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Hypertensive Disorders of Pregnancy in Women with Gestational Diabetes Mellitus on Overweight Status of Their Children

Shuang Zhang[1], **Leishen Wang**[1], **Junhong Leng**[1], **Huikun Liu**[1], **Weiqin Li**[1], **Tao Zhang**[1,2], **Nan Li**[1], **Wei Li**[1], **Huiguang Tian**[1], **Andrea A. Baccarelli**[3], **Lifang Hou**[4], and **Gang Hu**[2]

[1]Tianjin Women's and Children's Health Center, 96 Guizhou Road, Heping Districts, Tianjin, China

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

[3]Department of Environmental Health Sciences | Columbia University Mailman School of Public Health, New York, NY, USA

[4]Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

Abstract

Hypertensive disorders of pregnancy (HDP) as a group of medical complications in pregnancy are believed to be associated with an increased risk of poor fetal growth, but the influence on offspring's body composition is not clear. The aim of the present study was to evaluate the association between maternal hypertensive disorders of pregnancy and overweight status in the offspring of mothers with gestational diabetes mellitus (GDM).

A cross-sectional study among 1263 GDM mother-child pairs was performed in Tianjin, China. General linear models and logistic regression models were used to assess the associations of maternal hypertension in pregnancy with anthropometry and overweight status in the offspring from birth to 1–5 years old.

Offspring of GDM mothers who were diagnosed with hypertensive disorders during pregnancy had higher mean values of Z scores for birth weight for gestational age and birth weight for length, and higher mean values of Z scores for weight for age, weight for length/height, and body mass index for age at 1–5 years old than those of GDM mothers with normal blood pressure during pregnancy. Maternal hypertensive disorders of pregnancy were associated with increased risks of large for gestational age (OR 1.74, 95%CI 1.08–2.79) and macrosomia (OR 2.02, 95%CI 1.23–3.31) at birth and childhood overweight/obesity at 1–5 years old age (OR 1.88, 95%CI 1.16–3.04).

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

Conflict(s) of Interest/Disclosure Statement

None

For offspring of mothers with GDM, maternal hypertension during pregnancy was a risk factor for macrosomia at birth and childhood overweight and obesity, and controlling the maternal hypertension may be more important for preventing large for gestational age babies and childhood obesity.

Introduction

Hypertensive disorders of pregnancy as a group of medical complications in pregnancy remain to be a major cause of maternal and infant morbidity and mortality worldwide.[1] Several studies have indicated that offspring of women with hypertensive disorders of pregnancy are at increased risk for cardiovascular disease at early adults.[2, 3] Other studies have found that maternal hypertensive disorders of pregnancy predict large offspring size at birth and increase the risk of cardio metabolic diseases in the offspring during childhood and adolescence.[3, 4] A retrospective cohort study of 16,936 births found that maternal preeclampsia increased the risk of intrauterine growth restriction and low birth weight,[5] which in turn is reported to predispose to central obesity, hypertension, coronary heart disease and insulin resistance.[6, 7] Another 20-year prospective follow-up birth cohort study found that young adult offspring of maternal hypertensive pregnancies were more likely to be obese or overweight.[3] However, most of the studies were focused on the association of hypertensive disorders of pregnancy with fetal growth or offspring cardiovascular disease status in young adults, few studies have assessed the relationship between hypertensive disorders of pregnancy and childhood overweight status at early young years, especially less than 5 years old.

Gestational diabetes mellitus (GDM), defined as glucose intolerance with onset or first recognition during pregnancy, [8] is one of the most common complications in pregnancy affecting 2–10% of the pregnancies in the US.[9] In urban china, the prevalence of GDM has increased from 2.3% in 1999 to 8.1% in 2010.[10, 11] Some studies have found that offspring of mothers exposed to GDM are at increased risk of neonatal adiposity and childhood obesity,[12] and women with GDM are associated with an increased risk of hypertensive disorders of pregnancy.[13] Our objective was to evaluate the association between maternal hypertensive disorders of pregnancy and overweight status in the offspring of GDM mothers.

