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Complete List of Authors:	Zou, Zhi-Yong; Peking University School of Public Health, Institute of Child and Adolescent Health Yang, Zhongping; Peking University School of Public Health Institute of Child and Adolescent Health Yang, Zhaogeng; Peking University, Institute of Child and Adolescent Health & School of Public Health Wang, Xijie; Peking University Health Science Centre, Institute of Child and Adolescent Health, School of Public Health Gao, Di; Institute of Child and Adolescent Health, School of Public Health, Peking University Dong, Yanhui; Peking University Health Science Centre, Institute of Child and Adolescent Health, School of Public Health, Ma, Jun; Institute of Child and Adolescent Health, Peking University Health Science Center, Ma, Yinghua; Peking University,
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The association of high birth weight with overweight and obesity in Chinese students aged 6 to 18 years: a national cross-sectional study in China.

Zhiyong Zou*, Zhongping Yang*, Zhaogen Yang, Xijie Wang, Di Gao, Yanhui Dong, Jun Ma△, Yinghua Ma△

Author affiliations
Institute of Child and Adolescent Health, School of Public Health, Peking University, Beijing, 100191, China

△JM and YM are co-corresponding authors.
Corresponding authors: Jun Ma, Ph.D., Professor; Yinghua Ma, Ph.D., Professor; Institute of Child and Adolescent Health, School of Public Health, Peking University Health Science Center, No. 38 Xue Yuan Road, Haidian District, Beijing, 100191, China. Tel: +86-10-82801624, Fax: +86-10-82801178, Email: majunt@bjmu.edu.cn; yinghuama@bjmu.edu.cn

Abstract

Objectives: This paper aims to evaluate the association of high birth weight (HBW) with overweight and obesity in Chinese students aged 6-18 years.

Methods: All the students with HBW (n=4981) were selected from a national intervention program against obesity in Chinese students aged 6-18 years, and other 4981 students with normal birth weight were randomly sampled with matched gender and age. Anthropometric parameters were measured and characteristics were collected by questionnaires. *M*ulti-variance logistic regression was used to estimate the odds ratio (OR) of overweight and obesity and high birth weight in unadjusted and adjusted for confounding factors.

Results: Students aged 6-18 years with HBW revealed higher body mass index (BMI) values in childhood. The prevalence of overweight and obesity was significantly higher in HBW group than normal group in both sexes (boys: 16.8% versus 14.6%; 20.0% versus 12.7%; girls: 13.0% versus 10.8%; 12.1% versus 7.4%). Additionally, birth weight was positively associated with overweight and obesity in both genders [boys: OR 1.24 (1.05-1.47); OR 1.61 (1.36-1.92); girls: OR 1.31 (1.05-1.62); OR 1.66(1.30-2.13)] after adjustment for covariates.

Conclusions: HBW may lead to childhood overweight and obesity in this study, and early health education before and during pregnancy should be paid more attention to in the prevention of overweight and obesity.

Key Words: high birth weight; body mass index; overweight; obesity

Trial registration: January 22, 2015; Registration number: NCT02343588

Strength and limitation of this study

- This study used a national multi-centered sample covering all-age children and adolescents in school
- The 1:1 matching of gender, age and province in birth weight was used to enhance the study.
- This study offered evidence for early prevention of obesity.
- The way of collecting birth weight is a limitation of the study.

Introduction

Overweight and obesity in childhood has become a critical health issue with the continuous increase of prevalence worldwide [1], especially in China [2, 3]. The prevalence of obesity in Chinese students aged 7-18 years has increased from 0.1% in 1985, 2.6% in 2000 to 5.0% in 2010 [4], and the prevalence of overweight increased from 6.3% in 1991, 8.8% in 2000 and to 17.1% in 2011[5]. Overweight and obesity were considered as high-risk factors of cardiovascular and metabolic complications [6-8], and students with overweight and obesity were more likely to suffer physical and psychosocial problems in adulthood [9-11].

The hypothesis of Developmental Origins of Health and Disease (DOHaD), focusing on the early developmental phase of life, has offered a new way to the mechanism of overweight and obesity [12-13]. The hypothesis stated that adverse influence in intrauterine life can led to permanent readjustments in physiology and metabolism, which further caused increased risk of diseases in later life [13-14].

In childhood and puberty, the association between birth weight and obesity has been continually observed in cross-sectional [15-16], longitudinal [17] and cohort [18] studies. Most study has found that high birth weight was related to elevated risk of obesity in children or adolescents [15-18]. One study focusing on primary school students found high birth weight (≥4000 g) was significantly associated with higher risk of overweight and obesity (OR=2.48, 95% CI: 1.62-3.81) [19]. A Chinese study focusing on the large-scale population divided the subjects by 500 g intervals in birth weight, and found positive results in high birth weight (compared with 3000-3499 g group, 4000-4499 g: OR=1.39, 95% CI: 1.19-1.63; 4500-4999 g: OR=1.36, 95% CI: 1.06-1.76) [15]. However, another cohort study found no significant association between high birth weight and obesity after adjusted for parental education level and parental obesity [20]. Moreover, to our knowledge, very few studies focused on Chinese school-age children and adolescents aged 6-18 years, and a national multi-centered study has not been reported yet.

