The effect of high birth weight on overweight and obesity in childhood and adolescence

A cohort study in China

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ABSTRACT

الأهداف: دراسة العلاقة بين زيادة وزن المولود وارتفاع مخاطر الإصابة بالسمنة في مرحلة الطفولة والمراهقة وعرض التفاعلات بين ارتفاع وزن المولود والنشاط الجسمي والعادات الغذائية.

الطريقة: أجريت دراسة استباقية في عام 1993م، 1994م ، 1995م في ولاية ويكسي، الصين للمواليد الذين تتراوح أوزانهم أعلى من 4000 غرام مجموعة المعرضة، وفي المقابل تم اختيار مواليد مماثلين للمجموعة الأولى في سنة الميلاد، جهة الولادة، والجنس تتراوح أوزانهم من 3999–2500 غرام. أجريت متابعة لهم خلال الفترة من اكتوبر 2005م حتى فبراير 2007م ويونيو 2010م حتى نوفمبر 2011م.

النتائج: من بين 1108 طفل من المجموعة المعرضة و1128 من مجموعة غير معرضة تم إدراجهم في الدراسة. ارتفع معدل السمنة والوزن الزائد لدى المجموعة المعرضة (16.2% في الطفولة، 14.2% في المراهقة) أكثر من المجموعة الغير معرضة (12.1% في الطفولة، 8.2% في المراهقة). لم تظهر هنالك أي علاقة إحصائية بين وزن المولود وفترة النمو (F=2.10, p=0.147)، وكان هنالك زيادة في الاختطار النسبي نظراً لوجود علاقة بين وزن المولود الزائد والنشاط الجسمي -(95% CI=-2.85-2.45) 0.20 وزن المولود الزائد والنشاط الجسمي (95% CI=0.14-2.23) 1.19 .

خاتمة: ارتفاع خطورة الأصابة في السمنة لدى الطفولة والمراهقة لدى الأطفال المواليد بوزن زائد وليس لها أي علاقة مع فترة النمو. كما أنه لا يوجد تفاعل بين ارتفاع وزن المولود والعادات الغذائية.

Objectives: To determine the association of high birth weight (HBW) with the risk of obesity in childhood and adolescence. We also aimed to explore the interactions of HBW with physical activity and dietary habits.

Methods: In a birth cohort born in 1993, 1994, and 1995 in Wuxi, China, subjects with a birth weight (BW) of ≥4000 g were selected as the exposed group. For each exposed subject, one non-exposed subject with a BW of 2500-3999 g, matched by year of birth, gender, and type of institute at birth was chosen. Two follow-ups were performed from October 2005 to February 2007 and July 2010 to December 2011.

Results: A total of 1108 exposed and 1128 non-exposed subjects were included. Overweight/obesity rates were significantly higher in the exposed group (16.2% in childhood and 14.2% in adolescence) than those in the non-exposed group (12.1% in childhood and 8.2% in adolescence). There was no significant interaction between BW and the growth period (F=2.10, p=0.147). The relative excess risk due to interaction (RERI) of HBW with physical activity was -0.20 (95% CI=-2.85-2.45), and the RERI of HBW with dietary habits was 1.19 (95% CI=0.14-2.23).

Conclusion: Infants with HBW are at increased risk of childhood and adolescent overweight/obesity, and this relationship is not influenced by the growth period. There is an additive interaction between HBW and dietary habits.