Methods

Tianjin GDM screening project

Tianjin is the fourth largest city of China with over 13 million residents in 16 country-level administrative areas.[14] About 4.3 million people live in six central urban districts. Since 1999, all pregnant women who live in six urban districts have participated in the universal screening for GDM. The average proportion of screened pregnancies was over 91% during 1999–2008.[11] Following the WHO's GDM diagnosis criteria, all pregnant women at 26–30 gestational weeks participated in a 1-hour oral glucose tolerance test (OGTT) with 50-g glucose load. [15] Women who had a glucose reading ≥7.8 mmol/l were invited to undergo a 2-hour OGTT with a 75-g glucose load at the Tianjin Women's and Children's Health Center. [15] All women confirming either diabetes (fasting glucose ≥7 mmol/l or 2-hour

glucose ≥11.1mmol/l) or impaired glucose tolerance (IGT) (2-hour glucose ≥7.8 and <11.1 mmol/l) were regarded as having GDM.[15]

Study samples

A total of 4644 pregnant women diagnosed with GDM between 2005 and 2009 in six urban districts were eligible for the Tianjin Gestational Diabetes Mellitus Prevention Program (TGDMPP),[15] and 1263 GDM women and their children (participation rate=27%) had completed the baseline survey for the TGDMPP from August 2009 to July 2011.[14, 16–18] A total of 1263 women with GDM had fasting and 2 h glucose measured at 26–30 weeks 'gestation, and 1108 women measured HbA1c at 26–30 gestational weeks because HbA1c measurements were available from 2006. There were no differences in the OGTT at 26–30 weeks' gestation with regard to age (28.9 vs. 28.7 years), fasting glucose (5.34 vs. 5.34 mmol/L), 2-h glucose (9.23 vs. 9.16 mmol/L), and the prevalence of IGT (90.9% vs. 91.8%) and diabetes (9.1% vs. 8.2%) between the participated and not participated women with GDM. [11] The study was approved by the Human Subjects Committee of the Tianjin Women's and Children's Health Center. Informed consent was obtained from each participant.

Examinations

At the baseline survey, all GDM mothers and their children completed a self-administered questionnaire and underwent a physical examination that included anthropometric and blood pressure measurements. [11] The questionnaire and measurements were collected and checked by health workers from the Tianjin Women's and Children's Health Center, who were intensively trained in meetings and in practical sessions. The mothers' questionnaire included questions on the mothers' socio-demographics (age, marital status, education, income, and occupation), history of GDM, family history of chronic diseases, medical history (hypertension, pregnancy-induced hypertension, diabetes, and hypercholesterolemia), pregnancy outcomes (prepregnancy weight, weight gain during pregnancy, and number of children), dietary habits (a self-administered food frequency questionnaire to measure the frequency and quantity of intake of 33 major food groups and beverages during the past year),[19] alcohol intake, smoking habits, passive smoking, and physical activity (the frequency and duration of leisure time and sedentary activities) .[16–18] Women who reported doctors-diagnosed hypertension after 20 weeks (including gestational hypertension, preeclampsia, severe preeclampsia, or eclampsia) of gestation on the questionnaire were classified as having a history of hypertensive disorders of pregnancy.[20] The children's questionnaire included questions on the child's birth date, sex, gestational weeks of birth, birth weight, birth recumbent length, and Apgar score (above questions related to birth were copied from the birth certificate), as well as the mode and duration of infant feeding (exclusive breast feeding, mixed breast and formula feeding, weaned from breast feeding, and exclusive formula feeding), health characteristics (history of illness status and current health status), dietary habits (usual habits of eating breakfast, lunch, and dinner, usual frequency of intake of vegetables, fruits, sugar-sweetened beverages, and fast food), and other lifestyle habits (duration of usual sleep, and television or computer viewing). The questionnaire has been used in a longitudinal study in the same areas of Tianjin.[21]