Using the data from a national school-based health lifestyles intervention program against obesity among Chinese children, the present study aimed to evaluate the association of HBW with overweight and obesity among school children aged 6-18 years, and also to investigate the strength of association between HBW and BMI z-score.

Methods

Sample and Participants

The sampling was based on a national multi-centered intervention trial against obesity involving nearly 70, 000 children and adolescents aged 6–18 years from 7 provinces in China (Liaoning, Tianjin, Ningxia, Shanghai, Chongqing, Hunan, and Guangdong), which covered all seven geographical areas of China. The protocol of the cluster randomized controlled trial was previously published [21]. This study was approved by the medical ethical committee of the Peking University (IRB00001052-13034), and written informed consent was given by all students and their guardians before the investigation.

Given the most common criteria of macrosomia [22], all the students aged 6-18 years with birth weight over 4.0 kg (n=4981) were selected from the baseline database of the national intervention program against obesity in Chinese students, and other 4981 students with normal birth weight (2.5 kg ≤ birth weight < 4.0 kg) were randomly sampled with matched age, gender and province. Finally, 9962 students including 4981 students in HBW group and 4981 students in normal group

were enrolled in the present study.

Birth weight data

Birth weight was collected using a standard parent questionnaire. Parents were required to record their children's birth weight of children based on the record of birth certificate or health clinic. If they do not have, they were asked to recall the birth weight based on the measurements by themselves. About 70.9% of parents of participants were required to record the information of birth weight based on the health clinic card or birth certificate, and the proportions in the HBW group and normal birth weight group were 73.4% (3655/4981) and 68.4% (3406/4981), respectively. To ensure the reliability of birth weight data, parents were asked to repeat the same process of questionnaire survey six months later. The error in birth weight value between the baseline and six months later was lower than 10% and participants with the error over 10% were eliminated in this study.

BMI and blood pressure

Height and weight were measured by trained project members and experienced research nurses and doctors in line with the standardized procedure. During the measurement, students were asked to stand straight in light clothing and without shoes. A portable stadiometer and a lever type weight scale were validated and used to measure height and weight, respectively. Height was measured to the nearest 0.1 cm and weight was measured to the nearest 0.1 kg. The mean value for both height and weight was recorded after measuring twice. When rechecking 5% of students, the error was less than 10% or otherwise all students were re-measured according to the protocol. Body mass index (BMI) was calculated as body weight divided by height (m) squared (kg/m^2), and overweight and obesity were defined using the cut-offs references developed by the Working Group on Obesity in China (WGOC) [23].

Blood pressure was measured using a standardized mercury sphygmomanometer (model XJ1ID) recommended by National High Blood Pressure Education Program (NHBPEP) Working Group in children and adolescents. The cuff size was selected according to the NHBPEP working group, and placed approximately 2 cm above the crease of the elbow. The first reading was implemented after students were seated easefully for no less than 5 minutes, and the students were asked to keep quiet through the whole measurement. Systolic blood pressure (SBP) was determined by onset of the first Korotkoff sound and diastolic blood pressure (DBP) was defined by the fifth Korotkoff sound. An average of twice blood pressure measurement was recorded in this study. Elevated blood pressure in children and adolescents was defined as SBP or DBP or both are higher than the corresponding cut-offs. The cut-offs were age-, gender- and height-percentile-specific recommended by NHBPEP Working Group in 2004[24].

Questionnaires

Self-developed child-reported and parent-reported questionnaires were designed to collect information of obesity-related factors. Child-reported questionnaires were filled by students in the classroom with the interpretation by trained research staff, except that children under the third grade completed questionnaires at home with guardians' assistance. Parent-reported questionnaires were all finished by students' guardians.

Child-reported questionnaires contained diet intake (fruit, vegetable and sugar-sweetened beverage), moderate physical activity (PA), vigorous PA, sedentary time of students. For diet intake, students were asked how many days they eat fruits, vegetables or drink sugar-sweetened beverages and how many servings or cups for each day in the past 7 days. The average intake was

calculated: (days × servings/cups for each day)/7. One serving of fruits and vegetables was both defined as the amount of one fist of adults, while one cup of sugar-sweetened beverage as almost 250 ml. Moderate PA and vigorous PA were collected by asking how many days students do moderate or vigorous PA and how many hours for each day over the past 7 days. The average PA followed the calculation of (days × hours for each day)/7. Moderate PA included light activities (e.g. walking) while vigorous PA included high-load activities on musculoskeletal tissues in the body (e.g. sports and games)[25]. Sedentary time, consisting of doing homework, watching TV and using a computer, asked how many days and how many hours for the three separate portions over the past 7 days. Following the calculation of (days × hours for each day)/7 for each portion, the average sedentary time was the sum of homework, TV and computer time.

