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Gestational diabetes and Offspring's growth from birth to 6 years old

Jing Wang^{1,2}, Lei Pan¹, Enqing Liu¹, Hongyan Liu¹, Jin Liu¹, Shuting Wang¹, Jia Guo¹, Nan Li¹, Cuilin Zhang³, and Gang Hu²

¹Tianjin Women's and Children's Health Center, Tianjin, China, 300070

²Chronic Disease Epidemiology Laboratory, Pennington Biomedical Research Center, Baton Rouge, LA, USA, 70808

³Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA, 20852.

Abstract

Objectives: To compare the children's body mass index (BMI) growth between offspring exposed to maternal gestational diabetes mellitus (GDM) and those not exposed, and assess the associations between maternal hyperglycemia and their offspring's overweight risk from 1 to 6 years old.

Methods: Using the healthcare records data from the *Tianjin maternal and child healthcare system*, we conducted a population-based cohort study, which is composed of 27,155 mother-child pairs with all mothers undergoing GDM screening test in pregnancy.

Results: After adjustment for maternal and children's characteristics, children born to mothers with abnormal glucose (including GDM or abnormal glucose challenge test [GCT] but normal oral glucose tolerance test [OGTT] results) during pregnancy had higher mean values of Z scores for BMI-for-age at 1, 2, 3, 5, and 6 years of age, in comparison with those born to mothers with normal glucose (all P values <0.05). Moreover, maternal abnormal glucose was associated with a higher risk of childhood overweight with multivariate-adjusted hazard ratios of 1.07 (95% confidence interval [CI] 1.01–1.14), 1.09 (95% CI 1.04–1.15), 1.10 (95% CI 1.04–1.15), 1.08 (95% CI 1.03–1.14), 1.08 (95% CI 1.03–1.13), and 1.07 (95% CI 1.02–1.12) at 1–6 years old compared with children of mothers with normal glucose.

Conclusions: Abnormal maternal glucose tolerance during pregnancy was independently associated with children's higher BMI and overweight risk from 1 to 6 years old. Women with positive GCT results but negative OGTT can be neglected by the health system. More attention should be paid to the health of these mothers and their offspring.

Corresponding author: Gang Hu, Chronic Disease Epidemiology Laboratory, Pennington Biomedical Research Center, 6400 Perkins Road, Baton Rouge, LA° 70808, Tel: 225-763-3053, Fax: 225-763-3009, gang.hu@pbrc.edu.

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Keywords

Gestational Diabetes Mellitus; childhood growth; glucose intolerance; early childhood risk factors; OGTT

Introduction

Gestational diabetes mellitus (GDM), defined as any degree of glucose intolerance with onset or first recognition during pregnancy,¹ accounts for the majority of diabetic pregnancies. GDM affects about 7% of pregnancies in North America and has a global prevalence ranged from 5.8% to 12.9%.² The long-term risks of GDM concern both maternal and offspring's health: GDM is related to increased risk of hypertensive disorders of pregnancy, the need for cesarean delivery, and the possibility of fetal macrosomia;³ furthermore, women with a history of GDM have a 7-fold greater risk in developing type 2 diabetes in later life;⁴ children born to GDM mothers are also at risk of obesity, abnormal glucose metabolism^{5, 6} and adverse developmental outcomes.⁷

Unfortunately, with respect to the large number of GDM-affected population, very few studies have examined the long-term associations between the in utero exposures to maternal hyperglycemia and offspring's growth and development in early life. In the Northwestern Diabetes in Pregnancy Study in Chicago, diabetes during pregnancy (GDM and preexistent diabetes) was positively associated with the offspring's BMI at birth and after 5 years old.^{8, 9} The offspring of Pima Indian women with preexistent diabetes and GDM had much higher rates of obesity at age 5–19 years, compared with their counterparts born to prediabetic and nondiabetic women.^{10, 11} However, these differences may be due to the high type 2 diabetes (T2D) risk in the specialized population from the Pima Indians and a specialized pregnancy clinical population in Chicago.¹² Regarding the general population, two recent studies from the Hyperglycemia and Adverse Pregnancy Outcome study (HAPO)¹³ and Kaiser Permanente Northwest and Hawaii¹⁴ presented that maternal hyperglycemia increased the offspring's risk of overweight and obesity among 7-year-old girls and during the first decade among normal birth weight infants, respectively. Nonetheless, other studies did not find a clear association between maternal GDM and obesity in offspring of more than 5 years old.^{15–17} Moreover, at what age this association becomes apparent is unknown because very few previous studies were targeted at the GDM's offspring of less than 5 years old, and the existing results are conflicting. In the Project Viva, GDM's offspring showed a slower weight gain in the first 6 months of life,¹⁸ whereas the HAPO study in Belfast, UK, found little association between maternal glucose and obesity of offspring at 2 years old.¹⁹ Our previous study found that abnormal maternal glucose tolerance predicted a less weight gain in the first 3 months and more weight gain in the 9–12 months of life.²⁰ Discrepancies in these findings may be due to small sample sizes of GDM-exposed children, cross-sectional comparison of child's obesity, and adjustment for important confounders in both mothers and children. Therefore, the present study aimed to compare the children's BMI growth between offspring exposed to maternal GDM and those not exposed, and assess the associations between maternal hyperglycemia and their offspring's overweight risk from 1 to 6 years old in a large population.