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Among children and adolescents, the prevalence of overweight and obesity has reached epidemic proportions worldwide. Globally, in 2010, the number of overweight and obese children under the age of 5 years has been estimated to be greater than 42 million.[1] Overweight and obese children are likely to stay obese into adulthood. The World Health Organization[2] projected that by 2015, approximately 2.3 billion adults will be overweight and more than 700 million will be obese. Overweight and obesity are associated with increased risks of type 1 diabetes mellitus,[3] hypertension,[4] cardiovascular disease,[5] and some cancers.[6,7] Overweight and obesity are now globally recognized as one of the major health concerns, affecting a large part of the world's population, irrespective of age, gender, or ethnicity.[8,9] Obesity is a complex, multifactor condition with genetic and environmental etiology, and currently, there is no clear comprehensive understanding of its determinants. Early life factors, such as intrauterine growth, may contribute to the development of obesity.[10] Birth weight (BW), which is frequently used as an indicator of intrauterine growth,[11] is positively associated with subsequent obesity.[12,13] However, investigators have identified a J- or U-shaped association in the study,[14] while others have observed no association.[14,15] Therefore, the relationship between BW and later obesity is still controversial, and continuous follow-up data on this relationship from birth to childhood and to adolescence are still insufficient. These inconsistent results may be due to other unadjusted potential factors or complex interactions among these factors. The purpose of the study was to determine the association of high birth weight (HBW) with the risk of obesity in childhood and adolescence and the dependence of this association on the growth period. We also explored the interactions of HBW with physical activity and dietary habits.

Methods. We conducted a longitudinal study of the birth cohort in Wuxi, a suburban area of Shanghai, who participated in the US-China collaborative study of periconceptional folic acid supplementation and neural tube defects in the 1990s.[16] The birth cohort included live-born neonates born in 1993, 1994, and 1995 in 3 districts (Jiangyin, Huishan, and Xishan) of Wuxi. We excluded subjects who were stillbirths, those who died before their 12th birthday, those who had major congenital malformations, and those who moved outside of the study area before the scheduled follow-up. From the original birth cohort, subjects with a BW of ≥4000 g were selected as the exposed group. For each exposed subject, one non-exposed subject with a BW of 2500-3999 g, matched by year of birth, gender, and type of institute at birth (township hospital, regional central hospital, and tertiary center hospital) was chosen. The first follow-up was performed between October 2005 and February 2007, and detailed results have already been reported.[17] The present study performed between July 2010 to December 2011 was the second follow-up. The parents who agreed to participate after a full explanation of the purposes and procedures of the study were asked to sign a consent form and to take their children to participate in the study. This study was according to the principles of Helsinki Declaration and approved by the Ethics Committee of Shanghai Institute of Planned Parenthood Research, China.

Gestational and perinatal data were obtained from records maintained by the local Maternal and Children Health Bureaus. Data on socio-demography, current household income, physical activity, and dietary habits were collected face-to-face with a structured questionnaire at each phase. The subjects' height, weight, waist circumference, and hip circumference were measured according to the methods recommended by WHO.[18] All the data were collected by trained nurses.

We analyzed the data of the second follow-up and also performed a secondary analysis of the first follow-up data of the subjects who also took part in the second follow-up. Overweight/obesity was the main outcome variable of the study, which was defined as body mass index (BMI) higher than the sex-age-specific criteria (**Table 1**), set by the Working Group on Obesity in China.[19] Post-term pregnancy was defined as gestational

Table 1 - Gender-age-specific criteria of body mass index for defining overweight and obesity (kg/m^2) (10-18 years old).

Age	Boy		Girl	
	Overweight	Obesity	Overweight	Obesity
10	19.6	22.5	20.0	22.1
11	20.3	23.6	21.0	23.3
12	21.0	24.7	21.9	24.2
13	21.9	25.7	22.6	25.6
14	22.6	26.4	23.0	26.3
15	23.1	26.9	23.4	26.9
16	23.5	27.4	23.7	27.4
17	23.8	27.8	23.8	27.7
18	24.0	28.0	24.0	28.0
>18	24.0	28.0	24.0	28.0

