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Adverse birth outcomes and childhood overweight at age of 3–8 years in a prospective cohort study in Tianjin, China

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ABSTRACT

Objectives To explore associations between adverse birth outcomes and childhood overweight at 3–8 years of age.
Design A prospective cohort study.
Setting Six central urban districts of Tianjin, China.
Participants 1681 woman–child pairs.
Methods 1681 woman–child pairs were followed up for 8 years in Tianjin, China. Demographic and clinical information including birth outcomes was collected longitudinally, commencing from first antenatal care visit till postpartum period. Offspring height and weight were measured at 3–8 years of age. High and low weight/length ratios (WLR) at birth were, respectively, defined as ≥90th and ≤10th gestational week and sex-specific percentiles. Overweight for children at 3–5 and 6–8 years of age were, respectively, defined as body mass index (BMI)-for-age and -sex above the 2 z-score and 1 z-score curves of the WHO's child growth standards. Binary logistic regression analysis was used to obtain ORs and 95% CI with a stepwise backward selection method to select independent predictors.
Primary outcomes measures Childhood overweight.
Results Of 1681 children, 10.7% (n=179) and 27.8% (n=468) developed overweight at 3–5 and 6–8 years of age, respectively. Large for gestational age (LGA) was associated with increased risk of overweight at 3–5 years of age (aOR: 1.86, 95% CI: 1.27 to 2.72) while high WLR at birth was associated with increased risk of overweight at 6–8 years of age (1.82, 1.41 to 2.34). Low WLR at birth was associated with decreased risk of overweight at 6–8 years of age (0.52, 0.30 to 0.90).
Conclusions LGA and high WLR at birth predicted childhood overweight at 3–5 and 6–8 years of age, respectively. Low WLR at birth was associated with decreased risk of childhood overweight at 6–8 years of age.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study was conducted in the three-tier antenatal care system in urban Tianjin, China and the representativeness of the study population is good.
⇒ This study had documented detailed demographic and clinical information of pregnant women from their first antenatal care visit till postpartum period, thus available for analysis.
⇒ This study did not record lifestyle factors of children such as physical activities, sleep time, and dietary habits, which may exist residual confounding.
⇒ Most of women with gestational diabetes mellitus in our study were from a randomised controlled trial and half of them received intensive care (IC). Although we had carefully adjusted for IC, its confounding effect may have not been removed completely.

INTRODUCTION

Alongside adulthood overweight, childhood overweight has emerged as a serious public health issue worldwide. In 2019, WHO estimated that 38.2 million or 5.6% of children under 5 years of age were overweight globally. Furthermore, the prevalence of overweight among children and adolescents aged 5–19 years had risen dramatically from just 4% in 1975 to over 18% in 2016.[1] As we all know, overweight during childhood is likely to continue into adulthood and is associated with increased risk of many short-term and long-term adverse health outcomes, including psychosocial comorbidity, cardiovascular diseases, type 2 diabetes as well as premature mortality.[2] Consequently, it is of utmost importance to identify early risk factors for effective intervention and prevention of childhood overweight.

Childhood overweight is a complex, multifactorial condition stemming from interactions between genetic and non-genetic factors, including unhealthy dietary patterns, inadequate physical activities, shortened sleep duration, increased sedentary time, and excessive psychological stress.[3 4] It has also been reported that the intrauterine and early postnatal conditions can have a significant impact on increased risk of developing overweight in later life.[5 6] Therefore, the exploration for risk factors of childhood overweight could be extended to infant adverse birth outcomes.

Currently, only a few studies have explored the risk association between adverse birth outcomes and childhood overweight with inconsistent findings. For example, a cross-sectional analysis from Australia found that low birth weight was associated with decreased risk of overweight among girls at 4–5 years of age.[7] However, a retrospective study in Tianjin, China observed that low birth weight was not associated with overweight among children aged 3–6 years.[8] On the other hand, a retrospective study in Xiamen, China failed to find a significant association between infants with large for gestational age (LGA) of women with gestational diabetes mellitus (GDM) and later overweight at 1–6 years of age.[9] However, a large cohort study from Canada found that children born with LGA of mothers with GDM were 2.79 times more likely to be overweight at 4–6 years of age compared with children born with appropriate for gestational age (AGA) of mothers without diabetes.[10] Therefore, it deserves further investigation of the risk association between adverse birth outcomes and childhood overweight.

