Letter to the Editor

Intrauterine Exposure to Maternal Diabetes is Associated with Adiposity in Children at 6 Years of Age in China

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Children born to mothers with gestational diabetes mellitus (GDM) are more likely to exhibit congenital malformations, high birth weight, and obesity and have an increased risk of developing type 2 diabetes in later life. Children who are exposed to maternal diabetes in utero may be 'programmed' for later development of obesity at a critical period of development. Therefore, the purpose of the present study was to examine the associations among adiposity and systolic blood pressure in children and abnormal maternal glucose levels during pregnancy. A total of 856 mother-child pairs were included in the present retrospective study. Eligible pregnant women underwent a standard 75 g oral glucose tolerance test between 24 and 28 weeks' gestation. Anthropometric characteristics of their children were measured at 6 years of age, including body mass index, the sum of subscapular and tricep skinfold thickness, and systolic blood pressure. The result suggests that children exposed to GDM have higher adiposity; prevention of childhood obesity needs to begin early in life for these children.

Children born to mothers with gestational diabetes mellitus (GDM) are more likely to exhibit congenital malformations, high birth weight, and obesity and have an increased risk of developing type 2 diabetes in later life. Prospective cohort studies have demonstrated that prenatal exposure to gestational diabetes is a significant predictor of obesity by adolescence[1]. Although maternal glucose freely crosses the placenta, maternal insulin does not pass the placenta[2]. Thus, during exposure to maternal diabetes in the intrauterine environment, these children may be 'programmed' in utero for later development of obesity at a critical period of development[3]. In China, the prevalence of diabetes was 9.7% in 2009, and nearly 1 billion individuals worldwide now have diabetes[4]. With the incidence of diabetes increasing, intrauterine exposure to hyperglycemia affects an increasing number of children every year. Although some well-known research validates the link between maternal glucose and children adiposity, fewer studies have suggested associations of exposure to gestational diabetes with offspring obesity and systolic blood pressure (SBP) in the Chinese population. The purpose of the present study was to evaluate the correlation between intrauterine exposure to hyperglycemia, and offspring adiposity and blood pressure at 6 years of age in Tianjin, China.

Between January 2005 and December 2005, 856 mother-child pairs were recruited for the present study. Anthropometric characteristics were measured, including for 356 GDM mother-child pairs at a six-year follow-up. There were 12,000 women who completed a 50 g oral glucose tolerance test at 24 to 28 weeks' gestation in Tianjin Center Hospital of Obstetrics and Gynecology. If this result was abnormal (blood glucose level >7.8 mmol/L), the woman was referred for a fasting 3 h 75 g oral glucose tolerance test. Abnormal results were blood glucose level >5.3 mmol/L at baseline, >10 mmol/L at 1 h, >8.6 mmol/L at 2 h, and >7.8 mmol/L at 3 h[5]. Abnormal results in at least two measures were considered to be diagnostic of GDM. A total of 356 women were diagnosed with GDM and were followed by doctors, instructed to check their fasting and postprandial glucose value daily, and treated with diet, exercise and insulin in some cases. Maternal pre-pregnancy BMI, level of education, household income, and family history were collected and calculated by self-reported during the clinical visits. Research assistants collected these data. Sparks reported that body fat is a more specific representation of the effects of the intrauterine environment[6]; therefore, we measured subscapular (SS) and triceps (TR) skinfold thickness and calculated the sum of these (SS+TR) to estimate subcutaneous fat distribution. We measured children's blood pressure up to four times in 1 min intervals using Omol automated monitors in bilateral

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limbs, respectively.