Children's body weight was measured with a beam balance scale with participants wearing light indoor clothing without shoes. Body height was measured by a stadiometer. Weight was measured to the nearest 0.1kg and height to the nearest 0.1cm. Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. Z scores for weight for age, height for age, and weight for length and BMI for age, were calculated based on the standards for the WHO growth reference. [22] Children's overweight and obesity was defined as a BMI more than or equal to the 85th percentile for age and gender using the WHO BMI growth reference (≥1.035 Z score).[22] Z scores for birth weight for gestational age and birth weight for length for gestational age were calculated using our own study population means and standard deviation (n=57,454) in 2009–2011.[23] A large-for-gestational-age infant was defined as an infant having a standardized birth weight >90th percentile, whereas a small-for-gestational-age infant was defined as an infant having a standardized birth weight <10th percentile. Macrosomia was defined as birth weight ≥4000 grams. Gestational weight gain was classified according to the Chinese maternal pre-pregnancy BMI classification standard and the 2009 IOM GWG recommendations.[24]

Statistical analyses

The general characteristics of GDM mothers with and without a history of self-reported hypertensive disorders of pregnancy and their children were compared using T test and chi-square test. General Linear Models were used to compare the difference in Z scores for birth weight for gestational age and birth weight for length for gestational age, Z scores for weight for age, height for age, weight for height, and BMI for age at the baseline survey (1–5 years of offspring age), and changes in Z scores for weight for age and weight for height from birth the baseline survey between offspring of GDM mothers with and without history of self-reported hypertensive disorders of pregnancy. Logistic regression was used to estimate the odds ratios (ORs) and 95% confidence intervals (95% CIs) of large for gestational age and macrosomia at birth, and childhood overweight and obesity at baseline survey associated with self-reported maternal hypertensive disorders of pregnancy status. We set up three models: Model 1 adjusted for maternal age, family history of hypertension, family history of diabetes, history of GDM treatments, education, income, gestational weeks of birth, smoking, pre-pregnancy BMI, and gestational weight gain, and infant feeding; Model 2 additionally adjusted for birth variables for gestational age Z score; Model 3 adjusted for all variables in model 2 and also adjusted for HbA1c at 26–30 gestational weeks, which was measured from 2006 in 1108 of 1263 women, including 79 women with maternal hypertensive disorders of pregnancy. All statistical analyses were performed with PASW for Windows, version 23.0 (Statistics 23, SPSS, IBM, USA).

Results

Maternal and offspring's general characteristics were presented in Table 1. Of 1263 GDM mothers, 91 (7.2%) mothers had a history of self-reported hypertensive disorders of pregnancy. GDM mothers with a history of self-reported hypertensive disorders of pregnancy had higher mean values of pre-pregnancy BMI, gestation weight gain, fasting and 2-hour glucose at 26–30 gestational weeks compared with those with normal blood pressure during pregnancy (Table 1).

Offspring of GDM mothers who were diagnosed with hypertensive disorders during pregnancy had higher mean values of Z scores for birth weight for gestational age and birth weight for length than those of GDM mothers with normal blood pressure during pregnancy (Table 2). Self-reported maternal hypertensive disorders of pregnancy were associated with increased risks of childhood large for gestational age (OR 1.74, 95%CI 1.08–2.79) and macrosomia (OR 2.02, 95%CI 1.23–3.31) at birth.

After adjustment for maternal age, family history of hypertension, family history of diabetes, history of GDM treatment, education, income, smoking, gestational weeks of birth, pre-pregnancy BMI, gestational weight gain, and infant feeding, children born to GDM mothers with self-reported hypertensive disorders during pregnancy had higher mean values of Z scores for weight for age, weight for length/height, and body mass index for age at 1–5 years old, and greater changes in Z scores for weight for age, and weight for height from birth to 1–5 years old, compared with those born to mothers with normal blood pressure during pregnancy (Table 3). After additional adjustment for Z score for birth weight for gestational age, or birth weight for length, these associations did not change. Offspring born to GDM mothers with self-reported hypertensive disorders of pregnancy were associated with increased risks of overweight and obesity at 1–5 years old (OR 1.88, 95%CI 1.16–3.04) compared with those born to GDM mothers with normal blood pressure during pregnancy. This association did not change after additional adjustment for maternal HbA1c during 16–30 gestational weeks (n=1108). In addition, the association of maternal hypertensive disorders of pregnancy with the risk of childhood overweight and obesity was the same among children less than 3 years old (OR 1.77, 95%CI 1.04–3.04) and in children of 3–5 years old (OR 4.56, 95%CI 1.26–16.5).