Using the long-term follow-up data of children born to women enrolled in a population-based prospective cohort in Tianjin, China, we aimed to explore the risk associations between adverse birth outcomes and childhood overweight at 3–8 years of age.

SUBJECTS, MATERIALS, AND METHODS

Study settings and population

The study settings and population has been published previously.[11] Briefly, we established a universal screening and management system for GDM in six central urban districts of Tianjin, China in 1998.[12] The antenatal care was delivered by a three-tier antenatal care system, consisting of 65 primary hospitals, six district-level Women and Children's Health Centres (WCHC) and other secondary obstetric hospitals, and a city-level WCHC, that is, Tianjin WCHC (TWCHC) and other tertiary obstetric hospitals. On the basis of the GDM screening and management system and the three-tier antenatal care network, we set up a cohort of pregnant women and their offspring.

From 2010 to 2012, a total of 22 302 pregnant women were registered at the primary care hospital near their residence. They were offered a 50 g 1 hour glucose challenge test (GCT) at 24–28th gestational weeks. Women with plasma glucose (PG)≥7.8 mmol/L were referred to the TWCHC GDM Clinic to undergo a 75 g 2 hour Oral Glucose Tolerance Test (OGTT) after an overnight fasting of at least 8 hours. GDM was diagnosed according to the International Association of Diabetes and Pregnancy Study Group (IADPSG)'s cut-points: fasting PG≥5.1 mmol/L or 1 hour PG≥10.0 mmol/L or 2 hour PG ≥8.5 mmol/L.[13] Of them, 1251 women without a GCT result and 891 women with a positive GCT but without a standard OGTT result were excluded. Among the remaining 20 160 participants, 1535 women were diagnosed with GDM and 1040 of them were invited to participate in the study. Among the 18 625 women without GDM, 1100 women were randomly selected into this study as the controls. In the 1040 women with GDM, 948 of them participated in a randomised controlled trial (RCT) to test the effectiveness of intensive care (IC) of GDM during pregnancy on adverse pregnancy outcomes. The details of the RCT and IC have been published previously.[14] After further excluding 42 women who had stillbirth, neonatal death or non-singleton pregnancy, a total of 2098 woman–child pairs were included in the long-term follow-up study.

At postpartum, 2098 children born to the included women were invited to participate in the follow-up study and measured their body height and weight each year from 1 to 8 years of age. Finally, a total of 1681 children underwent at least one postpartum follow-up visit and completed body height and weight measurements at 1 to 8 years of age (figure 1).

Ethics

Ethical approval was obtained from the Ethics Committee for Clinical Research of Tianjin Women and Children's Health Centre (approval code: 2009-02). Written informed consent was obtained from all participants before data collection.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Data collection and clinical measurement

Before the study, all researchers received uniform training to standardise the anthropometric and clinical measurements. Data were collected longitudinally from a series of questionnaires or extracted from the database of Maternal and Child Health Information System. At registration for pregnancy, we collected information on maternal height, weight, age, systolic blood pressure (SBP), diastolic blood pressure (DBP), education attainment, parity, family history of diabetes in first-degree relatives, smoking and drinking during pregnancy. Maternal height and weight were measured with light clothing and without shoes. Body weight at the first antenatal visit was regarded as the prepregnancy weight as the maternal weight was relatively stable during the first trimester of pregnancy.[15] Blood pressure was measured in a sitting position after at least 10 min of rest. Children's information including birthday, sex, body length, and weight at birth and breastfeeding status were also obtained through questionnaires from their mothers. Body height and weight of offspring were measured at each of postpartum follow-up visits from 1 to 8 years of age. BMI was calculated as weight in kilograms divided by the square of height in metres. Weight/length ratio (WLR) at birth was calculated as weight in kilograms divided by body length in metres.[16]

Definition of adverse birth outcomes

Preterm birth and post-term pregnancy were defined as delivery at <37 and ≥42 weeks of gestation,[17,18] respectively.

