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ORIGINAL ARTICLE

Relationship of maternal birth weight on maternal and neonatal outcomes: a multicenter study in Beijing

R Su[1], W Zhu[1,2], Y Wei[1], C Wang[1], H Feng[1], L Lin[1], M Hod[3,4], E Hadar[3,4] and H Yang[1]

OBJECTIVE: Birth weight is an important indicator for childhood and adulthood diseases. Published studies lack information on the relative contribution of women's own birth weight to the course of her pregnancy, not only for maternal but especially to neonatal outcome. The aim of the study was to evaluate the relationship of maternal birth weight on maternal and perinatal complications during pregnancy.

STUDY DESIGN: Medical and obstetrical data were collected from 5479 women at 15 hospitals in Beijing, by a systemic cluster sampling survey conducted from 20 June 2013 to 30 November 2013. These women were categorized into five groups, according to their own birth weight: low birth weight (⩽2500 g, $n = 275$), sub-optimal birth weight (2500 to 2999 g, $n = 1079$), optimal birth weight (3000 to 3499 g, $n = 2590$; 3500 to 3999 g, $n = 1085$) and high birth weight (⩾4000 g, $n = 450$). The occurrence of maternal and neonatal complications was recorded and compared among the groups. Statistical analysis was performed by SPSS 20.0 and values of $P < 0.05$ were considered to be statistically significant.

RESULTS: Low maternal birth weight was associated with higher rates of gestational diabetes mellitus ($\chi^2 = 21.268$, $P = 0.006$) and hypertensive disorders ($\chi^2 = 10.844$, $P = 0.028$). The latter association was strongest in women with a pre-pregnancy body mass index above 25 kg m^{-2}. Low maternal birth weight was also associated with an apparently higher incidence of preterm labor ($\chi^2 = 18.27$, $P = 0.001$) and hypertriglyceridemia ($\chi^2 = 2.739$, $P = 0.027$) in pregnancy. An association between women with low birth weight and a significantly higher rate of small for gestational age infants ($\chi^2 = 93.507$, $P < 0.001$) and low birth weight ($\chi^2 = 36.256$, $P < 0.001$) was detected. High maternal birth weight was associated with an increased risk of pre-pregnancy overweight and obesity ($P < 0.001$), as well as for large for gestational age infants ($\chi^2 = 93.507$, $P < 0.001$) and macrosomia ($\chi^2 = 72.594$, $P < 0.001$).

CONCLUSIONS: In our study, high or low maternal birth weight was strongly associated with maternal and perinatal adverse pregnancy outcomes. This suggests that by controlling the birth weight of female infants among the normal range, adverse outcomes may be decreased in the future and for the following generations.

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INTRODUCTION

Birth weight is an important indicator for childhood and adulthood diseases.[1] Clinical and animal model studies have repeatedly showed that birth weight, as a marker of fetal growth, correlates with a number of diseases in adult life. These include primarily obesity, diabetes and cardiovascular diseases, but also chronic kidney disease and stroke.[2–4] These findings support the hypothesis of the developmental origins of adult disease, which states that susceptibility to chronic diseases in later life may be programmed *in utero*.[5]

Recently, some studies have examined the association between a woman's own birth weight, not only to future metabolic disorders, but to some extent to subsequent risk for pregnancy complications. Several large population-based epidemiological studies demonstrated that birth weight showed a U-shaped relationship to a woman's risk of gestational diabetes mellitus (GDM) and type 2 diabetes.[6,7] Other studies have demonstrated that low birth weight is inversely related to subsequent risk for hypertension, obesity and the metabolic syndrome.[8,9] However, this relationship has not been found in all ethnic population.[1] Conflicting results have been demonstrated by other researchers, particularly among populations from developing countries.[10] Also, research has mainly been emphasized on the effect of high birth weight.[11] Furthermore, various studies failed to evaluate the effect of maternal birth weight on neonatal complications.[12]

The incidence of such chronic non-communicable diseases has risen extremely worldwide, therefore understanding the impact of fetal growth on future health status is important. Clarifying the specific metabolic responses to pregnancy could unmask underlying susceptibility to future metabolic disorders. As such, it may be beneficial to control *in utero* fetal growth in order to decrease future risks to both the mother and infant. Published studies lack information on the relative contribution of women's own birth weight to the course of her pregnancy, not only for maternal but especially to neonatal outcome. Thus, in this study, we attempted to evaluate the relationship between mother's own birth weight and adverse pregnancy outcome.