Parent-reported questionnaire collected child's birth information (delivery, single birth or not and breast-feeding), single child or not, socioeconomic status (patents' education levels) and family history (hypertension, diabetes, obesity). Delivery mode included spontaneous delivery and cesarean delivery. Breast-feeding was categorized as ≥1 month and <1 month. Socioeconomic status was featured in education levels of children's parents, involving 3 levels: primary school or below, secondary school, and college or above. Family history covered parents' history in hypertension, diabetes and obesity in this study. Whether diagnosed with hypertension or diabetes was directly answered according to their medical history, while BMI was calculated by weight/height^2 (kg/m^2) for height and weight values provided in the questionnaire. Adult obesity was defined as BMI ≥28 kg/m^2 in the Chinese reference [26].

Statistical Analyses

All the analyses were performed by IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY, USA). Age, birth weight, height, weight, BMI, DBP, SBP, sweet drinks, MVPA were recorded as the mean value (SD). Gender, delivery, single birth, breast feeding, elevated blood pressure, parental education, and family history were displayed as categorical variables (the number and percentage). *T*-test was conducted for the P value of BMI between HBW group and normal group by gender and age group and *Chi-square* test was verified for the percentage of overweight and obesity. Multivariate logistic regression was used to calculate the odds ratios (*OR*) and 95% confidence intervals (*CI*) of different birth weight groups for overweight and obesity by gender and age group, further adjusted for province, urban-rural area, single child, delivery, sedentary time, elevated blood pressure, paternal education level, maternal education level, paternal obesity, maternal obesity and maternal diabetes in different models. The criterion for statistical significance was *P* value <0.05.

Results

A total of 9962 children and adolescents aged 6-18 years were recruited in this study, 4981 in study group (macrosomia) and 4981 in control group (normal birth weight). The distribution of characteristics in two groups was presented in Table 1. Gender and age were controlled in the design and thus there was no difference (*P*>0.05). The mean value of birth weight was 4.22±0.29 kg in study group and 3.24±0.36 kg in control group. Students in study group was observed with higher BMI average than those in control group (19.57 kg/m2 >18.64 kg/m2, P<0.001). Among all those factors, urban area, single child, spontaneous delivery, single birth, gestational age, fruit, family history (hypertension, diabetes and obesity) showed significant difference between study group and control group (*P*<0.05).

As presented in Table 2, students in HBW group revealed higher BMI values than those in normal group. Boys in HBW group were observed with significantly higher BMI than in normal group (HBW group: 19.80±4.26 kg/m^2; normal group: 18.77±3.86 kg/m^2; P<0.001). The similar result was found among girls (HBW group: 19.21±3.95 kg/m^2; normal group: 18.45±3.50 kg/m^2; P<0.001). When categorized by gender and age, BMI in all sub-groups were observed higher in HBW group than in normal group and all difference was statistically significant except for 6~7 age group and 8~9 age group in girls.

The associations between birth weight and BMI z-score in boys and girls were documented in Table 3. Both boys and girls were observed with a significant association between BMI z-score and birth weight (β=0.253 for boys, 95% *CI:* 0.211-0.296; β=0.210 for girls, 95% *CI:* 0.157-0.264). When adjusted for province, urban-rural area, single child, delivery, sedentary time, elevated blood pressure, paternal education level, maternal education level, paternal obesity, maternal obesity, maternal diabetes in Model 2, the associations remained to be significant both in boys and girls.

Table 4 presented the rate and odds ratio (OR) for overweight and obesity on current weight by gender and age. Overall, both boys and girls revealed a significantly higher rate of overweight and obesity in HBW group than those in normal group and the *OR* was 1.32 (95% *CI*: 1.14-1.52) and 1.81 (95% *CI*: 1.57-2.09) for boys and 1.31 (95% *CI*: 1.08-1.60) and 1.79 (95% *CI*: 1.44-2.23) for girls, respectively. After adjusted for province, urban-rural area, single child, delivery, sedentary time, elevated blood pressure in Model 2 and further adjusted for paternal education level, maternal education level, paternal obesity, maternal obesity and maternal diabetes in Model 3, both boys and girls of *OR* remained significant. Finally a slightly decreased but still significant association was observed with the *OR* of 1.24 (95% *CI*: 1.05-1.47) and 1.61 (95% *CI*: 1.36-1.92) for boys and 1.31 (95% *CI*: 1.05-1.62) and 1.66 (95% *CI*: 1.30-2.13) for girls.