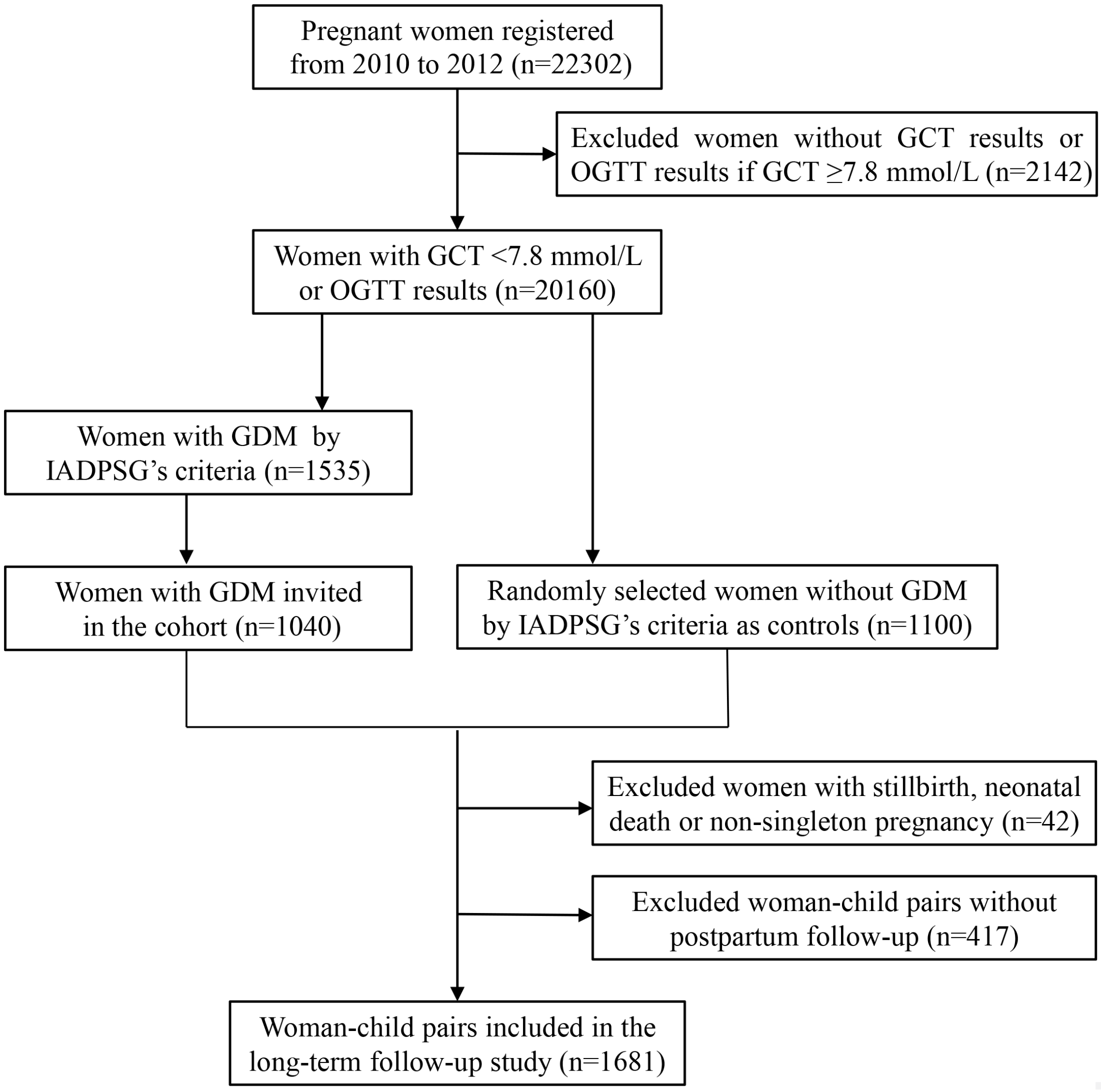

Figure 1 Flow diagram of participants included in the analysis. IADPSG, International Association of Diabetes and Pregnancy Study Group; GCT, glucose challenge test; GDM, gestational diabetes mellitus; OGTT, Oral Glucose Tolerance Test.