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age ≥42 weeks, and normal term pregnancy was definded as <37 weeks gestational age <42 weeks. Relative risks (RRs) and confidence intervals (CIs) were performed to evaluate risks and associations between BW and overweight/obesity in childhood and adolescence. Multiple logistic regression models were used to adjust for confounding factors. The effects of HBW on waist circumference (as a measure of abdominal obesity) and the waist-hip ratio (WHR) in adolescence were also examined by the above-mentioned methods. According to the criteria set by the Working Group on Obesity in China,[19] abdominal obesity was defined as a waist circumference in females ≥80 cm or a waist circumference in males ≥85 cm. An abnormal WHR was defined as a WHR in males >0.95 or a WHR in females >0.85. Waist circumference and hip circumference were not measured in childhood. Therefore, the effects of HBW on waist circumference and WHR in childhood were not analyzed. We pooled data from all 3 investigations and used longitudinal, generalized linear mixed models (GLMMs) to examine the association between BW and overweight/obesity in childhood and adolescence. Since we observed a nonlinear relation between BW and obesity, we categorized BW as normal (2500-3999 g [reference]) or high (≥4000 g).

In the present study, 250 adolescents were overweight or obese, and were chosen to examine the interactions of HBW with physical activity and dietary habits in the development of overweight or obesity. A total of 250 subjects with normal weight, matched by year of birth, gender, and type of institute at birth were chosen as controls. Interactions were investigated using a multiplicative model and an additive model. Interactions based on the multiplicative model were estimated using a logistic regression model with overweight or obesity as the dependent variable and BW x physical activity (dietary habits) as the interactive variable. In the additive model, the relative excess risk due to interaction (RERI) was used to measure the departure from additivity of effects on a relative risk scale. For a pair of dichotomous exposure variables, A and B, Hosmer and Lemeshow[20] defined this quantity as RR (AB) - RR (A) - RR (B) + 1. We estimated the RERI according to the method reported by Andersson.[21]

All the data were entered and checked using the software EpiData 3.1 (The EpiData Association, Odense, Denmark). All analyses were performed using Statistical Analysis Software version 9.2 (SAS Institute, Inc., Cary, NC, USA, 2009). Statistical significance was set at $p<0.05$. We used the key words of "birth weight" and "obesity" or "overweight" to search prior related research in Pubmed database, Chinese database, and so on.

Results. A total of 1503 pairs of exposed and non-exposed subjects were recruited. Among them, 2236 subjects responded to 2 follow-ups, corresponding to a response rate of 74.4%, and were included in the final analysis. The age of the subjects was between 11 and 14 years in the first follow-up and between 15 and 18 years in the second follow-up. Data were available for 748 girls and 1488 boys, among whom there were 1108 in the exposed group and 1128 in the non-exposed group. All available data were used at each step of the analyses, but the sample size varied due to some missing data.

Table 2 shows the demographic characteristics of the exposed and non-exposed subjects at baseline. The exposed and non-exposed subjects were significantly different in terms of post-term pregnancy and height, weight, and BMI of their mothers ($p<0.05$). Therefore, in the following calculation of RRs, post-term pregnancy and BMI of the subject's mothers were adjusted.

Association between HBW and childhood overweight/obesity. Overall, 14.2% of the participants were overweight or obese in childhood. A total of 18.1% of boys were overweight or obese, and 6.4% of girls were overweight or obese. **Table 3** shows the childhood overweight/obesity rates of the 2 groups. The rate of overweight/obesity was significantly higher in the exposed group than in the non-exposed group (16.2% versus 12.1%, $p=0.006$). For boys, HBW increased the risk of childhood overweight/obesity, which was not found in girls. The HBW-associated increase in childhood overweight/obesity remained essentially the same when some potential factors were adjusted.

Association between HBW and adolescent overweight/obesity. Overall, 11.2% of the participants were overweight or obese in adolescence. The rate of overweight/obesity was 12.4% in boys and 8.8% in girls. **Table 4** shows the rates of adolescent overweight/obesity of the 2 groups. Similar results were found in adolescence to those in childhood. However, HBW increased the risk of adolescent overweight/obesity not only for boys but also for girls. The RRs of overweight/obesity were increased in adolescence compared with those in childhood.

Aggregate analysis of the data from all 3 investigations. We pooled data from all 3 investigations and used GLMMs to examine the association between BW and overweight/obesity in childhood and adolescence. The HBW was related to increased overweight/obesity in childhood and adolescence ($F=20.69$, $p<0.001$). There was a significant difference in overweight/obesity rates in childhood and in adolescence, and the rate of overweight/obesity in childhood was higher than

Table 2 - Comparison of baseline characteristics between the exposed and non-exposed groups.