Discussion

We evaluated the association of high birth weight and overweight and obesity using the baseline database of a school-based intervention program in China. In the present study, high birth weight was significantly associated with the increase risk of overweight and obesity among Chinese children and adolescents after adjusting for the co-variables. More specifically, we found boys born with HBW were at an increasing risk of 1.24 and 1.61 times for overweight and obesity than those with normal birth weight, and girls born with HBW had a higher risk of 1.31 and 1.66 for overweight and obesity, respectively.

A significantly positive association between high birth weight and overweight and obesity was concluded in this study, which consists with the results in previous studies [27-29]. A meta-analysis gathering 643,902 persons aged 1 to 75 from 66 studies has proved that low birth weight and high birth weight were followed by opposite long-term effects on overweight compared with normal birth weight, and high birth weight predisposed for overweight in later life with OR of 1.66 (95% CI 1.55~1.77) [27]. Many studies also have verified high level of birth weight as one strong predictor of obesity among children or adolescents. A 12-country study assessed the full range of birth weight with obesity in children aged 9-11 and found high birth weight (≥ 4.0kg) was associated with increased odds of 2.08 (95% CI 1.47~2.93) on obesity [28]. Ren et al. [29] matched the exposed group with the non-exposed group by birth, gender, and type of institute at birth in Wuxi, China, which is the same as our study. Even though those studies have

explored the association between high birth weight and overweight or obesity, most studies in China, to our knowledge, have limited in one specific age group or one parochial area, which cannot reveal the overall association among children and adolescents aged 6-18 in China. This study was based on a national multi-centered intervention trial against obesity involving nearly 70, 000 children and adolescents in China, recruited a national representative samples ranging from 6 to 18 years old, which possibly avoided any missing in age or region.

The association of low birth weight and obesity was not evaluated in our study. However, no consistent result was reached in that filed [15, 27, 30]. Some studies verified that low birth weight had the same effect as high birth weight on obesity [30], while others found no significant association [27] or low birth weight was the protective factor for obesity [15]. One possible reason for those contradictions was the small sample. Birth weight seemed to be higher because of the better nutritious environment during the pregnancy [31], thus leading to lower prevalence of low birth weight and higher prevalence of macrosomia.

Other factors such as sedentary time might also influence the risk of obesity in children and adolescents [12]. Some studies focused on the interaction of birth weight and diet and behavioral factors [27-28]. No interaction between high birth weight and physical activity was found in the two studies. However, Ren and his colleagues found the synergy effect of high birth weight and unhealthy diet on the high risk of obesity [29]. Thus high birth weight students were more likely to be the targeted population for diet intervention.

Birth weight is commonly regarded as an important indicator to depict development status in intrauterine environments [13-14]. The mechanism of how birth weight influences overweight and obesity in later life has also been explored [32-34]. Even though obesity-associated gene expression was found positively associated with birth weight, no systematic explanation for birth weight and obesity has been given. This may be one way for further study. One possible explanation was that hyper-nutrition in pregnancy led to the increase of lean body mass or fat mass in the fetus, which might play an important role in obesity [34-35]. Another way was that birth weight might modify the genetic susceptibility in the later life and thus affected the risk of obesity [32-33]. Even though underlying mechanisms were raised, no systematic explanation for birth weight and obesity has been given. How birth weight affected obesity was a long process of life for further study.

There are two limitations in this study. Firstly, the information of birth weight was retrospectively obtained from their parents by questionnaire. In this way, there was possibly memory bias. However, we have tried to weaken the bias though collecting information on their certificate or the health clinic card and repeating the survey after six months. Subjects with difference of birth weight in the two investigations over 10% were eliminated in the study. Secondly, some maternal confounders were not adjusted in the study because those factors were not collected in the survey, such as maternal age of pregnancy, and gestational weight gain, which may also influence the results.

Conclusion

This study explored the association of HBW with overweight and obesity among students aged 6-18 years, based on a national survey of seven provinces in China. The results showed that high birth weight was positively associated with overweight and obesity in children. Both boys and girls with HBW held a higher risk of overweight and obesity in childhood, and birth weight

remained positively associated with higher BMI z-score even after the adjustment. This study indicates that HBW is a high-risk influence factor of overweight and obesity in children, and thus early intervention of intrauterine environments is necessary in the prevention and control of overweight and obesity.

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Contributors

ZZY and YZP contributed equally to this paper. JM and YM were both co-corresponding authors.

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Competing interests

None of the authors had any personal or financial conflict of interest.