Macrosomia and low birth weight were, respectively, defined as birthweight ≥4000 and <2500 g.[14 19] LGA and small for gestational age (SGA) were, respectively, defined as birthweight ≥90th gestational week and sex-specific percentiles and birthweight ≤10th gestational week and sex-specific percentiles of Chinese standards.[20] High and low WLR at birth were, respectively, defined as WLR at birth ≥90th and ≤10th gestational week and sex-specific percentiles of Chinese standards.[16]

Definition of childhood overweight

According to the WHO's child growth standards, overweight for children at 3–5 and 6–8 years of age were defined as BMI-for-age and -sex above the 2 z-score and 1 z-score curves, respectively.[21 22] In this study, childhood overweight at 3–5 years of age was defined as overweight at either of 3, 4, or 5 years of age and childhood overweight at 6–8 years of age was defined as either overweight at 6, 7, or 8 years of age.

Statistical analysis

All statistical analyses were conducted using the Statistical Analysis System (Release V.9.4, SAS Institute, Cary, NC). Continuous variables were described as mean±SD or median (IQR). Categorical variables were expressed as number (percentage). The differences of continuous variables between two groups were compared by Student's t-test or Mann-Whitney U test where appropriate. The differences of categorical variables between two groups were compared by χ^2 test or Fisher's exact test. We used binary logistic regression to obtain the ORs and 95% CI of adverse birth outcomes for overweight in children at 3–5 years of age and 6–8 years of age. First, we calculated unadjusted ORs in univariable analysis. Second, we performed multivariable analysis to control for confounders. The variables adjusted in the multivariable model included maternal prepregnancy BMI, SBP, education attainment, family history of diabetes in first-degree relatives, GDM, IC status during pregnancy, unintentional intervention, child's sex, breastfeeding status, and birth weight (for caesarean delivery only). At last, backward stepwise selection approach in the multivariable logistic regression (p=0.05 for exit) was used to identify adverse birth outcomes that have independent predictive values for childhood overweight. All the tests were two-tailed and p values<0.05 were considered to be statistically significant.

Reporting guidelines

We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) cohort checklist when writing our report.[23]

RESULTS

Characteristics of study participants

A total of 1681 children turned up at least one follow-up visit after delivery, with an overall response rate of 80.1%. Of them, 10.7% (n=179) and 27.8% (n=468) developed overweight at 3–5 and 6–8 years of age, respectively. At the first antenatal care visit, the mean age and BMI of their mothers were 28.9 (SD: 3.0) years and 23.1 (SD: 3.5) kg/m^2. Compared with children with normal weight, mothers of children who developed overweight at 3–5 years of age had higher prepregnancy BMI, SBP/DBP, were less likely to have education>12 years, and were more likely to have family history of diabetes in first-degree relatives and to have GDM; mothers of children who developed overweight at 6–8 years of age had higher prepregnancy BMI and higher SBP/DBP and were more likely to have GDM and to receive IC during pregnancy but less likely to have education>12 years. Other characteristics including parity, smoking and drinking during pregnancy, and unintentional intervention were not significantly different between the two groups (table 1).

Associations of adverse birth outcomes with offspring overweight at 3–5 years of age

Children who developed overweight at 3–5 years of age had a higher birth weight, higher rates of male sex, caesarean delivery, macrosomia, LGA, and high WLR at birth than children with normal weight (table 2). In univariable analysis, caesarean delivery, macrosomia, LGA, and high WLR at birth were associated with markedly increased risk of offspring overweight (OR: 1.96, 95% CI: 1.36 to 2.84 and 2.63, 1.79 to 3.87 and 2.37, 1.66 to 3.39 and 2.09, 1.51 to 2.91, respectively). After adjusting for confounding factors, the associations of macrosomia, LGA and high WLR at birth with offspring overweight at 3–5 years of age were slightly attenuated but still significant (aOR: 1.89, 1.25 to 2.85 and 1.86, 1.27 to 2.72 and 1.67, 1.18 to 2.37, respectively). The multivariable backward stepwise logistic regression analysis revealed that LGA was independently associated with increased risk of offspring overweight at 3–5 years of age (aOR: 1.86, 1.27 to 2.72) (table 3).