METHODS

This study was a retrospective analysis of 5479 women, stratified according to their birth weight, and compared for adverse maternal and neonatal outcomes. The study was approved by the ethics review board of the Peking University First hospital (resolution 2013(578)). Informed written consent was obtained from the pregnant women before enrollment.

[1]Department of Obstetrics and Gynecology, Peking University First Hospital, Beijing, China; [2]National Institute of Hospital Administration, Beijing, China; [3]Helen Schneider Hospital for Women, Rabin Medical Center, Petach-Tikva, Israel and [4]The Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. Correspondence: Professor H Yang, Department of Obstetrics and Gynecology, Peking University First Hospital, Xianmen Street No. 1, Xicheng District, Beijing 100034, China.
E-mail: yanghuixia@bjmu.edu.cn
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Study population

Eligible subjects were defined as all women who delivered a live born singleton infant between 20 June 2013 and 30 November 2013 and that were born at 1970 or later.

Data collection

Medical and obstetrical data for each participant was collected from 15 hospitals in Beijing by a systemic cluster sampling survey conducted from 20 June 2013 to 30 November 2013. Hospital discharge records for each pregnant woman were matched using a unique combination of the mother's medical record number and hospital number. Maternal birth weight was known by means of written medical record. About 5479 were successfully matched to the woman's own birth records.

Collected data for each eligible woman included independent and dependent variables for maternal characteristics such as age, height, pre-pregnancy weight, parity, gestational age at delivery and mode of delivery. The following laboratory parameters were collected: hemoglobin, first trimester of pregnancy fasting glucose, oral glucose tolerance test, lipid values of triglycerides, high-density lipoprotein and low-density lipoprotein.

Plasma glucose (Glucose GOD-PAP; Roche Diagnostic, Mannheim, Germany), the values of triglycerides, high-density lipoprotein and low-density lipoprotein were detected in a fully automatic biochemical analyzer. The reagents used in the assays were provided by SEKISUI Medical and Biosino Bio-technology and Science (Osaka, Japan).

Outcome measures

The following maternal and perinatal complications were assessed and collected from the medical records: GDM (diagnosed according to China's ministry of health criteria published at 2011),[13] hypertensive disorders (inclusive of gestational hypertension, preeclampsia, HELLP syndrome and eclampsia), overweight (pre-pregnancy body mass index (BMI) $\geqslant 24\ kg\ m^{-2}$), obesity (BMI $\geqslant 28\ kg\ m^{-2}$), anemia (defined as hemoglobin $\leqslant 110\ g\ l^{-1}$) and preterm labor (delivery < 37 completed weeks of gestation, $n = 274$). Perinatal and neonatal outcome were considered for all of the following: low birth weight (⩽2500 g), macrosomia (⩾4000 g), small for gestational age (SGA, defined as birth weight below the 10th percentile for the gestational age), large for gestational age (LGA, defined as birth weight over the 90th percentile for the gestational age), neonatal intensive care unit admission and congenital malformations.

Data analysis

All eligible women were subdivided into groups according to maternal birth weight—low birth weight (⩽2500 g), sub-optimal birth weight (2500 to 2999 g), optimal birth weight (3000 to 3499 g; 3500 to 999 g) and high birth weight (⩾4000 g). The occurrence of maternal and neonatal complications was recorded and compared among the groups. The occurrence of GDM and hypertensive disorders was detected among women in different groups with a pre-pregnancy BMI $\geqslant 28\ kg\ m^{-2}$.