Variables	Exposed (n=1108)		Non-exposed (n=1128)		Total		*P*-value
Mother's age (year)							
<25	814	(73.5)	836	(74.1)	1650	(73.8)	0.693
25~	231	(20.8)	237	(21.0)	468	(20.9)	
30~	63	(5.7)	55	(4.9)	118	(5.3)	
Father's age (year)							
<25	579	(52.3)	541	(48.0)	1120	(50.1)	0.104
25~	397	(35.8)	450	(39.9)	847	(37.9)	
30~	132	(11.9)	137	(12.1)	269	(12.0)	
Mother's job							
Peasant	395	(35.6)	435	(38.6)	830	(37.1)	0.359
Worker	672	(60.7)	652	(57.8)	1324	(59.2)	
Others	41	(3.7)	41	(3.6)	82	(3.7)	
Mother's education							
Junior high school or lower	995	(89.8)	1033	(91.7)	2028	(90.7)	0.130
Senior high school or higher	113	(10.2)	94	(8.3)	207	(9.3)	
Gravidity							
1	775	(69.9)	794	(70.4)	1569	(70.2)	0.850
2	220	(19.9)	227	(20.1)	447	(20.0)	
3~	113	(10.2)	107	(9.5)	220	(9.8)	
Post term pregnancy							
Yes	231	(20.8)	119	(10.5)	350	(15.7)	<0.001
No	877	(79.2)	1009	(89.5)	1886	(84.3)	
Family hypertension history							
Yes	3	(0.3)	8	(0.7)	11	(0.5)	Fisher P=0.226
No	1105	(99.7)	1120	(99.3)	2225	(99.5)	
Family diabetes history							
Yes	1	(0.1)	1	(0.1)	2	(0.1)	Fisher P=1.000
No	1107	(99.9)	1127	(99.9)	2234	(99.9)	
Mother	Mean±SD		Mean±SD		t		*P*-value
Height (cm)	160.67±4.31		159.38±4.17		3.95		<0.001
Weight (kg)	54.22±6.07		52.40±5.33		4.12		<0.001
Body mass index (kg/m^2)	21.00±2.17		20.64±2.07		2.20		0.028

Table 3 - Association between HBW and childhood overweight/obesity.

Variables	Normal n (%)	Overweight or obesity n (%)	*P*-value	RR (95%CI)
Exposed	928 (83.8)	180 (16.2)	0.006	1.34 (1.09-1.64)
Non-exposed	991 (87.9)	137 (12.1)		
Boy				
Exposed	586 (79.5)	151 (20.5)	0.017	1.30 (1.05-1.62)
Non-exposed	633 (84.3)	118 (15.7)		
Girl				
Exposed	342 (92.2)	29 (7.8)	0.121	1.55 (0.89-2.72)
Non-exposed	358(95.0)	19 (5.0)		
Normal term pregnancy				
Exposed	732 (83.5)	145 (16.5)	0.005	1.38 (1.10-1.72)
Non-exposed	888 (88.0)	121 (12.0)		
Postterm pregnancy				
Exposed	196 (84.8)	35 (15.2)	0.668	1.13 (0.65-1.95)
Non-exposed	103 (86.6)	16 (13.4)		
Model I*			0.009	1.79 (1.15-2.77)
Model II†			0.015	1.39 (1.07-1.82)

*Model I, adjusted for the gestational age and mother's BMI before pregnancy,
†Model II, adjusted for the gestational age, gender, household income, father's BMI, mother's BMI, mother's education, high calorie food intake, midnight snack, dietary bias, TV time, computer usage time and physical activity time

Table 4 - Association between high birth weight and adolescent overweight/obesity.