Associations of adverse birth outcomes with offspring overweight at 6–8 years of age

Children who developed overweight at 6–8 years of age had a higher birth weight, higher rates of male sex, caesarean delivery, macrosomia, LGA and high WLR at birth, and lower rates of low birth weight, SGA, and low WLR at birth than children with normal weight (table 2). In univariable analysis, caesarean delivery, macrosomia, LGA, and high WLR at birth were associated with markedly increased risk of offspring overweight (OR: 1.69, 95% CI: 1.33 to 2.14 and 2.59, 1.91 to 3.50 and 2.42, 1.84 to 3.19 and 2.18, 1.72 to 2.77, respectively). Conversely, low birth weight, SGA, and low WLR at birth were associated with decreased risk of offspring overweight (OR: 0.41, 0.17 to 0.98 and 0.48, 0.27 to 0.83 and 0.47, 0.28 to 0.80, respectively). In multivariable analysis, the associations of macrosomia, LGA, and high WLR at birth with offspring overweight were slightly attenuated but still significant (aOR: 1.92, 1.39 to 2.65 and 1.99, 1.49 to 2.67 and 1.82, 1.41 to 2.34, respectively). On the other hand, low birth weight, SGA and low WLR at birth were still associated with decreased risk of offspring overweight (aOR: 0.41, 0.17 to 0.98 and 0.53, 0.30 to 0.95 and 0.52, 0.30 to 0.90, respectively). The backward stepwise logistic regression in the multivariable analysis revealed that high WLR at birth was independently associated with increased risk of offspring overweight at 6–8 years of age (aOR: 1.82, 1.41 to 2.34), whereas low WLR at birth was associated with decreased risk of offspring overweight at 6–8 years of age (aOR: 0.52, 0.30 to 0.90) (table 3).

DISCUSSION

In the present study, we found that (1) LGA predicted offspring overweight at 3–5 years of age; (2) high WLR at birth predicted offspring overweight at 6–8 years of age; and (3) low WLR at birth was associated with decreased risk of offspring overweight at 6–8 years of age.

Several studies have investigated the association between LGA and offspring overweight but have inconsistent conclusions. A retrospective study in Xiamen, China (n=33 157) did not observe a significant association between LGA and childhood overweight among women with GDM at 1–6 years of age.[9] A cohort study in Greece (n=1667) also did not find any significant association between LGA and childhood overweight from 3 to 5 years of age.[24] However, a large cohort study in Alberta, Canada (n=81 226) found that infants with LGA of women with GDM had a 179% higher risk of being overweight at 4–6 years of age than infants with AGA of mothers without GDM. However, that study did not adjust for maternal prepregnancy BMI.[10] To the best of our knowledge, our study is the first to evaluate the association between WLR at birth and long-term risk of childhood overweight. WLR at birth was found to correlate strongly with skinfold thickness and body fat store in newborn infants.[25 26] Moreover, the INTERGROWTH-21st Project demonstrated that WLR at birth was more closely associated with fat

Table 1 Maternal clinical characteristics stratified by offspring overweight status at 3-8 years of age

Characteristics	Normal	Overweight	P value
At 3–5 years of age (1502/179)			
Age (years, means±SD)	28.9±3.0	28.7±2.9	0.355*
Height (cm, means±SD)	163.0±4.9	162.5±5.4	0.328*
Prepregnancy BMI (kg/m^2, means±SD)	22.8±3.3	25.4±4.4	<0.001*
SBP (mm Hg, means±SD)	106.0±10.7	108.4±10.5	0.005*
DBP (mm Hg, means±SD)	68.8±7.6	70.8±7.9	0.001*
Education>12 years (%)	1255 (83.6)	139 (77.7)	0.047†
Parity≥1 (%)	62 (4.1)	5 (2.8)	0.388†
Family history of diabetes in first-degree relatives (%)	137 (9.1)	28 (15.6)	0.006†
Smoking during pregnancy (%)	14 (0.9)	1 (0.6)	0.935†
Drinking during pregnancy (%)	8 (0.5)	1 (0.6)	1.000†
Gestational diabetes mellitus (%)	718 (47.8)	103 (57.5)	0.014†
IC status during pregnancy (%)	322 (21.4)	42 (23.5)	0.534†
Unintentional intervention (%)	172 (11.5)	22 (12.3)	0.740†
At 6–8 years of age (1213/468)			
Age (years, means±SD)	28.9±2.9	28.9±3.2	0.983*
Height (cm, means±SD)	162.9±4.8	162.8±5.3	0.615*
Prepregnancy BMI (kg/m^2, means±SD)	22.5±3.2	24.5±3.9	<0.001*
SBP (mm Hg, means±SD)	105.7±10.8	107.6±10.4	0.002*
DBP (mm Hg, means±SD)	68.6±7.7	70.2±7.7	<0.001*
Education>12 years (%)	1030 (84.9)	364 (77.8)	0.001†
Parity≥1 (%)	45 (3.7)	22 (4.7)	0.352†
Family history of diabetes in first-degree relatives (%)	113 (9.3)	52 (11.1)	0.268†
Smoking during pregnancy (%)	8 (0.7)	7 (1.5)	0.179†
Drinking during pregnancy (%)	7 (0.6)	2 (0.4)	1.000†
Gestational diabetes mellitus (%)	543 (44.8)	278 (59.4)	<0.001†
IC status during pregnancy (%)	240 (19.8)	124 (26.5)	0.003†
Unintentional intervention (%)	135 (11.1)	59 (12.6)	0.400†