Ethics approval

Medical Ethical Committee of the Peking University

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Table 1. Characteristics of study subjects in the study

	HBW group (4981)	Normal group (4981)	*P*
Male, n (%)	3014 (60.5)	3014 (60.5)	
Age (year) / mean ± SD	11.04 ± 3.34	11.00 ± 3.34	0.541
Urban area, n (%)	3209 (64.4)	2849 (57.2)	<0.001
Single child, n (%)	3095 (62.1)	3377 (67.8)	<0.001
Birth information			
Birth weight (kg) / mean ± SD	4.22 ± 0.29	3.24 ± 0.36	<0.001

Caesarean birth, n (%)	2499 (48.9)	2149 (39.6)	<0.001
Single birth, n (%)	4792 (98.1)	4594 (97.1)	<0.001
Breast feeding, n (%)	4244 (86.6)	4047 (85.4)	0.089
Anthropometry, mean ± SD			
Height (cm)	148.59 ± 17.01	146.29 ± 17.06	<0.001
Weight (kg)	44.74 ± 16.89	41.38 ± 15.47	<0.001
WC (cm)	67.41 ± 11.46	65.04 ± 10.76	<0.001
Systolic pressure (mmHg)	105.70 ± 12.11	105.28 ± 12.12	0.086
Diastolic pressure (mmHg)	66.71 ± 8.56	66.50 ± 8.67	0.228
Body mass index (kg/m^2)	19.57 ± 4.15	18.64 ± 3.72	<0.001
Diet and physical activity, mean ± SD			
Fruit (serving/day)	1.28 ± 1.06	1.22 ± 1.02	0.012
Vegetable (serving/day)	1.81 ± 1.44	1.78 ± 1.42	0.430
Sugar-sweetened beverage (cup/day)	0.44 ± 0.78	0.42 ± 0.76	0.226
Moderate PA (hour/day)	0.52 ± 0.81	0.49 ± 0.80	0.098
Vigorous PA (hour/day)	0.47 ± 0.74	0.46 ± 0.75	0.566
Sedentary time (hour/day)	5.83 ± 3.71	5.75 ± 3.74	0.305
Socioeconomic status, n (%)			
Parental education level			
none/primary	409 (8.4)	379 (8.1)	0.859
secondary	3172 (65.3)	3100 (65.9)	
college and above	1274 (26.2)	1227 (26.1)	
Maternal education level			
none/primary	540 (11.1)	457 (9.8)	
secondary	3177 (65.5)	3155 (67.3)	0.464
college and above	1137 (23.4)	1073 (22.9)	
Family history, n (%)			
Parental hypertension	214 (4.5)	200 (4.4)	0.745
Maternal hypertension	151 (3.2)	95 (2.1)	0.001
Parental diabetes	69 (1.5)	61 (1.4)	0.614
Maternal diabetes	62 (1.4)	27 (0.6)	<0.001
Parental obesity	623 (13.1)	519 (11.4)	0.012
Maternal obesity	311 (6.5)	182 (4.0)	0.000

Table 2. Gender- and age-specific BMI of study subjects in different groups

Group		HBW group			Normal group			*P*
		N	Mean	SD	N	Mean	SD	
Boys	6~7	551	17.44	2.86	551	16.59	2.84	<0.001
	8~9	729	18.73	3.68	729	17.53	3.22	<0.001
	10~11	401	20.17	4.22	401	18.55	3.63	<0.001
	12~13	621	20.88	4.27	621	19.94	3.97	<0.001
	14~15	352	21.05	4.32	352	20.20	3.46	0.004
	16~18	360	22.08	4.78	360	21.43	4.01	0.047
	total	3014	19.80	4.26	3014	18.77	3.86	<0.001
Girls	6~7	320	16.35	2.64	320	15.97	2.35	0.052
	8~9	419	17.69	3.26	419	16.70	2.88	<0.001
	10~11	237	18.68	3.35	237	18.20	3.35	0.123
	12~13	395	19.92	3.68	395	19.20	3.18	0.004
	14~15	299	21.19	3.67	299	20.24	2.98	0.001
	16~18	297	21.91	4.08	297	21.01	3.27	0.003
	total	1967	19.21	3.95	1967	18.45	3.50	<0.001

Table 3. The association between birth weight and BMI z-score in boys and girls by general linear regression model

	Model 1[a]			Model 2[b]		
	β	95% *CI*	*P*	*β*	95% *CI*	*P*
Boys (n=6028)						
Normal birth weight	Ref			Ref		
High birth weight	0.276	0.226-0.326	<0.001	0.221	0.157-0.286	<0.001
Birth weight[c]	0.253	0.211-0.296	<0.001	0.234	0.178-0.290	<0.001
Girls (n=3934)						
Normal birth weight	Ref			Ref		
High birth weight	0.225	0.163-0.287	<0.001	0.212	0.131-0.292	<0.001
Birth weight[c]	0.210	0.157-0.264	<0.001	0.198	0.128-0.268	<0.001

[a] Model 1 was unadjusted for any covariates.

[b] Model 2 was adjusted for province, urban-rural area, single child, delivery, sedentary time, elevated blood pressure, paternal education level, maternal education level, paternal obesity, maternal obesity, maternal diabetes.

[c] Continuous variable.