Discussion

The present study indicated that offspring born to GDM mothers with a history of hypertensive disorders of pregnancy had higher risks of large for gestational age and macrosomia at birth, and childhood overweight and obesity at 1–5 years old compared with those born to GDM mothers with normal blood pressure during pregnancy.

Only a few epidemiologic studies have assessed the association between maternal hypertensive disorders of pregnancy and fetal growth, and the results are inconsistent. A US prospective study found that maternal preeclampsia reduced the risk of large for gestational age infants.[25] However, another Canadian study indicated that maternal preeclampsia and gestational hypertension were associated with increased risks of both large for gestational age and small for gestational age infants. [26] The present study investigated the association of maternal hypertensive disorders of pregnancy with the growth of offspring of GDM mothers, and found a significant positive association between maternal pregnancy-induced hypertension and the risks of infant large for gestational age and macrosomia at birth.

Few studies have investigated the association between hypertensive disorders of pregnancy and childhood overweight and obesity. A recent meta-analysis has indicated that there was a significant increase in BMI in children aged ≥10 years who born to mothers with preeclampsia compared with those who born to mothers with normal blood pressure, but no

difference in BMI was found in the studies that included only children aged <10 years.[27] An Australia birth cohort study found that maternal pregnancy-induced hypertension was associated with an increased risk of obesity and high blood pressure in young adult offspring.[3] To our knowledge, almost no studies investigated the association of hypertensive disorders of pregnancy of GDM mothers with overweight/obesity risk of their children aged less than 5 years. The present study found that offspring of GDM mothers who were diagnosed with hypertensive disorders of pregnancy had higher mean values of Z scores of weight for age, weight for length and BMI for age at 1–5 years old, and higher mean values of changes in Z scores of weight for age and weight for height from birth to age 1–5 years, as well as a higher risk of childhood overweight and obesity at 1–5 years old than those of GDM mothers without a history of hypertensive disorders of pregnancy. Our findings suggest that maternal pregnancy-induced hypertension in GDM mothers is an important risk factor for childhood overweight at an early age.

Some studies have found a significant positive association between high birth weight and childhood obesity.[21, 28] The present study also found that offspring born to GDM mothers with a history of hypertensive disorders of pregnancy had higher risks of large for gestational age and macrosomia at birth, and childhood overweight and obesity at 1–5 years old compared with those born to GDM mothers with normal blood pressure during pregnancy. To control for the potential mediating effect of maternal hypertensive disorders of pregnancy on childhood overweight risk via infant high birth weight or length, we additionally adjusted for birth weight for gestational age Z score, birth length for gestational age Z score, and birth weight for length Z score in the multivariable-adjusted analyses, and found that the positive association between maternal hypertensive disorders of pregnancy and the risk of childhood overweight and obesity at 1–5 years old was independent of fetal growth.

Several studies have indicated that pre-pregnancy overweight and excessive gestational weight gain were associated with offspring's childhood overweight and obesity among the general population.[29, 30] One study from our team has got the same findings in children of GDM mothers.[10] In the present study, we found that maternal pre-pregnancy overweight, excessive gestational weight gain and maternal history of hypertensive disorders of pregnancy were all associated with offspring's overweight and obesity when maternal pre-pregnancy overweight, excessive gestational weight gain and maternal history of hypertensive disorders of pregnancy were entered into the multivariable-adjusted model simultaneously (Model 1 – adjusted for maternal age, family history of hypertension, family history of diabetes, history of GDM treatments, education, income, smoking, gestational weeks of birth, and infant feeding). After additional adjustment for BMI for age Z score in Model 2 and HbA1c at 26–30 gestational weeks in Model 3, we still found that maternal pre-pregnancy BMI and maternal history of hypertensive disorders of pregnancy were associated with offspring's overweight and obesity. However, there was no association of gestational weight gain with offspring's overweight and obesity. This might indicate that maternal history of hypertensive disorders of pregnancy and pre-pregnancy BMI were independent risk factors for childhood obesity.