Statistical analysis

SPSS software version 20.0 (IBM Co., USA) was used for all statistical analyses. Univariate associations between multiple pregnancy and maternal and neonatal complications were explored with Pearson's χ^2-test. Categorical variables were expressed as frequencies and percentages. Continuous variables are presented as the mean ± s.d., and two groups were compared using a one-way analysis of variance. *P*-values < 0.05 were considered as statistically significant. Logistic regression was used to evaluate the effect of maternal birth weight on the perinatal complications. Included in the multivariate model were the risk factors that have been associated with perinatal complications (maternal height, gestational age, pre-pregnancy BMI and weight gain during pregnancy).

RESULTS

Of the 5479 eligible women, 275 were with low birth weight ⩽2500 g, 1079 with birth weight between 2500 and 2999 g, 2590 with birth weight between 3000 and 3499 g, 1085 with birth weight between 3500 and 3999 g and 450 with birth weight ⩾4000 g. Basic characteristics of the study population, stratified by maternal birth weight categories, are shown in Table 1. Maternal age, parity and mode of delivery did not present significant differences between the groups. Pre-pregnancy weight ($F = 31.109$, $P < 0.001$), maternal height ($F = 49.025$, $P < 0.001$) and gestational age at delivery ($F = 7.368$, $P < 0.001$) were significantly increased as maternal birth weight was higher.

Maternal complications, stratified according to maternal birth weight categories, are presented in Table 2. The prevalence of GDM was significantly higher (28.7%) in the group of women born at low birth weight (⩽2500 g) compared with other birth weight categories ($\chi^2 = 21.268$, $P < 0.001$). Interestingly, women at the high-birth weight group (⩾4000 g) were at decreased risk of GDM (18.4%). Women with a low birth weight who reached a high BMI ($\geqslant 28\ kg\ m^{-2}$) in adult life had the highest risk of GDM, and the increased risk also be found in women with high birth weight (Figure 1a).

Women born at low birth weight (⩽2500 g) were significantly more likely to develop hypertensive disorders during pregnancy (7.7%, $\chi^2 = 10.844$, $P < 0.001$) than the normal- and high-weight groups. The association was increased in women with a pre-pregnancy BMI $\geqslant 28\ kg\ m^{-2}$ between the low-birth weight and normal-birth weight group, but not detected in the high-birth weight group (Figure 1b)

The incidence of preterm labor (9.8%, $\chi^2 = 18.270$, $P < 0.001$) was much higher in the group of mothers with low birth weight compared with those born at a normal or high birth weight (Table 2).

Table 1. Basic maternal characteristics stratified according to maternal own birth weight categories

Variables	*⩽2500 g* n = *275*	*2500–2999 g* n = *1079*	*3000–3499 g* n = *2590*	*3500–3999 g* n = *1085*	*⩾4000 g* n = *450*	χ^2/F	P-*value*
Age, years	28.70 ± 3.66	28.45 ± 3.88	28.26 ± 3.89	28.37 ± 3.81	28.28 ± 3.96	70.558	0.317
Height, cm	160.75 ± 4.54	161.69 ± 4.92	162.58 ± 4.77	163.90 ± 4.80	164.04 ± 5.17	49.025	< 0.001
Pre-pregnancy weight, kg	55.49 ± 8.58	55.96 ± 9.33	57.24 ± 9.56	59.70 ± 10.02	59.91 ± 10.55	31.109	< 0.001
Gestational age (Weeks)	38.59 ± 1.82	38.94 ± 1.53	38.99 ± 1.58	39.11 ± 1.51	39.14 ± 1.50	7.368	< 0.001
Parity							
Uniparous	207 (75.3%)	806 (74.7%)	1888 (72.9%)	804 (74.1%)	345 (76.7%)	3.789	0.435
Multiparous	68 (24.7%)	273 (25.3%)	702 (27.1%)	281 (25.9%)	105 (23.3%)		
Mode of delivery							
Vaginal delivery	155 (57.8%)	609 (56.4%)	1503 (58.0%)	615 (56.6%)	241 (53.6%)	15.729	0.204
Cesarean section	120 (43.2%)	470 (43.6%)	1087 (42.0%)	470 (43.4%)	209 (46.4%)		

Data are presented as mean ± s.d. or *n* (%).