Methods

Using the healthcare records data from the *Tianjin maternal and child healthcare system*, we conducted a population based cohort study in Tianjin, China.

Tianjin maternal and child healthcare system is a three-tier care system, consisting of community-based health centers, district-level Women's and Children's Health Centers (also including secondary hospitals), and a city-level (Tianjin) Women's and Children's Health Center (also including tertiary hospitals). All women are registered at their community health centers everytime they get pregnant and then referred to a secondary hospital or a tertiary hospital for healthcare from the 32nd gestational week till delivery. All children are given the health examinations at birth (<3 days after birth), and then annual examinations until 7 years old. Every woman is assigned a unique identification number (maternal healthcare ID) at the first time she registers at the community health center and every child is assigned another unique identification number (child healthcare ID) linked with his/her biological mother's maternal healthcare ID, when he/she is born in the hospital in Tianjin. In different phases and examination locations, trained healthcare practitioners conduct the necessary examinations for pregnant women and their children, collect the data, and enter into an electronic health information system.^{20, 21} Both maternal healthcare ID and child healthcare ID are "key chains" to link all the mothers' pregnancy healthcare records and their children's healthcare records until 7 years of age. Healthcare records for both pregnant women and their children have been collected and available in electronic form since 2009.²²

Healthcare records for pregnant women begin within the first 12 weeks of pregnancy, including general information (age, education, occupation, date of the first visit, numbers of pregnancy/infants, last menstrual period, expected delivery date, and smoking habits), medical history, family history of diseases, clinical measurements (height, weight, blood pressure, fasting glucose, gynaecological examinations, ultrasonography, gestational diabetes screening test and other lab tests), complications during pregnancy, pregnancy outcomes (delivery modes and labor complications), and postnatal period examinations (<42 days after delivery).

Healthcare records for children begin with children's birth, including information from newborns (date of birth, sex, gestational week of birth, birth weight, birth recumbent length, and Apgar score), postnatal period (names of the child and his/her parents, family history of diseases, feeding modalities, weight, and recumbent length), infancy (date of examination, weight, recumbent length before 24 months and height from 24 months, head circumference, number of teeth, and blood hemoglobin), and preschool (date of examination, weight, height, number of teeth, blood hemoglobin, and blood pressure), as well as the information of feeding modalities (exclusive breastfeeding, mixed breast and formula feeding, weaned from breastfeeding, and exclusive formula feeding) during the first 6 months.

Glucose testing and diagnosis

Based on recommendation from Tianjin routine prenatal care, the first antenatal visit usually happens within 4–12 gestational weeks when fasting glucose is tested among all pregnant women. At 26–30 gestational weeks, all mothers-to-be are screened for GDM by a two-step

approach.³ First, they submit to a glucose challenge test (GCT) by measuring the one-hour-serum glucose concentration after taking 50-g glucose load in their community health centers. Then, those who have a glucose reading ≥ 7.8 mmol/L are referred to the Tianjin Women's and Children's Health Center and undergo a 2-hour oral glucose tolerance test (OGTT) with 75-g glucose load. GDM was diagnosed according to the World Health Organization (WHO)'s criteria: women with a 75-g glucose 2-h OGTT result confirming either diabetes (fasting glucose ≥ 7 mmol/L or 2-h glucose ≥ 11.1 mmol/L) or impaired glucose tolerance (IGT) (2-h glucose ≥ 7.8 mmol/L and <11.1 mmol/L). In the present study, 12 pregnant mothers were defined as isolated impaired fasting glucose (IFG), failed GCT and fasting glucose ≥ 6.1 and <7.0 mmol/L and 2-hour glucose <7.8 mmol/L, and these 12 mothers were included in the IGT group and treated as IGT in the clinical. Thus in the present study, we defined women with pregnancy diabetes, IGT or IFG as GDM or "glucose intolerance in pregnancy". For the participants with failed GCT results (1-h glucose reading ≥ 7.8 mmol/L) and negative OGTT results (fasting glucose <6.1 mmol/L and 2-h glucose <7.8 mmol/L), we categorized them into a group as "GCT+ OGTT-". All other participants free of GDM or "GCT+ OGTT-" were grouped into "normal glucose". (Figure 1)