Table 4. Odds ratio of high birth weight group for overweight and obesity in boys and girls, China

	study group (n=4981)	control group (n=4981)	Model 1[a]		Model 2[b]		Model 3[c]	
	n (%)	n (%)	*OR*	95% *CI*	*OR*	95% *CI*	*OR*	95% *CI*
Boys (n=6028)								
Overweight	505 (16.8)	441 (14.6)	1.32*	1.14-1.52	1.27*	1.09-1.49	1.24*	1.05-1.47
Obesity	603 (20.0)	383 (12.7)	1.81*	1.57-2.09	1.80*	1.53-2.11	1.61*	1.36-1.92
Girls (n=3934)								
Overweight	255 (13.0)	212 (10.8)	1.31*	1.08-1.60	1.31*	1.07-1.60	1.31*	1.05-1.62
Obesity	238 (12.1)	145 (7.4)	1.79*	1.44-2.23	1.78*	1.42-2.23	1.66*	1.30-2.13

[a] Model 1 was unadjusted for any covariates.

[b] Model 2 was adjusted for province, urban-rural area, single child, delivery, sedentary time, elevated blood pressure for boys, and single child, delivery, elevated blood pressure for girls.

[c] In Model 3, boys were further adjusted for paternal education level, paternal obesity, maternal obesity and maternal diabetes, while girls further adjusted for maternal education level, paternal obesity, maternal obesity and maternal diabetes.

* $P<0.05$

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The association of high birth weight with overweight and obesity in Chinese students aged 6 to 18 years: a national cross-sectional study in China.

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The association of high birth weight with overweight and obesity in Chinese students aged 6 to 18 years: a national cross-sectional study in China

Zhiyong Zou, Zhongping Yang, Zhaogeng Yang, Xijie Wang, Di Gao, Yanhui Dong, Jun Ma△, Yinghua Ma△

Author affiliations

Institute of Child and Adolescent Health, School of Public Health, Peking University, Beijing, 100191, China

△JM and YM are co-corresponding authors.

Corresponding authors: Jun Ma, Ph.D., Professor; Yinghua Ma, Ph.D., Professor; Institute of Child and Adolescent Health, School of Public Health, Peking University Health Science Center, No. 38 Xueyuan Road, Haidian District, Beijing, 100191, China. Tel: +86-10-82801624, Fax: +86-10-82801178, Email: majunt@bjmu.edu.cn; yinghuama@bjmu.edu.cn

Abstract

Background: Childhood overweight and obesity prevalence in China has drastically increased 57 times during the past 30 years, and to control birth weight was an effective way to reduce the risk of overweight and obesity across the lifecourse.

Objectives: This paper aims to evaluate the association of high birth weight (HBW) with overweight and obesity in Chinese students aged 6-18 years.

Methods: All the students with HBW (n=4981) aged 6-18 years were selected from a cross-sectional survey from 7 provinces in China, and other 4981 students with normal birth weight (NBW) were randomly sampled with matched gender, age and province. Anthropometric parameters were measured and characteristics were collected by questionnaires. *M*ultiple logistic regression was used to estimate the odds ratio (OR) of overweight and obesity with high birth weight in unadjusted and adjusted for confounding factors.

Results: Students aged 6-18 years with HBW revealed higher body mass index (BMI) values in childhood. The prevalence of overweight and obesity was significantly higher in HBW group than NBW group (overweight 15.3% versus 13.1%, $p<0.05$; obesity 16.9% versus 10.6%, $p<0.05$), and results were similar in all age groups except age 6-7, age 14-15 and age 16-18 for overweight. Additionally, HBW was positively associated with overweight (OR=1.230; 95%CI: 1.056-1.432) and obesity (OR=1.611; 95%CI: 1.368-1.897) after adjustment for covariates.

Conclusions: HBW may lead to childhood overweight and obesity in this study, thus weight management during pregnancy to control children's birth weight may play an important role in the prevention and control of childhood overweight and obesity.

Key Words: high birth weight; body mass index; overweight; obesity

Trial registration: January 22, 2015; Registration number: NCT02343588

Strength and limitation of this study

- This study used a national multi-centered sample covering all-age children and adolescents in school.
- The 1:1 matching of gender, age and province in birth weight was used to enhance the study.
- Some maternal information such as maternal age of pregnancy, and gestational weight gain, were not collected in the survey, which may influence the results.
- 70.9% of birth weight was reported based on the health clinic card or birth certificate, with the other 29.1% recalled by their parents twice during six months which may have recall bias.