*Derived from t-test.
†Derived from χ^2 test or Fisher's exact test.
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; IC, intensive care.;

mass, fat-free mass, and body fat percentage than BMI or ponderal index in neonates.[27] Therefore, the WLR at birth is a good parameter for evaluating the nutritional status of intrauterine growth and predicting metabolic complications in newborns with abnormal intrauterine growth.[25 26] In this connection, we observed that high WLR at birth was positively associated with overweight in children at 6–8 years of age, while low WLR at birth was negatively associated with childhood overweight at 6–8 years of age.

The mechanisms by which LGA increases the risk of childhood overweight are not yet fully understood. However, it is becoming increasingly clear that GDM, maternal prepregnancy overweight, and excessive pregnancy weight gain all predispose women to an elevated risk of LGA.[28] These risk factors are accompanied with insulin resistance and hyperglycaemia during pregnancy,[29 30] which can cause fetal hyperinsulinaemia and maternal hypertriglyceridemia, and then lead to fetal overnutrition and high risk of LGA.[31 32] Intrauterine overnutrition may affect fat metabolism, insulin, and leptin secretion by altering the development of the appetite control centre in the fetal hypothalamus, thus leading to an imbalance of the fetal energy system and increasing the risk of childhood overweight.[33 34] Furthermore, a longitudinal study in Hungary found a positive correlation between cord serum leptin levels and WLR at birth.[35] Cord blood leptin levels were found to be closely related to fetal fat store and may serve as an important regulator of fetal growth and development, energy intake, storage and expenditure, thus contributing to long-term childhood overweight.[35 36]

Table 2 Adverse birth outcomes stratified by offspring overweight status from 3 to 8 years of age

	Normal	Overweight	P value
At 3–5 years of age (1502/179)			
Gestational age at delivery (weeks, median (IQR))	39.0 (38.0, 40.0)	39.0 (38.0, 40.0)	0.867*
Birth weight (kg, means±SD)	3.4±0.5	3.6±0.5	<0.001*
Infant male sex (%)	796 (53.0)	115 (64.3)	0.004†
Caesarean delivery (%)	971 (64.7)	140 (78.2)	<0.001†
Gestational week at delivery (%)			0.630†
Preterm birth	66 (4.4)	7 (3.9)	
Post-term pregnancy	27 (1.8)	5 (2.8)	
Weight at birth (%)			<0.001†
Macrosomia	155 (10.3)	42 (23.5)	
Low birth weight	45 (3.0)	3 (1.7)	
Gestational age specific weight at birth (%)			<0.001†
Large for gestational age	207 (13.8)	51 (28.5)	
Small for gestational age	103 (6.9)	4 (2.2)	
Weight/length ratio at birth (%)			<0.001†
High weight/length ratio at birth	335 (22.3)	69 (38.6)	
Low weight/length ratio at birth	120 (8.0)	7 (3.9)	
Breastfeeding status (%)			0.393†
Exclusive breastfeeding	242 (16.1)	23 (12.9)	
Mixed breastfeeding	328 (21.8)	45 (25.1)	
Artificial feeding	932 (62.1)	111 (62.0)	
At 6–8 years of age (1213/468)			
Gestational age at delivery (weeks, median (IQR))	39.0 (38.0, 40.0)	39.0 (38.0, 40.0)	0.036*
Birth weight (kg, means±SD)	3.4±0.5	3.6±0.5	<0.001*
Infant male sex (%)	612 (50.5)	299 (63.9)	<0.001†
Caesarean delivery (%)	764 (63.0)	347 (74.2)	<0.001†
Gestational week at delivery (%)			0.923†
Preterm birth	52 (4.3)	21 (4.5)	
Post-term pregnancy	24 (2.0)	8 (1.7)	
Weight at birth (%)			<0.001†
Macrosomia	104 (8.6)	93 (19.9)	
Low birth weight	42 (3.5)	6 (1.3)	
Gestational age specific weight at birth (%)			<0.001†
Large for gestational age	141 (11.6)	117 (25.0)	
Small for gestational age	92 (7.6)	15 (3.2)	
Weight/length ratio at birth (%)			<0.001†
High weight/length ratio at birth	236 (19.5)	168 (35.9)	
Low weight/length ratio at birth	110 (9.1)	17 (3.6)	
Breastfeeding status (%)			0.232†
Exclusive breastfeeding	200 (16.5)	65 (13.9)	
Mixed breastfeeding	275 (22.7)	98 (20.9)	
Artificial feeding	738 (60.8)	305 (65.2)	