Study population

We collected the records of both mothers and their infants who were born between June 2009 and May 2011 in the six urban districts of Tianjin. A total of 43,853 mother-child pairs' health care records were available. In the present study, we included 27,155 mother-child pairs (61.9%), after excluding multiple births ($n=987$), premature infants, gestational age <37 weeks ($n=1847$), the mother-child pairs missing mother's weight or height information at the first prenatal visit or gestational weight gain information ($n=12,429$, the mean maternal age was 28.2 years at delivery) or missing children's anthropometric data from 1 year old ($n=1185$), and the mother-child pairs with undetermined gestational glucose level due to missing GCT or OGTT results ($n=6111$). We also excluded 53 participants reporting their medical history of diabetes (diagnosed before the index pregnancy) in this study and another 64 participants, whose fasting glucose ≥ 7.0 mmol/L before 12 gestational weeks, because they were possible to be under-diagnosed diabetes cases before pregnancy. Compared with the excluded mother-child pairs, those included in this study had younger children and were younger mothers (6.11 vs. 6.24 years at the latest follow-up point and 27.9 vs. 28.3 years at delivery, respectively) and had less male children (51.7% vs. 52.9%). The rates of child health examination at 1 year, 2 years and 3 years (mainly administrated in community health centers) were 98.3%, 97.6%, and 98.6%, respectively, and the average rate of 4–6 years (mainly administrated in preschool) was 93.5% (6-year-data were still ongoing). Our study was approved by the Human Subjects Committee of Tianjin Women's and Children's Health Center (TWCHC) and conformed to the guidelines of the Helsinki agreement and its amendments. Since we used the electronic health care records in this study, TWCHC agreed to waive the need for written informed consent from all participants.

Patient involvement

We used the electronic health care records from *Tianjin maternal and child healthcare system*. No patients were involved in this study.

Measurements

Using the standardized protocol, all mothers' height and weight were measured in light indoor clothing and without shoes by trained practitioners in community health centers during the pregnancy. Women's gestational weight gain (GWG) was calculated as the difference between pre-pregnancy and delivery weight. Maternal body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. We treated maternal BMI using the weight and height measured at the first prenatal visit within the first 12 weeks of the index pregnancy as pre-pregnancy BMI.²³ According to the Chinese BMI cut-offs,²⁴ maternal pre-pregnancy BMI was further categorized as four groups: <18.5, 18.5–23.9, 24.0–27.9, and ≥28.0 kg/m². Meanwhile, we categorized the women according to the WHO classification and IOM (Institute of Medicine) guidelines.²⁵ Women with a GWG within the IOM-recommended range were categorized as having an adequate GWG, those with a GWG less than the lower-limit were categorized as having an inadequate GWG, and those with a GWG greater than the upper-limit were categorized as having an excessive GWG.

Children's anthropometric data, including body weight, height or recumbent length (before 24 months) were collected at birth (<3 days after birth) in delivery hospitals by nurses, every year between 1 year and 3 years in community health centers by trained health practitioners, and every year between 3 years and 7 years in preschool by Tianjin or district-level Women's and Children's Health Center(s), using the same devices. Measurement devices and standards have been described elsewhere.^{21, 26} Validity studies were also conducted to compare the healthcare records and measurements.²¹ The correlations between electronic healthcare records and measurement data for pregnancy women and children are 0.998 and 0.999 (for body weight) as well as 0.997 and 0.999 (for height/recumbent length), respectively.

Children's Z-scores for body mass index and childhood overweight

Z-score for BMI-for-age (Z-BMI) was used to describe the change in the offspring's BMI. It is a gender-independent classification system, representing equivalent BMI-for-age percentile based on the World Health Organization (WHO) growth reference.²⁷ Children's Z-BMI (from 1 to 6 years old) was calculated based on the protocol from the WHO. We also defined childhood obesity by Z-scores. Although BMI under 2 years old was not recommended for clinical use²⁸ and there was no universal agreement on the definition of obesity in toddlers under 2 years of age,²⁹ in order to describe a child's growth using the same standard from 1 to 6 years of age (weight-for-length Z-score is not available after 5 years old), we defined normal weight as a BMI less than the 85th percentiles for age and gender based on the WHO growth reference (Z-score <1.035) and overweight as a BMI above the 85th percentiles (Z-score ≥1.035).²⁹ Childhood overweight was evaluated as a time-to-overweight analysis;¹⁴ we counted the first measurement of overweight as a case and accumulated the cases from age 1 to 6 years.