Introduction

Overweight and obesity in childhood has become a critical health issue with the continuous increase of prevalence worldwide [1], especially in China [2, 3]. The prevalence of obesity in Chinese students aged 7-18 years has increased from 0.13% in 1985 to 7.26% in 2014 [4], while the prevalence of overweight increased from 6.3% in 1991 to 17.1% in 2011[5]. Overweight and obesity are considered high-risk factors of cardiovascular and metabolic complications [6-8], and students with overweight and obesity were more likely to suffer physical and psychosocial problems in adulthood [9-11]. Previous studies have shown that an improvement to physical activity or dietary intake can produce stronger effects than those without it, while the number of health behaviors was inversely related to the intervention effects for obesity [12-13], and the difficulty in preventing obesity is that obesity is the result of many factors, including genetics, unhealthy lifestyles, the family environment as well as heavy marketing of unhealthy food products [13-14].

The hypothesis of Developmental Origins of Health and Disease (DOHaD) that adverse influence in intrauterine life can lead to permanent readjustments in physiology and metabolism, which further caused increased risk of diseases in later life. Thus, focusing on the early developmental phase of life, offered a new way to the mechanism of overweight and obesity [15]. In childhood and puberty, the association between birth weight and obesity has been continually observed in cross-sectional [16-17], longitudinal [18] and cohort [19] studies. Most studies have found that high birth weight (HBW) was related to elevated risk of obesity in children or adolescents [16-19], and healthy lifestyle before and during pregnancy could be effective to reduce the risk of HBW, which means a balanced diet with low glycemic load, light to moderate intensity physical activity, and moderate weight gain during pregnancy [20-21]. However, very few studies have focused on Chinese school-age children aged 6-18 years, nor they have accounted for regional difference and provincial disparities, thus a multicenter study is needed to clarify the associations.

Using the baseline survey data from 7 provinces in China, the present study aimed to evaluate the association of HBW with overweight and obesity among school children aged 6-18 years, and also to investigate the strength of association between HBW and BMI z-score.

Methods

Sample and Participants

The sampling was based on a cross-sectional baseline survey from 7 provinces in China (Liaoning, Tianjin, Ningxia, Shanghai, Chongqing, Hunan, and Guangdong) prior to the commencement of a national multi-centered intervention trial beginning, and these provinces covered all seven geographical areas of China. The protocol of the cluster randomized controlled trial was previously published [22]. This study was

approved by the medical ethical committee of the Peking University (IRB00001052-13034), and written informed consent was given by all students and their guardians before the baseline survey commence.

Using the most common criteria of high birth weight (HBW) [16,18-19], all the students aged 6-18 years with birth weight over 4.0 kg (n=4981) were selected from the baseline survey in 65 347 students, and other 4 981 students with normal birth weight (NBW, 2.5 kg ≤ birth weight < 4.0 kg) were randomly sampled with matched age, gender and province. Finally, 9 962 students including 4 981 students in HBW group and 4 981 students in NBW group were enrolled in the present study, and were further divided into six groups in Table 1 and Table 2: NBW Normal weight group (n=3800), NBW Overweight group (n=653), NBW Obesity group (n=528)， HBW Normal weight group (n=3380), HBW Overweight group (n=760) and HBW Obesity group (n=841), while overweight and obesity were defined using the cut-offs references developed by the Working Group on Obesity in China (WGOC) [23].

Birth weight data

Birth weight was collected using a standard parent questionnaire. Parents were required to record their children's birth weight based on the record of birth certificate or health clinic. If they did not have, parents were asked to recall the birth weight based on their own measurements. About 70.9% of parents record the information of their children's birth weight based on the health clinic card or birth certificate, and the proportions in the HBW group and NBW group were 73.4% (3655/4981) and 68.4% (3406/4981), respectively. To ensure the reliability of birth weight data, parents were asked to repeat the same process of questionnaire survey six months later. The error in birth weight value between the baseline and six months later was lower than 10% and participants with the error over 10% were eliminated in this study.

BMI and blood pressure

Height and weight were measured by trained project members and experienced research nurses and doctors according the standardized procedure. To record these measurements, students were asked to stand straight in light clothing and without shoes. A portable stadiometer and a lever type weight scale were validated and then used to measure height and weight, twice respectively. The mean value for both height and weight measurements was calculated using the duplicate measures. Height was measured to the nearest 0.1 cm and weight was measured to the nearest 0.1 kg. In rechecking 5% of students, the error was less than 10% or if higher all students were re-measured according to the protocol. Body mass index (BMI) was calculated as body weight divided by height (m) squared (kg/m^2),

Blood pressure was measured using a standardized mercury sphygmomanometer (model XJ1ID) recommended by National High Blood Pressure Education Program (NHBPEP) Working Group in children and adolescents. The cuff size was selected according to the NHBPEP working group, and placed approximately 2 cm above the crease of the elbow. The first reading was taken after students had sat at ease for at least 5 minutes, with the students asked to keep quiet through the whole measurement. Systolic blood pressure (SBP) was determined by onset of the first Korotkoff sound and diastolic blood pressure (DBP) was defined by the fifth Korotkoff sound. This

was performed twice, with the average recorded and used in this study. Elevated blood pressure in children and adolescents was defined as SBP or DBP or both are higher than the corresponding cut-offs. The cut-offs were age-, gender- and height-percentile-specific was recommended by NHBPEP Working Group in 2004[24].