*Derived from t-test or Mann-Whitney U test.
†Derived from χ^2 test or Fisher's exact test.

Table 3 ORs of adverse birth outcomes for offspring overweight status from 3 to 8 years of age

	Overweight at 3–5 years of age (n=179)		Overweight at 6–8 years of age (n=468)	
	OR (95% CI)	**P value**	**OR (95% CI)**	**P value**
Model 1				
Caesarean delivery	1.96 (1.36 to 2.84)	<0.001	1.69 (1.33 to 2.14)	<0.001
Gestational week at delivery				
Preterm birth	0.90 (0.40 to 1.98)	0.784	1.05 (0.62 to 1.76)	0.865
Term birth	Reference		Reference	
Post-term pregnancy	1.56 (0.59 to 4.11)	0.366	0.86 (0.39 to 1.94)	0.721
Weight at birth				
Macrosomia	2.63 (1.79 to 3.87)	<0.001	2.59 (1.91 to 3.50)	<0.001
Normal weight	Reference		Reference	
Low birth weight	0.65 (0.20 to 2.11)	0.472	0.41 (0.17 to 0.98)	0.045
Gestational age specific weight at birth				
Large for gestational age	2.37 (1.66 to 3.39)	<0.001	2.42 (1.84 to 3.19)	<0.001
Appropriate for gestational age	Reference		Reference	
Small for gestational age	0.37 (0.14 to 1.03)	0.057	0.48 (0.27 to 0.83)	0.009
Weight/length ratio at birth				
High weight/length ratio at birth	2.09 (1.51 to 2.91)	<0.001	2.18 (1.72 to 2.77)	<0.001
Normal weight/length ratio at birth	Reference		Reference	
Low weight/length ratio at birth	0.59 (0.27 to 1.31)	0.194	0.47 (0.28 to 0.80)	0.006
Model 2				
Caesarean delivery	1.36 (0.91 to 2.01)	0.131	1.20 (0.93 to 1.56)	0.162
Gestational week at delivery				
Preterm birth	0.90 (0.40 to 2.03)	0.800	1.01 (0.59 to 1.74)	0.975
Term birth	Reference		Reference	
Post-term pregnancy	1.41 (0.50 to 3.95)	0.518	0.83 (0.35 to 1.94)	0.662
Weight at birth				
Macrosomia	1.89 (1.25 to 2.85)	0.002	1.92 (1.39 to 2.65)	<0.001
Normal weight	Reference		Reference	
Low birth weight	0.68 (0.20 to 2.26)	0.528	0.41 (0.17 to 0.98)	0.046
Gestational age specific weight at birth				
Large for gestational age	1.86 (1.27 to 2.72)	0.002	1.99 (1.49 to 2.67)	<0.001
Appropriate for gestational age	Reference		Reference	
Small for gestational age	0.45 (0.16 to 1.26)	0.128	0.53 (0.30 to 0.95)	0.032
Weight/length ratio at birth				
High weight/length ratio at birth	1.67 (1.18 to 2.37)	0.004	1.82 (1.41 to 2.34)	<0.001
Normal weight/length ratio at birth	Reference		Reference	
Low weight/length ratio at birth	0.67 (0.30 to 1.50)	0.329	0.52 (0.30 to 0.90)	0.018
Model 3				
Weight at birth				
Macrosomia	–	–	–	–
Normal weight				
Low birth weight	–	–	–	–
Gestational age specific weight at birth				
Large for gestational age	1.86 (1.27 to 2.72)	0.002	–	–
Appropriate for gestational age	Reference			