Statistical analyses

We used one-way ANOVA and chi-square test to compare the general characteristics (continuous and categorical variables) of both mothers and children according to maternal

glucose level in pregnancy (normal glucose, GCT+ OGTT-, and GDM). General Linear Models were applied to assess the differences in children's Z-BMI at 1 year (± 6 months), 2 years (± 6 months), 3 years (± 6 months), 4 years (± 6 months), 5 years (± 6 months) and 6 years (± 6 months) of age according to maternal glucose level in pregnancy. Cox proportional hazards models were used to estimate hazards ratios for childhood overweight at 1 to 6 years old according to maternal glucose level in pregnancy. We also stratified the participants by children's gender and assessed the associations of maternal glucose level in pregnancy and childhood overweight among boys and girls, respectively. The analyses included three multivariable-adjusted models: Model 1 adjusted for maternal age, gestational age, education, smoking status, and infant feeding modes; Model 2 adjusted for the variables in Model 1 and also for maternal gestational weight gain; Model 3 adjusted for the variables in Model 2 and also for maternal prepregnancy BMI. All the analyses were performed using IBM SPSS Statistics 24.0 (IBM SPSS, Chicago, IL) with a statistical significance at 0.05.

Results

Of all the 27,155 mother-child pairs, 5.5% of mothers were diagnosed with GDM (including pregnancy DM with fasting glucose level ranging from 4.16 to 12.22, and 2-hour glucose level ranging from 7.80 to 20.56, IGT with fasting glucose level ranging from 3.63 to 6.85, and 2-hour glucose level ranging from 7.80 to 11.09, and IFG with fasting glucose level ranging from 6.10 to 6.51, and 2-hour glucose level ranged from 6.10 to 7.68), whereas 8.0% of mothers had a failed GCT test and passed the OGTT test (GCT+ OGTT-). The general maternal and child characteristics according to maternal glucose level in pregnancy (normal glucose, GCT+ OGTT-, and GDM) are presented in Table 1. Mothers with GDM were older, had a higher prepregnancy BMI and less gestational weight gain compared with mothers with normal glucose during pregnancy. Children born to mothers with normal glucose during pregnancy had lower means of Z-BMI, in comparison with those children born to mothers with GDM or GCT+ OGTT- at 1 year, 2 years, 3 years and 5 years of age in an unadjusted model.

Table 2 presents the comparison of children's Z-BMI from 1 to 6 years of age according to maternal glucose level in pregnancy. After adjustment for maternal age, education, smoking status, gestational age, weight gain during pregnancy and infant feeding modes (multivariable-adjusted Model 2), children born to mothers with normal glucose during pregnancy had lower mean values of Z-BMI at 1 to 6 years of age, in comparison with those children born to mothers with GDM or GCT+OGTT- (all P values <0.05). The multivariable-adjusted mean values of Z-BMI in children born to mothers with normal glucose, GCT+OGTT-, and GDM during pregnancy were 0.65, 0.75, and 0.75 at 1 year old (P value <0.001), 0.42, 0.52, and 0.54 at 2 years old (P value <0.001), 0.26, 0.35, and 0.38 at 3 years old (P value <0.001), 0.16, 0.21, and 0.25 at 4 years old (P value =0.007), 0.18, 0.28, and 0.34 at 5 years old (P value <0.001), and 0.25, 0.35, and 0.40 at 6 years old (P value =0.003), respectively. When introducing maternal prepregnancy BMI into the model (multivariable-adjusted Model 3), the differences were still significant among children at 1, 2, 3, and 5 years old, and disappeared among children at 4 and 6 years old.

Since the mean values of Z-BMI had no significant differences between children born to mothers with GCT+OGTT- and those born to mothers with GDM during pregnancy at each age group of 1–6 (P values for difference >0.05), we combined children born to mothers with GCT+OGTT- and GDM into one group and regrouped all mother-child pairs into two groups: children with normal-glucose mothers and children with abnormal-glucose (GCT+OGTT- or GDM) mothers in the analyses (Figure 2). In multivariable-adjusted Model 3, children born to mothers with normal glucose during pregnancy had significantly lower mean values of Z-BMI at 1, 2, 3, 5, and 6 years old (but not 4 years old) than those born to mothers with abnormal glucose.