Variables	Normal n (%)	Overweight or obesity n (%)	*P*-value	RR (95%CI)
Exposed	951 (85.8)	157 (14.2)	<0.000	1.72 (1.35-2.19)
Non-exposed	1035 (91.8)	93 (8.2)		
Boy				
Exposed	623 (84.5)	114 (15.5)	<0.001	1.66 (1.25-2.20)
Non-exposed	681 (90.7)	70 (9.3)		
Girl				
Exposed	328 (88.4)	43 (11.6)	0.008	1.90 (1.17-3.09)
Non-exposed	354 (93.9)	23 (6.1)		
Normal term pregnancy				
Exposed	755 (86.1)	122 (13.9)	<0.001	1.80 (1.37-2.36)
Non-exposed	931 (92.3)	78 (7.7)		
Postterm pregnancy				
Exposed	196 (84.8)	35 (15.2)	0.519	1.20 (0.68-2.11)
Non-exposed	104 (87.4)	15 (12.6)		
Model I*			0.000	2.36 (1.44-3.88)
Model II†			0.005	1.52 (1.14-2.04)

* Model I, adjusted for the gestational age and mother's BMI before pregnancy,
†Model II, adjusted for the gestational age, gender, household income, father's BMI, mother's BMI, mother's education, high calorie food intake, midnight snack, dietary bias, TV time, computer usage time and physical activity time

that in adolescence (F=11.41, p=0.001). There was no interaction between BW and the growth period (F=2.10, p=0.147).

Association between HBW and waist circumference and WHR in adolescence. Waist circumference and the WHR were 74.32±8.54 cm and 0.83±0.08 in the exposed group, and 73.62±8.49 cm and 0.83±0.08 in the non-exposed group, respectively, with no significant differences between the 2 groups. The waist circumference of girls in the exposed group (71.11±7.55 cm) was bigger than that in the non-exposed group (69.87±7.35 cm, p=0.023). After stratifying by gestational age, the waist circumference of the normal term pregnancy population in the exposed group (74.37±8.34 cm) was significantly bigger than that in the non-exposed group (73.54±8.42 cm, p=0.032).

There were no significant differences of the abdominal obesity (the exposed versus no-exposed, 14.8% versus 13.2%, p=0.274) and abnormality of the WHR (the exposed versus no-exposed, 14.5% versus 15.4%, p=0.553) rates between the 2 groups.

Interactions of HBW with physical activity and dietary habits. No interactions were found between HBW and physical activity (OR=1.08, 95% CI=0.53-2.20, p=0.835) and between HBW and dietary habits (OR=1.93, 95% CI=0.93-3.98, p=0.076) based on the multiplicative model (**Table 5**). Based on the additive model, adolescents with a HBW and unhealthy dietary habits had an increased risk of overweight/obesity (RERI=1.19, 95% CI=0.14-2.23),

Table 5 - Interactions of birth weight with other factors based on the multiplicative model.

Factor	ß	*P*-value	OR (95%CI)
Birth weight	0.47	0.068	1.60 (0.97-2.66)
Physical activity	0.03	0.906	1.03 (0.60-1.77)
Birth weight x physical activity	0.08	0.835	1.08 (0.53-2.20)
Birth weight	0.22	0.396	1.25 (0.75-2.09)
Dietary habits	0.02	0.937	1.02 (0.59-1.76)
Birth weight dietary habits	0.66	0.076	1.93 (0.93-3.98)

while an interaction of HBW with physical activity was not found (RERI=-0.20, 95% CI=-2.85-2.45, **Table 6**).

Discussion. In the present study, 14.2% of the participants were overweight or obese in childhood, and 11.2% were overweight or obese in adolescence. In boys, 18.1% were overweight or obese in childhood, and 12.4% were overweight or obese in adolescence. In girls, 6.4% were overweight or obese in childhood, and 8.8% were overweight or obese in adolescence. The overweight/obesity rates observed in our study are lower than the rates reported from various non-Chinese childhood and adolescent populations.[22-24] Obesity is known as a multifactor condition. The different rates observed in different populations may be due to different ethnicities, dietary habits, and different development levels of economy. The rates observed in our study are lower than those reported from a city population in China, and are similar to those reported

Table 6 - Interaction of birth weight (BW) with other factors based on the additive model.