Continued

Table 3 Continued

	Overweight at 3–5 years of age (n=179)		Overweight at 6–8 years of age (n=468)	
	OR (95% CI)	P value	OR (95% CI)	P value
Small for gestational age	0.45 (0.16 to 1.26)	0.128	–	–
Weight/length ratio at birth				
High weight/length ratio at birth	–	–	1.82 (1.41 to 2.34)	<0.001
Normal weight/length ratio at birth			Reference	
Low weight/length ratio at birth	–	–	0.52 (0.30 to 0.90)	0.018

Model 1: univariable analysis.
Model 2: multivariable analysis, adjusted for prepregnancy body mass index, systolic blood pressure, education attainment, family history of diabetes in first-degree relatives, gestational diabetes mellitus, intensive care status during pregnancy, unintentional intervention, child gender, breastfeeding status, and birth weight (for caesarean delivery only).
Model 3: adjusted for the variables listed in model 2 and backward stepwise approach was used to select pregnancy outcomes (p=0.05 for exit).

Our findings have strong public health and clinical implications. It is well established that childhood overweight can persist into adulthood and has been implicated in many chronic diseases. Hence, there is a strong need for taking measures to prevent childhood overweight to reduce the burden of overweight-related diseases in adulthood. This long-term follow-up study supports that LGA and high WLR at birth need to be recognised as risk factors for childhood overweight. On the one hand, our findings highlighted the importance of improving adverse birth outcomes, including LGA and high WLR at birth, for benefits of childhood overweight and possible well-being in adulthood. Our previous RCT demonstrated that IC for pregnant women with GDM can improve adverse birth outcomes, including LGA.[14] Therefore, to reduce the incidence of adverse birth outcomes by dietary and physical activity education during pregnancy is one of the possible measures to prevent childhood overweight. On the other hand, special attention should also be given to infants born with LGA and high WLR to help reduce the prevalence of childhood overweight and related chronic disease later in life. Our findings suggest that more efforts should be shifted to early lifestyle interventions for children at high risk of overweight, especially those born to be LGA and high WLR. Indeed, given to the high prevalence of childhood overweight, it is worthwhile to test the effect and cost-effectiveness of healthy lifestyle intervention for prevention of childhood overweight among high-risk children. In addition, our study also indicates that low WLR at birth had a protective effect on childhood overweight at 6–8 years of age. However, it is still unclear of its benefits and possible harms in late childhood and adulthood. Further investigations are needed to evaluate the association of WLR with long-term overweight in the future.

Our study had strengths and limitations. The strength of this study was conducted in the three-tier antenatal care system in urban Tianjin, China and the representativeness of the study population is good. The second strength of the study was that we had documented detailed demographic and clinical information of pregnant women from their first antenatal care visit till postpartum period, thus available for analysis. Our study also has several limitations. First, some variables regarding lifestyle in the children were not recorded in the study, such as detailed information of breastfeeding duration, physical activities, sleep time, and dietary habits, which may exist residual confounding. Second, most of women with GDM in our study were from an RCT and half of them received IC. In this respect, our previous meta-analysis failed to show that IC of GDM during pregnancy had a detectable effect on the risk of offspring overweight.[37] Although we had carefully adjusted for IC, its confounding effect may have not removed completely.

CONCLUSION

In summary, in the long-term follow-up study of Chinese children, we found that LGA and high WLR at birth were predictive of overweight in children at 3–5 and 6–8 years of age, respectively. Special attention should be paid to children born with LGA and/or high WLR for prevention of childhood overweight. It is worthwhile to test the effectiveness and cost-effectiveness of lifestyle intervention for children at high risk of being overweight. We also observed some benefits for childhood overweight associated with low WLR at birth. Its long-term benefits and possible harms need further investigations in the future, especially for overweight in adulthood.

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