Table 2. Maternal complications stratified according to maternal own birth weight categories

Variables	*⩽2500 g* n = *275*	*2500–2999 g* n = *1079*	*3000–3499 g* n = *2590*	*3500–3999 g* n = *1085*	*⩾4000 g* n = *450*	*χ2*/F	P-*value*
Gestational diabetes mellitus	79 (28.7%)	246 (22.8%)	505 (19.5%)	230 (21.2%)	83 (18.4%)	21.268	0.006
Hypertensive disorders	21 (7.7%)	47 (4.4%)	120 (4.7%)	39 (3.6%)	14 (3.1%)	10.844	0.028
Preterm labor	27 (9.8%)	61 (5.7%)	125 (4.8%)	41 (3.8%)	20 (4.4%)	18.270	0.001
Overweight	35 (12.8%)	139 (13.1%)	370 (14.4%)	179 (16.6%)	77 (17.3%)	37.584	< 0.001
Obesity	16 (5.8%)	52 (4.9%)	140 (5.5%)	73 (6.8%)	34 (7.6%)	37.584	< 0.001
Anemia	41 (16.0%)	132 (12.8%)	296 (12.0%)	128 (12.4%)	50 (11.7%)	3.768	0.438
First trimester CHOL (mmol l^{-1})	4.84 ± 1.09	4.84 ± 1.11	4.82 ± 1.09	4.78 ± 1.04	4.80 ± 1.10	0.352	0.843
First trimester TG (mmol l^{-1})	1.61 ± 0.91	1.51 ± 1.01	1.51 ± 1.06	1.41 ± 0.89	1.40 ± 0.99	2.739	0.027
First trimester HDL (mmol l^{-1})	1.77 ± 0.43	1.79 ± 0.49	1.79 ± 0.49	1.75 ± 0.40	1.81 ± 0.46	1.274	0.278
First trimester LDL (mmol l^{-1})	2.46 ± 0.76	2.53 ± 0.83	2.51 ± 0.79	2.48 ± 0.78	2.50 ± 0.80	0.62	0.648

Abbreviations: CHOL, cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride. Data are presented as mean ± s.d. or *n* (%).