Even though the mechanisms of hypertensive disorders of pregnancy with the risk of childhood overweight and obesity in the offspring are poorly understood, several putative mechanisms may be proposed. Washburn et al[31] found that male adolescents born prematurely of women with preeclampsia had higher measurements of adiposity than those born prematurely of normotensive pregnancies, and they speculated that the developmental programming such as the altering of leptin regulation system in the offspring born of women with preeclampsia may be associated with childhood postnatal adiposity. Another Germany study found that obesity-related genes such as leptin were considerably up-regulated in placental tissue of preeclampsia,[32] and the increased levels of leptin in cord blood of preterm infants could affect blood pressure and body weight of the offspring.[33] Other possible mechanisms included oxidative stress and mitochondrial dysfunction.[34] Several studies have shown that maternal preeclamptic pregnancies are associated with oxidative stress in the newborn,[35] and oxidative stress and mitochondrial dysfunction are associated with obesity.[36–38]

Our study has several strengths, including a large number of GDM mother-child pairs, and adjustment for multiple prenatal and perinatal factors in the analyses. However, there were several limitations. First, the maternal hypertensive disorders of pregnancy were based on the self-reported questionnaire which may bring retrospective bias. Nevertheless, validation studies in the United States and England have found good concordance between self-reported hypertensive disorder during pregnancy and clinical records.[39] Second, since hypertensive disorders of pregnancy could not be disaggregated into gestational hypertension, preeclampsia, and eclampsia in the present study, we cannot separately investigate the effects of different pathophysiology and severity disorders on the growth of offspring. Additionally, the samples were the offspring of GDM mothers, therefore the findings may not be generalizable to the normal population, and thus more studies are needed to confirm our findings.

Our study demonstrates that offspring born to GDM mothers with a history of hypertensive disorders of pregnancy had higher risks of large for gestational age and macrosomia at birth, and childhood overweight and obesity at 1–5 years old compared with those born to GDM mothers with normal blood pressure during pregnancy.

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Abbreviation List

HDP	Hypertensive disorders of pregnancy

GDM	Gestational diabetes mellitus
OR	odds ratios
OGTT	Oral glucose tolerance test
IGT	Impaired glucose tolerance
TGDMPP	Tianjin Gestational Diabetes Mellitus Prevention Program
BMI	Body mass index

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Summary Table

What is known about the topic?

- Hypertensive disorders of pregnancy as a group of medical complications in pregnancy remain to be a major cause of maternal and infant morbidity and mortality worldwide.
- Offspring of women with hypertensive disorders of pregnancy are at increased risk for cardiovascular disease at early adults. Maternal preeclampsia increased the risk of intrauterine growth restriction and low birth weight, which in turn is reported to predispose to central obesity, hypertension, coronary heart disease and insulin resistance.

What this study adds?

- Offspring born to GDM mothers with a history of hypertensive disorders of pregnancy had higher risks of large for gestational age and macrosomia at birth.
- Compared with offspring born to GDM mothers with normal blood pressure during pregnancy, the risk of childhood overweight and obesity is increasing among children born to GDM mothers with a history of hypertensive disorders of pregnancy.

Table 1

Characteristics of mother-child pairs according to self-reported maternal hypertensive disorders of pregnancy