In addition, we performed a sensitive analysis including 1632 mother-child pairs with mothers having failed GCT but without OGTT results (these mothers and children were both older than the originally included mothers and children: 28.5 vs. 27.9 and 6.3 vs. 6.1, respectively, but the distributions of children's gender were similar) in the abnormal glucose group (GCT+ OGTT-, or GCT+ but without OGTT, or GDM), and found that children born to mothers with abnormal glucose during pregnancy had significantly higher mean values of Z-BMI at 1, 2, 3, 4, 5, and 6 years old than those born to mothers with normal glucose during pregnancy (Online Table1).

The hazard ratios of childhood overweight according to maternal glucose level in pregnancy are shown in Table 3. Compared with children born to mothers with normal glucose during pregnancy, children with GDM mothers showed 10–17% increased multivariable-adjusted risks of childhood obesity from 1–6 years old, while children born to mothers with GCT+OGTT- status during pregnancy showed 12–16% increased multivariable-adjusted risks of childhood obesity. After additional adjustment for maternal prepregnancy BMI, the increased hazard ratios of childhood overweight somewhat attenuated but still remained significant in almost all groups of children born to mothers with GCT+ OGTT- or GDM at different age groups. Since we found little difference between GCT+ OGTT- and GDM on childhood overweight risk at all ages, we combined these two groups into one group, refit the models and found that maternal abnormal glucose (GCT+ OGTT- or GDM) during pregnancy was independently associated with a higher risk of childhood overweight at each age group of 1–6 years (multivariable-adjusted Model 3). Moreover, we conducted the models with GWG in categorical variables (inadequate, adequate, and excessive), instead of the continuous variables, and the associations were consistent (Online Table 2).

When stratified by sex of the child, the positive associations between maternal abnormal glucose in utero and the risk of childhood overweight were significant at almost each age groups of 1–6 years among boys and at 3 year old among girls (Online Table 3). There were no significant interactions between maternal abnormal glucose in utero and GDM and the child's sex with the risk of childhood overweight (P value for interaction is all over 0.05).

Discussion

In the present study, we found that maternal hyperglycemia including either GCT+ OGTT- or GDM during pregnancy was associated with higher values of Z-scores for BMI-for-age and increased risks of overweight in children at each year up to 6 years old, and these

associations were independent of maternal prepregnancy BMI and other related maternal and infant factors.

The worldwide rise in over-nutrition, sedentary life and obesity has resulted in a steep increase in the number of women who develop GDM during pregnancy.³ Previous studies have indicated that in utero exposure to GDM is a risk factor of macrosomia and large for gestational age at birth and developing obesity and type 2 diabetes during adolescence or young adulthood in the offspring.³⁰ There is a public debate of the associations between maternal hyperglycemia and offspring's overweight and obesity. Studies of Northwestern diabetes in pregnancy study in Chicago,^{8,9} Pima Indian,¹¹ HAPO¹³ and Kaiser Permanente centers¹⁴ claimed to find a positive association, while other studies argued that little association existed.^{15–17} However, most of previous studies were targeted at the GDM's offspring at birth or of more than 5 years old. Therefore, at what age these associations become apparent is still unknown.

Within the research conducted among children under 5 years old, the Project Viva observed that children born to mothers with GDM and IGT had a slower weight gain in the first 6 months of life, compared with those infants with normal-glucose-tolerance mothers.¹⁸ Our previous study found that abnormal maternal glucose tolerance during pregnancy predicted a less weight gain in the first 3 months and more weight gain in the 9–12 months of life in the offspring.²⁰ On the contrary, the HAPO study in Belfast¹⁹ and the Exploring perinatal Outcomes among Children (EPOCH) study in Colorado³¹ found no association of maternal hyperglycemia with the growth of offspring at 2 years old and before 26 months, respectively. The differences may be due to limited sample sizes of GDM and different adjustments in the analysis. The present study indicated that both maternal GCT+ OGTT- and maternal GDM during pregnancy were associated with higher values of Z-scores for BMI-for-age and increased risks of overweight in children at 1, 2, 3, 4, 5, and 6 years old, and these associations were independent of maternal prepregnancy BMI and other related maternal and infant factors. Our study was intended to contribute to the limited amount of literature examining this association, especially for large-population-based studies among children under 5 years old. In the present study, we also controlled various covariates in the multivariable-adjusted analysis, such as maternal social-economic characteristics, lifestyle, infant feeding status, maternal weight gain during pregnancy, and prepregnancy BMI, which were identified as important confounders of this association.³² Also, adjusting for maternal obesity could help to determine and understand the causes of offspring obesity: an altered intrauterine environment or obesity genes inherited from the mother.¹⁵