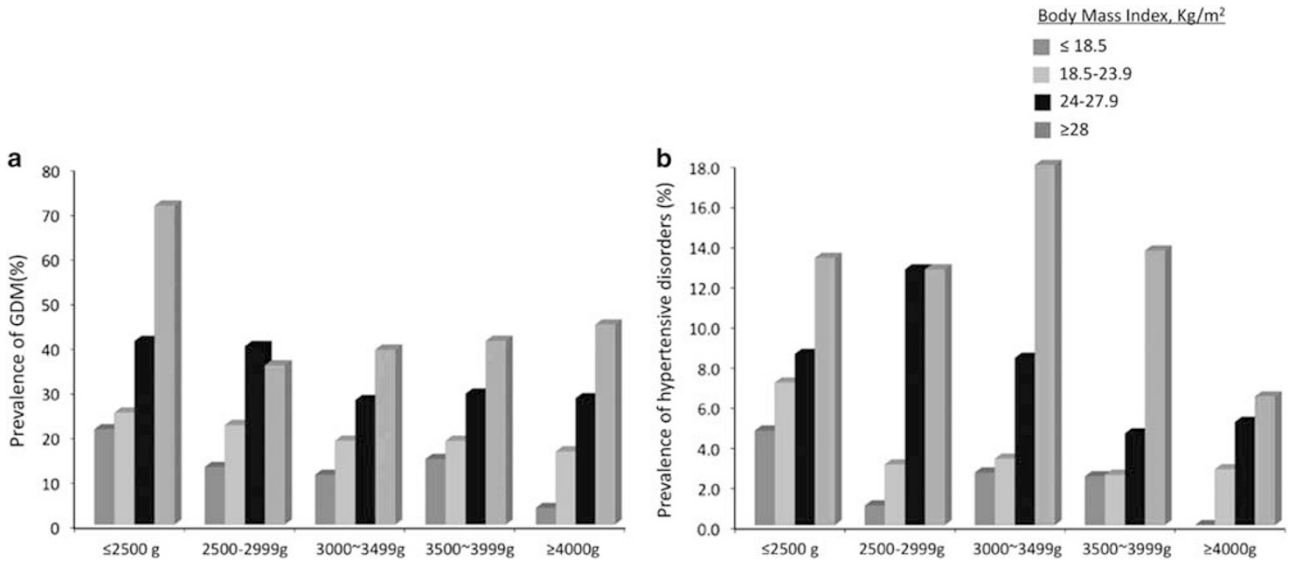

Figure 1. **(a)** Prevalence of GDM in pregnant women stratified by their birth weight as well as by their pre-pregnancy BMI. (**b**) Prevalence of hypertensive disorders in pregnant women stratified by their birth weight as well as by their pre-pregnancy BMI. BMI, body mass index; GDM, gestational diabetes mellitus.

Table 3. Neonatal complications stratified according to maternal own birth weight categories

Variables	*⩽2500 g* n = *275*	*2500–2999 g* n = *1079*	*3000–3499 g* n = *2590*	*3500–3999 g* n = *1085*	*⩾4000 g* n = *450*	*χ2*/F	P-*value*
Fetal weight, g	3155.98 ± 512.57	3253.82 ± 442.34	3331.16 ± 463.80	3452.31 ± 470.64	3475.90 ± 469.32	45.828	< 0.001
Low birth weight (< 2500 g)	26 (9.5%)	45 (4.2)	90 (3.5%)	24 (2.2%)	11 (2.4%)	36.256	< 0.001
Macrosomia (> 4000 g)	10 (3.6%)	52 (4.8%)	175 (6.8%)	127 (11.7%)	64 (14.2%)	72.594	< 0.001
Small for gestational age	31 (11.3%)	84 (7.8%)	135 (5.2%)	33 (3.0%)	13 (2.9%)	93.507	< 0.001
Large for gestational age	4 (1.5%)	47 (4.4%)	150 (5.8%)	104 (9.6%)	47 (10.4%)	93.507	< 0.001
NICU admission	34 (12.4%)	71 (6.6%)	172 (6.6%)	67 (6.2%)	27 (6.0%)	25.225	0.001

Abbreviation: NICU, neonatal intensive care unit. Data presented as mean ± s.d. or *n* (%).

A positive correlation between low birth weight and high triglycerides in first trimester, and a similar U-shaped relationship between maternal birth weight and risk of pre-pregnancy obesity was found in this study (Table 2). The highest prevalence of pre-pregnancy overweight (17.3%, $\chi^2 = 37.584$, $P < 0.001$) was, however, observed in individuals with high birth weight (Table 2). There were no significant differences in the mean cholesterol, high-density lipoprotein and low-density lipoprotein in the different groups.

Neonatal complications, stratified according to maternal birth weight categories, are presented in Table 3.

Infants from the maternal low-birth weight group had a significantly higher rate of SGA (11.3%, $\chi^2 = 93.507$, $P < 0.001$), low birth weight (9.5%, $\chi^2 = 36.256$, $P < 0.001$) and neonatal

Table 4. The adjusted effect of maternal own birth weight on the perinatal complications

Variables	β	*OR*	*95% CI*	P-*value*
Gestational diabetes mellitus[a]	−0.128	0.880	0.819–0.945	< 0.01
Hypertensive disorders[b]	−0.176	0.838	0.723–0.972	0.020
Preterm labor[c]	0.047	1.048	0.388–2.831	0.926
Low birth weight (< 2500 g)[d]	−0.305	0.737	0.597–0.910	0.005
Macrosomia (> 4000 g)[d]	0.321	1.378	1.231–1.543	< 0.01
NICU admission[e]	−0.077	0.926	0.855–1.004	0.062