	Self-reported maternal hypertensive disorders of pregnancy		P for differences
	No	Yes	
No. of subjects	1172	91	
Maternal characteristics			
Age (years)	32.3 (3.5)	33.0 (3.6)	0.108
Pre-pregnancy body mass index (kg/m^2)	22.9 (3.2)	25.1 (3.6)	<0.001
Fasting glucose at 26–30 gestational weeks (mmol/l)	5.3 (0.8)	5.5 (0.8)	0.037
2-hour glucose at 26–30 gestational weeks (mmol/l)	9.1 (1.3)	9.4 (1.3)	0.035
HbA1c at 26–30 gestational weeks (n=1108)[a]	5.8 (0.6)	5.9 (0.6)	0.073
History of gestational diabetes mellitus treatments (%)			0.079
Yes	83.7	91.1	
No	16.3	8.9	
Gestational weight gain			
Means (kg)	16.6 (5.8)	19.0 (7.0)	0.002
Categories (%)[b]			<0.001
Inadequate	12.8	6.6	
Adequate	32.4	15.4	
Excessive	54.8	78.0	
Current smoking (%)	1.9	3.3	0.349
Education (%)			0.216
<13 years	22.0	29.7	
13–16 years	70.4	64.8	
≥16 years	7.6	5.5	
Family income (yuan/month, %)			0.127
<5000	26.9	36.3	
5000–8000	37.0	35.2	
≥8000	36.1	28.6	
Family history of hypertension (%)	49.1	54.9	0.280
Family history of diabetes (%)	34.2	39.2	0.369
Offspring characteristics			
Newborn			
Gestational weeks of birth (weeks)	39.1 (1.5)	38.6 (1.8)	0.003
Sex (boys %)	52.3	62.6	0.057
Birth weight (g)	3540 (517)	3619 (613)	0.235
Birth recumbent length (cm)	50.8 (2.0)	51.1 (2.6)	0.206
At baseline survey of 1–5 years old			
Age (months)	26.8 (10.5)	28.1 (10.3)	0.273
Weight (kg)	13.4 (2.8)	14.6 (3.2)	<0.001
Height (cm)	90.5 (8.4)	92.2 (8.5)	0.056
Body mass index (kg/m^2)	16.1 (1.5)	16.9 (1.7)	<0.001

	Self-reported maternal hypertensive disorders of pregnancy		P for differences
	No	Yes	
Breast feeding (%)			0.008
Exclusive breast feeding ≥6 months	42.1	26.4	
Exclusive breast feeding <6 months	2.1	1.1	
Mixed feeding	42.2	49.5	
Exclusive formula feeding	13.7	23.1	

Data are means (SD) or percentage. T-test and chi-square tests were used to assess the difference between two groups.

[a]HbA1c measurements at 26–30 gestational weeks were available from 2006 among 1108 women including 79 women had maternal hypertensive disorders of pregnancy.

[b]Gestational weight gain categories: Inadequate (1): <12.5 kg (pre-pregnancy BMI <18.5 kg/m^2), <11.5 kg (BMI 18.5–23.9 kg/m^2), <7 kg (BMI 24.0–27.9 kg/m^2), and <5 kg (BMI >28 kg/m^2); Adequate (1): 12.5–18 kg (BMI <18.5 kg/m^2), 11.5–16 kg (BMI 18.5–23.9 kg/m^2), 7–11.5 kg (BMI 24.0–27.9 kg/m^2), and 5–9 kg (BMI >28 kg/m^2); Excessive (1): >18 kg (BMI <18.5 kg/m^2), >16 kg (BMI 18.5–23.9 kg/m^2), >11.5 kg (BMI 24.0–27.9 kg/m^2), and >9 kg (BMI >28 kg/m^2), according to the Chinese maternal pre-pregnancy BMI classification standard and the 2009 IOM GWG recommendations.

Table 2

Neonatal major outcomes according to self-reported maternal history of hypertensive disorders of pregnancy

	Maternal hypertensive disorders of pregnancy		P for differences
	No	Yes	
No. of subjects	1172	91	
Birth weight for gestational age Z score	0.38 (0.03)	0.74 (0.11)	0.005
Birth weight for length for gestational age Z score	0.34 (0.03)	0.63 (0.11)	0.019
Preterm delivery (%)[a]	4.4	7.7	0.156
Small for gestational age (%)[b]	5.0	3.2	0.444
Large for gestational age (%)[b]	20.5	30.8	0.021
Macrosomia (%)[c]	18.9	30.8	0.006
Odd ratio of large for gestational age [b]	1.00	1.74 (1.08, 2.79)	0.022
Odd ratio of macrosomia[c]	1.00	2.02 (1.23, 3.31)	0.005

Data are mean (SE), percentage or odds ratio (95% CI); adjusted for maternal age, family history of hypertension, education, family income, and gestational weeks of birth.