Complete data were available for 356 children exposed to GDM and 500 children who had not been exposed to GDM. All mothers with GDM were treated with dietary changes, while 146 women used insulin during pregnancy. Compared with normoglycemic mothers, mothers with GDM had significantly higher weight gain (*P*=0.001, Table 1) and prepregnancy body mass index (BMI) (*P*=0.002, Table 1) during pregnancy, and had lower education levels and family income (*P*=0.032, Table 1). Maternal age was similar in the entire study population. A history of diabetes in the mother was correlated with the incidence of GDM (*P*=0.005, Table 1). Children exposed to GDM had higher BMI at 6 years of age (*P*=0.001, Table 2) and larger SS+TR (*P*=0.025, Table 2) compared with the offspring of NP. However, the mean systolic blood pressure was not significantly increased among the children exposed to GDM (*P*=0.120). Associations between maternal glucose with SS+TR and BMI of offspring are presented in Table 3. With higher levels of maternal fasting and 2 h plasma glucose concentrations, SS+TR and BMI rose. The median thickness of SS+TR was 8.0 cm and BMI was 13.8 kg/m^2 if the fasting glucose level was ≤5.3 mmol/L, while the median thickness of SS+TR and BMI were significantly higher if maternal plasma glucose concentration increased. Fasting glucose and 2 h plasma glucose levels of women with GDM was significantly related to offspring BMI and SS+TR at 6 years of age.

Table 1. Characteristics of the Study Population

Characteristic	GDM	NP	*P*
Age, years	28.6±3.6	27.4±2.9	0.182
Prepregnancy BMI, kg/m^2	25.3±5.2	22.1±3.9	0.002
Weight gain during pregnancy, kg	52.4±8.3	42.5±6.7	0.001
Educational level, *n*			
University	50	120	0.002
High school	106	80	
Household income, *n*			
≥5000 RMB/M	66	132	0.032
<3000 RMB/M	90	68	
Maternal family history of diabetes, *n*	38	26	0.005

Note. Data are presented as means and standard deviations unless otherwise indicated. BMI, Body mass index; GDM, Gestational diabetes mellitus; NP, Normal pregnant.

Table 2. Characteristics of the Six-year-old Children

Characteristic	Offspring of GDM	Offspring of NP	*P*
Birth weight, kg	3.7±1.2	3.2±0.8	0.015
BMI, Kg/m^2	15.8±1.9	12.3±2.4	0.001
SS, cm	3.5±0.5	1.2±0.3	0.000
TR, cm	6.6±1.1	4.2±0.8	0.038
SS+TR, cm	8.2±1.5	4.8±1.3	0.025
SBP	92.5±10.2	90.3±9.8	0.120

Note. Data are presented as means and standard deviations unless otherwise indicated. BMI, Body mass index; SBP, Systolic blood pressure; SS, Subscapular skinfold thickness; TR, Triceps skinfold thickness.

Table 3. Relationship between Maternal Glucose Level and Sum of Skin Fold Thickness and BMI

Glucose Level	SS+TR, cm	BMI
FPG		
≤5.3 mmol/L	8.0±1.3	13.8±3.4
>5.8 mmol/L	11.2±2.2	17.6±2.8
P	0.012	0.002
2 h plasma glucose		
≤6.7 mmol/L	7.9±1.5	15.6±2.4
>7.8 mmol/L	12.2±3.1	18.6±2.5
P	0.011	0.000

Note. Data are presented as means and standard deviations unless otherwise indicated. BMI, Body mass index; FPG, Fasting plasma glucose; SS, Subscapular skinfold thickness; TR, Triceps skinfold thickness.

Anthropometric data at 6 years of age confirmed that children of mothers with GDM were more likely to have high adiposity and had higher BMI and skinfold thickness. This correlation persisted even taken into account potential confounding variables such as gestational age, maternal family history of diabetes, household income, and level of education. Previous studies have found an association between exposure to maternal GDM and obesity in the offspring[7-8]. Another study reported that maternal diabetes is a strong determinant of adiposity in Indian children[9]. Tight glycemic control after the diagnosis of GDM can decrease skinfold thickness and the risk of overweight later in life in the children exposed to GDM[10]. In the present study, we adjusted for paternal hypertension and maternal blood pressure, maternal family history of diabetes and socioeconomic factors, and found that SBP was not higher among children exposed to GDM in utero compared with offspring of nondiabetic mothers. In fact, the effect of intrauterine exposure to GDM on children's blood pressure may gradually increase over time. The long-term effects of GDM on blood pressure in the offspring may not be apparent until later in childhood.

In summary, we provide evidence that intrauterine exposure to diabetes is associated with adiposity in children in a population in northern China. With the increase in GDM, a growing number of children will be exposed to hyperglycemia before birth in China every year. Tight glycemic control may ameliorate the outcomes, but how tight is too tight during pregnancy? Future studies should determine the level of glycemic control that is suitable for Chinese pregnant women.

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