Abbreviations: BMI, body mass index; CI, confidence interval; GDM, gestational diabetes mellitus; NICU, neonatal intensive care unit; OR, odds ratio. [a]versus without GDM. [b]versus without hypertensive disorders. [c]versus gestation age over 37 weeks. [d]versus normal birth weight. [e]versus without NICU admission. All ORs were adjusted for maternal height, gestational age, pre-pregnancy BMI and weight gain during pregnancy.

intensive care unit admission (12.4%, $\chi^2 = 25.225$, $P < 0.001$) than infants from the other groups (Table 3). The prevalence of macrosomia (14.2%, $\chi^2 = 72.594$, $P < 0.001$) and LGA (10.4%, $\chi^2 = 93.507$, $P < 0.001$) was significantly higher in the maternal high-birth weight group than that in the group with normal or low birth weight (Table 3). The incidence of congenital malformations has no significant difference between the groups.

Adjusting for important risk factors, maternal own birth weight retained its strong relation to GDM, hypertensive disorders, neonatal low birth weight and macrosomia (odds ratio (OR) = 0.880, 95% confidence interval (CI): 0.819 to 0.945, OR = 0.838, 95% CI: 0.723 to 0.972, OR = 0.737, 95% CI: 0.597 to 0.910, OR = 1.378, 95% CI: 1.231 to 1.543, respectively). Maternal own birth weight appeared to be at reduced risk for preterm labor and neonatal intensive care unit admission after adjustment for maternal height, pre-pregnancy BMI, weight gain during pregnancy and gestational age (OR = 1.048, 95% CI: 0.388 to 2.831, OR = 0.926, 95% CI: 0.855 to 1.004) (Table 4).

DISCUSSION

This was a retrospective analysis of the impact of maternal birth weight on various maternal and neonatal complications during pregnancy in Beijing's population. Our main results confirmed the apparent relationship between maternal low birth weight and the risk of GDM and hypertensive disorders. Also we were able to demonstrate that low maternal birth weight is associated with other adverse pregnancy outcomes including preterm labor, SGA and low birth weight of the infant. High maternal birth weight is associated with maternal risk of overweight and obesity, as well as an increased neonatal risk to be born LGA and macrosomic.

The association between maternal low birth weight and GDM, as well as the lack of such correlation with maternal high birth weight is consistent with the previous reports. Seghieri *et al.*[14] demonstrated that low maternal birth weight was independently associated with a 2-fold higher risk for GDM, adjusted for age, parity, family history of diabetes and pre-pregnancy weight. A large population cohort of 138 714 Norwegian women reported that low birth weight (< 2500 g) may be a common risk factor for GDM and type 2 diabetes and that this association is not held true for a maternal weight of 4500 g or more at birth.[12]

It is known that adults born with low birth weight and later have a high BMI are more insulin resistant[15] and are at the highest risk for type 2 diabetes.[16] Our study shows concordant results with this observation, as we found that high pre-pregnancy BMI could enhance the risk of GDM associated with low birth weight. Furthermore, women with high birth weight and high BMI are also at an increased risk of GDM. Therefore, our data is a further demonstration that high pre-pregnancy BMI may have a major role in determining the distribution shape of risk for GDM in adult women with low or high birth weight.