[a]Preterm delivery was defined as gestational weeks of delivery <37 weeks.

[b]Small-for-gestational-age was defined as a standardized birth weight <10th percentile; large-for-gestational-age was defined as a standardized birth weight >90th percentile.

[c]Macrosomia was defined as birth weight ≥4000g

Table 3

Mean values of Z scores for weight for age, length/height for age, and body mass index for age, as well as prevalence and odds ratio of overweight/obesity among offspring at 1–5 years old according to self-reported maternal hypertensive disorders of pregnancy

	Maternal hypertensive disorders of pregnancy		P-value
	No	Yes	
No. of subjects	1172	91	
Weight for age Z score			
Model 1[a]	0.64 (0.03)	0.96 (0.10)	0.002
Model 2[b]	0.64 (0.03)	0.94 (0.09)	0.003
Model 3[c]	0.64 (0.03)	0.98 (0.10)	0.002
Length/height for age Z score			
Model 1[a]	0.79 (0.03)	0.91 (0.11)	0.272
Model 2[b]	0.79 (0.03)	0.88 (0.10)	0.388
Model 3[c]	0.82 (0.03)	0.89 (0.11)	0.547
Weight for length/height Z score			
Model 1[a]	0.31 (0.03)	0.68 (0.11)	0.001
Model 2[b]	0.31 (0.03)	0.67 (0.11)	0.001
Model 3[c]	0.30 (0.03)	0.72 (0.11)	0.001
Body mass index for age Z score			
Model 1[a]	0.24 (0.03)	0.60 (0.11)	0.002
Model 2[b]	0.24 (0.03)	0.59 (0.11)	0.002
Model 3[c]	0.22 (0.03)	0.62 (0.11)	0.001
Change in weight for age Z score from birth to 1–5 years old			
Model 1[a]	0.24 (0.04)	0.45 (0.14)	0.125
Model 2[b]	0.23 (0.03)	0.54 (0.10)	0.003
Model 3[c]	0.25 (0.03)	0.59 (0.10)	0.002
Change in weight for height Z score from birth to 1–5 years old			
Model 1[a]	−0.04 (0.04)	0.27 (0.15)	0.045
Model 2[b]	−0.04 (0.03)	0.32 (0.11)	0.001
Model 3[c]	−0.05 (0.03)	0.37 (0.11)	0.001
Prevalence of overweight/obesity (%)[d]			
Model 1[a]	19.0 (0.01)	31.9 (0.04)	0.003
Model 2[b]	19.0 (0.01)	31.7 (0.04)	0.004
Model 3[c]	18.8 (0.01)	31.2 (0.04)	0.008
Odds ratio of overweight/obesity			
Model 1[a]	1.00	1.90 (1.18, 3.06)	0.009
Model 2[b]	1.00	1.88 (1.16, 3.04)	0.010

	Maternal hypertensive disorders of pregnancy		P-value
	No	Yes	
Model 3[c]	1.00	1.86 (1.10, 3.13)	0.020

Data are mean (SE), percentage or odds ratio (95% confidence interval).

[a]Model 1 was adjusted for maternal age, family history of hypertension, family history of diabetes, history of GDM treatments, education, income, smoking, gestational weeks of birth, pre-pregnancy BMI, weight gain during pregnancy, and infant feeding.

[b]Model 2 was adjusted for all variables in model 1 and also birth weight for gestational age Z score in analyses of weight for age Z score and change in weight for age Z score from birth to 1–5 years old, birth length for gestational age Z score in analyses of length/height for age Z score, birth weight for length Z score in analyses of changes in weight for length/height Z score, body mass index for age Z score and change in weight for height Z score from birth to 1–5 years old and odd ratio of overweight/obesity.

[c]Model 3 was adjusted for all variables in model 2 and also adjusted for HbA1c at 26–30 gestational weeks (n=1108, 79 women had maternal hypertensive disorders of pregnancy).

[d]Overweight and obesity is defined as a body mass index higher than the 85th percentiles for age and gender using the WHO growth reference.