Moreover, a novel finding from the present study is that children exposed to maternal abnormal glucose in utero, including GDM and GCT+ OGTT- status, had the same risk of childhood overweight. Either GDM or GCT+ OGTT- mothers during pregnancy had an increased risk on offspring's overweight at 1–6 years old, compared mothers with normal glucose in pregnancy. According to the Pregnancy Infection and Nutrition study (PIN), a study performed among children born to the mothers with normal glucose level during pregnancy, maternal glucose concentration 130 mg/dL was independently associated with the development of overweight/obesity at 3 years old.³³ Therefore, more attention should be

paid on the health of children born to women with positive GCT results but negative OGTT results in pregnancy.

The possible explanation underlying these findings could be “maternal abnormal metabolic imprinting”, which represented a determinant of an over-nutritional status of fetus and further leading to offspring’s diseases later in life.³⁴ One of the mechanisms may be the delivery of excessive nutrients from mothers to the fetus; that maternal glucose but not insulin can cross the placenta would in turn influence the development of fetus in utero and even long-term health.³⁵ Simultaneously, we learned from the study of Pima-Indian families that a greater number of diabetes-susceptibility genes maybe inherited from mothers with hyperglycemia to their offspring.³⁶

In the present study, we also found little difference of children’s Z-BMI at 4 years old between the normal glucose group and abnormal glucose (GCT+ OTTT- or GDM) group. A possible explanation may be that the nadir of all children’s Z-BMI was around their 4 years old. The results were consistent with our previous work, which used a large health survey of 3–6 year-old children between 2006 and 2014 in Tianjin and suggested that the lowest mean value of Z-BMI appeared around 4 years old.³⁷

Our study is a large-scale population-based study of mother-child pairs from the prenatal period to early childhood with anthropometry measurements by trained health practitioners. Also, the data is based on the Asian population, who are of increasing burden of childhood obesity and diabetes; as such identification and understanding of early life risk factors are particularly relevant. However, there are some limitations in our study. First, 38.1% of mother-child pairs were excluded from the present study due to missing values. Although we have adjusted for maternal age and used Z-score independent of children’s age to describe the growth of children, the results still might differ from the true value because of the imbalance. Second, since we used healthcare records as a main source of data, some childhood lifestyle factors, such as physical activity and nutrition, were not available in this study. Third, we excluded premature and multiple birth infants and the information of assisted reproductive technology pregnancies was not available in this study, therefore, it should be cautious when generalizing the findings.

In conclusion, abnormal maternal glucose tolerance during pregnancy was independently associated with children’s higher BMI and overweight risk from 1 to 6 years old. Women with positive GCT results but negative OGTT can be neglected by the health system. Therefore, health services should pay more attention to the health of these mothers and to the health of their offspring.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Flow chart of Glucose testing and diagnosis. GDM: gestational diabetes mellitus; IGT: impaired glucose tolerance; IFG: impaired fasting glucose

Figure 2.

Comparison of Z-scores for body mass index-for-age at 1, 2, 3, 4, 5, and 6 years old between children born to mothers with normal glucose (GCT+ OGTT- or GDM) during pregnancy. Adjusted for maternal age, education, smoking status, prepregnancy body mass index, gestational age at delivery, gestational weight gain and infant feeding modes.

Table 1.

Characteristics of mother-child pairs according to maternal gestational diabetes status