Birth weight	Factor	Overweight/ obesity (n)	Control (n)	OR (95%CI)	RERI (95%CI)	AP (%)‡
Physical activity						
-	-	45	61	1.00		
-	+	48	63	1.03 (0.60-1.77)		
+	-	78	66	1.60 (0.97-2.66)		
+	+	79	60	1.79 (1.07-2.98)	-0.20 (-2.85-2.45)	-11.15
Dietary habits						
-	-	40	54	1.00		
-	+	53	70	1.02 (0.59-1.76)		
+	-	75	81	1.25 (0.75-2.09)		
+	+	82	45	2.46 (1.42-4.25)	1.19 (0.14-2.23)	48.29

RERI - relative excess risk due to interaction, AP - attributable proportion of interaction, negative sign - 2500g ≤BW <4000g, positive sign - BW ≥4000g, Physical activity with negative sign - ≥1 hour/day, Physical activity with positive sign - <1 hour/day, Dietary habits with negative sign - do not prefer high calorie food, Dietary habits with positive sign - prefer high calorie food.

from a rural population in China.[25] The present study population was from rural areas, which may partly explain the observed rates.

There has been increasing interest in conceptualizing disease etiology within a life course framework. A life course approach to chronic disease epidemiology has been defined as the study of long-term effects on chronic disease risk of physical and social exposures during gestation, childhood, adolescence, young adulthood, and later adult life.[26] Programming may be the underlying mechanism associating growth patterns during early life, with subsequent risk of later metabolic disease. Programming is defined as when the developing organism passes through "critical windows" of sensitivity or plasticity, during which environmental factors generate long-lasting variability in phenotype.[27] Fetal life has been proposed as a critical window for programming of later obesity risks. Birth weight, which is frequently used as an indicator of conditions experienced in uterus,[11] is used to research the relationship of early-life experience with later obesity.

The relationship between BW and childhood obesity is still controversial. Strufaldi et al[15] suggested that there was no association between BW and overweight or obesity in schoolchildren. The el al[28] reported that among persons with a non-obese mother, HBW participants were more likely than normal birth weight participants to become obese later in life (RR=1.46, 95%CI=1.28-1.67) in a longitudinal sibling and twin pair cohort. However, given the null associations observed in the sibling sample, they presumed that the commonly observed positive association between BW and later obesity from cohort analyses may be attributed to confounding by maternal characteristics. A systematic review and meta-analysis showed that HBW was associated with an increased risk of obesity (OR=2.0, 95% CI=1.91-2.24) compared with subjects with a BW ≤4000 g.[29] In the present study in boys, HBW increased the risk of childhood overweight/obesity, and a similar result was found in the normal term pregnancy population. However, in girls and the post-term pregnancy population, no significant difference was found in the incidence rate of childhood overweight/obesity among the 2 study groups. Therefore, we hypothesize that the association of HBW with overweight/obesity in childhood may be affected by gender and gestational age. However, we also might not have found an association in girls and the post-term pregnancy population due to the potential confounding factors. Recent studies suggest that there are gender differences in the association of BW with child overweight/obesity. Oldroyd et al[30] found that HBW was associated with a higher risk of overweight/obesity among girls with an adjusted OR of 1.76 and a 95% CI of 1.12-2.78; however, among boys, the adjusted OR was 2.42 and the 95% CI was 2.06-2.86.

The results of recent studies on the relationship of adolescence overweight/obesity with BW are relatively consistent.[31-33] Gillman et al[31] showed that a higher BW predicted increased risk of overweight in adolescence, with an OR of 1.4 (95% CI=1.2-1.6) for each 1-kg increment in BW. Vale et al[33] also highlighted that HBW was a predictor of overweight/obesity in adolescence. In the present study, HBW increased the risk of adolescent overweight/obesity. This relationship remained in the normal term pregnancy population. However, in the post-term pregnancy population, no significant difference was found in the incidence rate of adolescent overweight/obesity among the 2 study groups. Therefore, we speculate that gestational age affects the association of HBW with overweight/

obesity in adolescence. However, we might not have found an association in the post-term pregnancy population because the sample only included a small number of participants in this population. Further research is required to explore the association of HBW with adolescent overweight/obesity in the post-term pregnancy population.