In contrast to observations in other reports[17,18] showing a different relation between birth weight and glucose tolerance that demonstrated a U-shaped relationship between birth weight and GDM and type 2 diabetes risk, however, the U-shaped relation was converted to a reverse J shape after adjustment for history of maternal diabetes.[18]

The increased risk of hypertensive disorders of pregnancy among our study population with maternal low birth weight is similar to reports of other investigators, which showed that low birth weight has been linked to the development of hypertension in adult life.[19,20] It also has been proven that women born with low birth weight do have an elevated risk for the development of hypertensive pregnancy disorders, which is especially pronounced in those women who become obese in later life.[21,22] In our research, there were no significant differences in high pre-pregnancy BMI ($\geqslant 28\ kg\ m^{-2}$) between the low-birth weight and normal-birth weight group, however, high BMI could increase the risk of hypertensive disorders in the women with normal birth weight. Therefore, maternal birth weight was not an independent risk factor for hypertensive disorders of pregnancy. Some authors tried to find other perinatal parameters describing body proportions that better correlate with high blood pressure in later life.[23] Pre-pregnancy BMI may be independently associated with an increased risk of a hypertensive disorder during pregnancy.[24] However, an elevated hypertension risk among high birth weight with high pre-pregnancy was not observed in our study.

In this article, we distinguished maternal low birth weight was strongly related to hypertriglyceridemia, a finding supported by previous research.[25] Adipokines can serve as a measure of adipose tissue activity. Although birth weight correlates with neonatal adiposity, Yeung EH *et al.*[26] found that singletons in the lowest compared with the highest quintile of adiponectin were more likely SGA (1.81; 95% CI 1.18, 2.77). Another study found that leptin was positively associated with birth weight.[27] Our investigation also indicated the incidence of preterm labor to be 9.8% in the low-birth weight group, which was relatively higher than that in the normal- and high-birth weight groups. Likewise, a cohort study by Nohr *et al.*[28] showed that low birth weight was a good indicator for preterm birth.

The known association between women with high birth weight and the increased risk of the development of overweight and obesity was confirmed in our study.[6,29] We showed that even women with a birth weight over 4000 g were at an increased risk of developing overweight or obesity pre-pregnancy. Interestingly, we found an analogous U-shaped relationship between a woman's risk for obesity ($BMI \geqslant 28\ kg\ m^{-2}$) and birth weight. Maternal low birth weight was also associated with pre-pregnancy obesity. A nested cross-sectional study conducted in a cohort showed that rapid postnatal weight gain for the low birth weight determined higher BMI among school age children,[30] which supported the results of our study.

Our findings also suggest that women with low birth weight could give birth to smaller babies (SGA and low birth weight ⩽ 2500 g), whereas women with high birth weight could give birth to larger babies (LGA and high birth weight ⩾ 4000 g). These

outcomes are in concordance with a previous observation that showed maternal birth weight and the offspring's weight were linearly related.[31–33] Other large population studies also demonstrated that a mother's own intra-uterine growth was an important intergenerational predictor of her offspring's fetal growth. The mother's increased weight at birth and the prenatal overweight or obesity were correlated with increased weight and length at birth of the newborn.[34,35]

Our study suggested that knowledge of a woman's birth weight during pregnancy may be useful from an epidemiological point of view—first, to assess the global risk of being affected with GDM, hypertensive disorders, overweight or obesity; and second, to better predict the risk of giving birth to smaller or larger babies. Population strategies aimed at optimizing growth at birth require broader intergenerational considerations, in addition to focusing on the health of mothers in the immediate pregnancy period.

Nonetheless, the use of retrospective vital records and hospital discharge data has some inherent limitation. We were unable to adjust for certain known and potential risk factors for GDM, including family history of height, dietary intake and exercise habits. And the study does not take the woman's own gestational age into account. A child's birth weight can be low either because of low gestational age or low weight for gestational age. Further studies are needed to clarify the association between maternal birth weight, fetal growth and adverse outcome later in life and during pregnancies.

CONCLUSION

This large, multicenter study of Beijing's population demonstrated a strong association between a woman's own birth weight and the subsequent risk for GDM, hypertensive disorders, preterm labor, SGA, LGA, low birth weight and macrosomia. It seems reasonable, therefore, those infants born with high or low birth weight should remain under effective and competent health service provision through antenatal care to reduce maternal and perinatal morbidity and mortality.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

HY and WZ designed the study. RS did the literature search with support from YW. RS and WZ analysed the data. CW, HF and LL collected the data. RS, MH and EH wrote the report.

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