	Total	Maternal gestational diabetes status		P-value
		Normal glucose	GCT+ OGTT- GDM	
Number of subjects	27,155	23,471	2184	1500
Maternal characteristics				
Maternal age before pregnancy, y	27.9±2.9	27.9±2.9	28.1±3.0	29.1±3.2 <0.001
Gestational age at delivery, wk	39.2±1.1	39.3±1.1	39.2±1.1	39.1±1.1 <0.001
Prepregnancy BMI, kg/m ²	22.1±3.3	21.9±3.3	22.8±3.6	23.7±3.7 <0.001
Prepregnancy BMI category, %				<0.001
<18.5 kg/m ²	11.0	11.7	7.9	4.7
18.5–23.9 kg/m ²	64.8	66.0	59.3	53.1
24.0–27.9 kg/m ²	18.5	17.2	24.6	29.8
>28.0 kg/m ²	5.8	5.2	8.2	12.4
Gestational weight gain, kg	12.5±4.0	12.7±4.0	12.0±4.0	11.0±4.1 <0.001
Education, %				0.62
12 years	22.0	21.9	23.1	22.1
13–15 years	27.9	28.0	27.8	27.0
16 years	50.1	50.1	49.0	50.8
Smoking status, %				0.61
Smokers	1.2	1.1	1.2	1.6
Passive smokers	48.1	48.1	48.5	47.2
Child characteristics				
Boy, %	51.7	51.5	53.3	53.3 0.110
Mode of infant feeding within the first 6 months, %				
Exclusive breastfeeding	18.0	18.1	18.2	16.2 0.040
Mixed breast and formula	69.6	69.7	69.5	69.3
Weaned from breastfeeding	10.5	10.5	10.1	11.7
Exclusive formula feeding	1.9	1.8	2.2	2.7
Z-scores for body mass index-for-age				
12 months	0.67±1.0	0.65±1.0	0.74±1.0	0.72±1.0 <0.001

	Total	Maternal gestational diabetes status		P-value
		Normal glucose	GCT+ OGTT- GDM	
24 months	0.43±1.0	0.42±1.0	0.51±1.0	<0.001
3 years	0.28±1.1	0.27±1.1	0.33±1.1	0.003
4 years	0.17±1.1	0.16±1.1	0.20±1.1	0.23
5 years	0.20±1.2	0.19±1.2	0.27±1.3	<0.001
6 years	0.27±1.3	0.26±1.3	0.33±1.3	0.09

Values are means ± SD unless otherwise specified.

BMI: body mass index; GCT: glucose challenge test; OGTT: oral glucose tolerance test; GDM: gestational diabetes mellitus.

Table 2. Comparison of Z-scores for body mass index from 1 to 9 years of age according to maternal gestational diabetes status

Z score of BMI-for-age	Maternal gestational diabetes status			P-value
	Normal glucose	GCT+ OGTT-	GDM	
Age 1 years				
No. of participants	22,057	2093	1405	
Model 1	0.65 (0.01)	0.74 (0.02)	0.73 (0.03)	<0.001
Model 2	0.65 (0.01)	0.75 (0.02)	0.75 (0.03)	<0.001
Model 3	0.65 (0.01)	0.74 (0.02)	0.73 (0.03)	<0.001
Age 2 years				
No. of participants	21,513	2035	1397	
Model 1	0.42 (0.01)	0.51 (0.02)	0.51 (0.03)	<0.001
Model 2	0.42 (0.01)	0.52 (0.02)	0.54 (0.03)	<0.001
Model 3	0.42 (0.01)	0.50 (0.02)	0.51 (0.03)	<0.001
Age 3 years				
No. of participants	21957	2074	1426	
Model 1	0.27 (0.01)	0.34 (0.02)	0.35 (0.03)	0.001
Model 2	0.26 (0.01)	0.35 (0.02)	0.38 (0.03)	<0.001
Model 3	0.27 (0.01)	0.33 (0.02)	0.33 (0.03)	0.011
Age 4 years				
No. of participants	21221	1989	1351	
Model 1	0.16 (0.01)	0.20 (0.02)	0.22 (0.03)	0.097
Model 2	0.16 (0.01)	0.21 (0.02)	0.25 (0.03)	0.007
Model 3	0.17 (0.01)	0.18 (0.02)	0.19 (0.03)	0.640
Age 5 years				
No. of participants	20546	1913	1299	
Model 1	0.19 (0.01)	0.27 (0.03)	0.31 (0.03)	<0.001
Model 2	0.18 (0.01)	0.28 (0.03)	0.34 (0.03)	<0.001
Model 3	0.19 (0.01)	0.25 (0.03)	0.27 (0.03)	0.005
Age 6 years				
No. of participants	11517	999	727	

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Z score of BMI-for-age	Maternal gestational diabetes status			P-value
	Normal glucose	GCT+ OGTT-	GDM	
Model 1	0.26 (0.01)	0.34 (0.04)	0.36 (0.05)	0.028
Model 2	0.25 (0.01)	0.35 (0.04)	0.40 (0.05)	0.003
Model 3	0.26 (0.01)	0.31 (0.04)	0.31 (0.05)	0.326

Data are means (SE).

BMI, body mass index; GCT, glucose challenge test; OGTT, oral glucose tolerance test; GDM, gestational diabetes mellitus.