In the present study, HBW increased the risk of adolescent overweight/obesity in girls, but no significant difference was found in the incidence rate of childhood overweight/obesity among the 2 study groups. There may be an interaction among gender, the growth period, and HBW, but further research is required to determine this possibility. The overweight/obesity rate in adolescence was decreased compared with that in childhood (F=11.41, p=0.001). Adiposity rebound in childhood and changes in hormones in adolescence may partly explain the decreased overweight/obesity rate in adolescence. The RRs were increased in adolescence compared with those in childhood. However, we did not find an interaction between BW and the growth period (F=2.10, p=0.147). This finding showed that the association of HBW with later overweight/obesity is independent of the growth period.

Two mechanisms could partly explain the association between HBW and overweight/obesity in later life. 1) Genetic factors: HBW and obesity may partly share a common genetic background. Genetic factors contribute to variation in both traits.[34,35] However, a study that examined the associations of 12 established BMI variants and their additive score with BW suggested that obesity-susceptibility loci have a small or no effect on weight at birth, while some evidence of an association was found for the MTCH2 and FTO loci with lower and higher BW, respectively.[36] 2) Programming of the intrauterine environment: Animal studies showed that overfeeding in early life (in the uterus and early postnatal period) greatly affects nutrient balance and hormone responses, which can lead to a disturbance of appetite regulation.[37] Studies on humans also showed that hormonal changes during gestation could result in obesity in later life.[38,39]

A higher BMI may be the result of more fat tissue or more lean tissue. Information on waist and hip circumference may be a better reflection of the distribution of fat than BMI, and waist circumference and the WHR are usually used as measures of abdominal obesity, which is related to some chronic diseases. In our study, there was a significant difference in overweight/obesity defined by BMI between the HBW group and the normal body weight group, but no significant difference was found in waist circumference and WHR between the 2 groups. These results show that a higher BMI induced by HBW may not be due to more fat tissue but more lean tissue. This is consistent with the study by Singhal.[40] In our study, after stratifying by gender or gestational age, waist circumference was significantly higher in the exposed group than in the non-exposed group in girls and the normal term pregnancy group. In girls and the normal term pregnancy group, infants with a HBW were at increased risk of abdominal obesity and there was a sex differences in the effect of HBW on waist circumference.

In our study, the RERI of HBW with physical activity was -0.20 (95% CI=-2.85-2.45), and the RERI of HBW with dietary habits was 1.19 (95% CI=0.14-2.23). This suggests that there is an interaction between HBW and dietary habits in adolescence, and adolescents with a HBW and unhealthy dietary habits suffer from an increased risk of overweight or obesity. Some genes have been found to have interactions with some behaviors.[41,42] Lots of reports show that physical activity and dietary habits influence overweight.[43-45] However, there are only a few reports on interaction of HBW with some behavior, and further studies are required to confirm this finding.

Although our study has strengths, including the use of prospective data, integration, and analysis of 3 repeated investigations and relatively comprehensive information, we acknowledge some limitations. One limitation of our data is the absence of information on waist and hip circumference in childhood. Another limitation is the use of a traditional cohort, which cannot control the genetic effect compared with the sibling and twin pair cohort.

In summary, HBW may be associated with an increased risk of childhood and adolescent overweight/obesity. The relationship of HBW with overweight/obesity is not affected by the growth period. In girls or the normal term pregnancy , infants with a HBW suffer an increased risk of abdominal obesity in adolescence. There is an interaction between HBW and dietary habits. More attention should be paid to the population with a HBW in the process of preventing child and adolescent overweight/obesity, especially in girls with a HBW and normal term pregnancy. Additionally, controlling the diet may attenuate the effect of HBW on overweight/obesity.

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