Model 1: adjusted for maternal age, gestational age, education, smoking status, and infant feeding.

Model 2: adjusted for covariates in Model 1 and also for maternal gestational weight gain.

Model 3: adjusted for in Model 2 and also for maternal prepregnancy body mass index.

Table 3.
Hazard ratios of childhood overweight from 1 to 9 years of age according to maternal gestational diabetes status

	No. of participants	No. of overweight	Person-years	Hazard Ratios (95% CIs)		
				Model 1	Model 2	Model 3
Age 1 year						
Normal glucose	22,057	7562	22,014	1.00	1.00	1.00
GCT+OGTT- or GDM	3498	1327	3507	1.09 (1.03, 1.16)	1.11 (1.05, 1.18)	1.07 (1.01, 1.14)
GCT+ OGTT-	2093	791	2097	1.11 (1.04, 1.20)	1.13 (1.05, 1.21)	1.10 (1.02, 1.18)
GDM	1405	536	1410	1.06 (0.97, 1.16)	1.10 (1.00, 1.20)	1.04 (0.95, 1.13)
Up to age 2 years						
Normal glucose	22,971	9613	37,870	1.00	1.00	1.00
GCT+OGTT- or GDM	3632	1651	5877	1.12 (1.06, 1.18)	1.15 (1.09, 1.21)	1.09 (1.04, 1.15)
GCT+ OGTT-	2155	986	3491	1.12 (1.05, 1.19)	1.14 (1.06, 1.21)	1.10 (1.03, 1.17)
GDM	1477	665	2387	1.12 (1.04, 1.22)	1.17 (1.08, 1.26)	1.09 (1.01, 1.18)
Up to age 3 years						
Normal glucose	23,263	10,567	51,969	1.00	1.00	1.00
GCT+OGTT- or GDM	3658	1811	7953	1.13 (1.07, 1.18)	1.16 (1.10, 1.22)	1.10 (1.04, 1.15)
GCT+ OGTT-	2167	1080	4688	1.14 (1.07, 1.21)	1.16 (1.08, 1.23)	1.11 (1.04, 1.18)
GDM	1491	731	3265	1.11 (1.03, 1.20)	1.16 (1.07, 1.25)	1.07 (1.00, 1.16)
Up to age 4 years						
Normal glucose	23,391	11,121	63,994	1.00	1.00	1.00
GCT+OGTT- or GDM	3677	1886	9703	1.12 (1.06, 1.17)	1.14 (1.09, 1.20)	1.08 (1.03, 1.14)
GCT+ OGTT-	2180	1120	5740	1.11 (1.05, 1.18)	1.13 (1.06, 1.20)	1.08 (1.02, 1.15)
GDM	1497	766	3963	1.12 (1.04, 1.21)	1.17 (1.08, 1.26)	1.08 (1.00, 1.16)
Up to age 5 years						
Normal glucose	23,436	11,620	76,032	1.00	1.00	1.00
GCT+OGTT- or GDM	3679	1963	11,442	1.12 (1.06, 1.17)	1.14 (1.09, 1.20)	1.08 (1.03, 1.13)
GCT+ OGTT-	2182	1162	6768	1.11 (1.04, 1.18)	1.13 (1.06, 1.20)	1.08 (1.01, 1.15)
GDM	1497	801	4675	1.13 (1.05, 1.21)	1.17 (1.09, 1.26)	1.08 (1.00, 1.16)
Up to age 6 years (total overweight from 1 to 6 years)						
Normal glucose	23,448	12,015	82,763	1.00	1.00	1.00

	No. of participants	No. of overweight	Person-years	Hazard Ratios (95% CIs)		
				Model 1	Model 2	Model 3
GCT+OGTT- or GDM	3681	2011	12,361	1.11 (1.06, 1.17)	1.14 (1.08, 1.19)	1.07 (1.02, 1.12)
GCT+ OGTT-	2183	1189	7269	1.11 (1.04, 1.17)	1.12 (1.06, 1.19)	1.07 (1.01, 1.14)
GDM	1498	822	5092	1.12 (1.04, 1.20)	1.16 (1.08, 1.24)	1.06 (0.99, 1.14)

GCT, glucose challenge test; OGTT, oral glucose tolerance test; GDM, gestational diabetes mellitus.

Model 1 : adjusted for maternal age, gestational age, education, smoking status, and infant feeding.

Model 2: adjusted for covariates in Model 1 and also for maternal gestational weight gain.

Model 3: adjusted for in Model 2 and also maternal prepregnancy body mass index.