Questionnaires

The research team developed self-reported questionnaires for children and prarents to collect information of obesity-related factors. Child-reported questionnaires were filled by students in the classroom with the interpretation by trained research staff, with the exception that children at the third grade or under in primary school completed questionnaires at home with guardians' assistance. Parent-reported questionnaires were all finished by students' guardians.

Child-reported questionnaires contained diet intake (fruit, vegetable and sugar-sweetened beverage), moderate physical activity (PA), vigorous PA, sedentary time of students. For diet intake, students were asked how many days they eat fruits, vegetables or drink sugar-sweetened beverages and how many servings or cups of these for each day in the past 7 days. The average intake was calculated: (days × servings/cups for each day)/7. One serving of fruits or vegetables was defined as the size of an adult's fist, while one cup of sugar-sweetened beverage as almost 250 ml. Moderate and vigorous PA (MVPA) were collected by asking how many days students do moderate or vigorous PA and how many hours for each day over the past 7 days. The average PA followed the calculation of (days × hours for each day)/7. Moderate PA included light activities (e.g. walking) while vigorous PA included high-load activities on musculoskeletal tissues in the body (e.g. sports and games)[25]. Sedentary time, consisting of doing homework, watching TV and using a computer, asked how many days and how many hours for the three separate activities over the past 7 days. Following the calculation of (days × hours for each day)/7 for each activity, the average sedentary time was the sum of homework, TV and computer time.

Parent-reported questionnaire collected the child's birth information (delivery, single birth or not and breast-feeding), single child or not, socioeconomic status (patents' education levels) and family history (hypertension, diabetes, obesity). Delivery mode included spontaneous delivery and cesarean delivery. Breast-feeding was categorized as ≥6 month and <6 month. Socioeconomic status was defined as education levels of children's parents, involving 3 levels: primary school or below, secondary school, and college or above. In this study, family history covered parents' history in hypertension, diabetes and obesity in this study. This was established through a diagnoses of hypertension or diabetes according to their medical history, while BMI was calculated by weight/height^2 (kg/m^2) for height and weight values provided in the questionnaire. Adult obesity was defined as BMI ≥28 kg/m^2 in the Chinese guideline for adult obesity [26].

Patient and Public Involvement

Students and their parents were not involved in setting the research question or outcome measures, nor they involved in the recruitment and conduct of the study.

School doctors and class teachers help us to organize and maintain order of the physical examination by class held in the school.

Statistical Analyses

Epidata Software Version 3.02 was used to do data entry, and all the analyses were performed by IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY, USA). Age, birth weight, height, weight, BMI, DBP, SBP, sweet drinks, MVPA were recorded as the mean value (SD). Gender, delivery, single birth, breast feeding, elevated blood pressure, parental education, and family history were displayed as categorical variables (the number and percentage). T-test was conducted for the P value of BMI between HBW group and normal group by gender and age group and Chi-square test was verified for the percentage of overweight and obesity. Multivariate logistic regression was used to calculate the odds ratios (*OR*) and 95% confidence intervals (*CI*) of different birth weight groups for overweight and obesity by age group. This was further adjusted for urban-rural area, single child, delivery, food intake and physical activity, sedentary time, elevated blood pressure in Model 2, and adjusted for paternal and maternal education level, family history such as hypertension, diabetes and obesity in Model 3. Sensitivity analyses were conducted with different thresholds for HBW compared with NBW, which were displayed in Supplementary Table 1. The criterion for statistical significance was *P* value <0.05.

Results

A total of 9962 children and adolescents aged 6-18 years were recruited in this study, and the distribution of characteristics in all groups was presented separately in Table 1 and Table 2. As presented in Table 1, the mean value of birth weight was 3.22±0.35 kg, 3.25±0.36kg, 4.21±0.29 kg and 4.21±0.26 kg respectively for NBW Normal weight group, NBW Overweight group, HBW Normal group and HBW Overweight group. Compared with other three groups, students in HBW overweight group were observed with significantly higher rate of caesarean birth, urban area, single child, single birth, maternal hypertension, diabetes, obesity and parental obesity (*P*<0.05). Results in Table 2 were similar between HBW obesity group and other three groups, except the rate of parental hypertension and parental diabetes was also significant higher (*P*<0.05).

The associations between BMI z-score and birth weight in different age groups were documented in Table 3. All age groups were observed with significant positive associations between BMI z-score and birth weight, highest in age 8-9 group. When adjusted for urban-rural area, single child, fruit and vegetable intake, sugar-sweetened beverage, moderate and vigorous physical activity, sedentary time, elevated blood pressure in Model 2, the associations remained significant in overall as well as different age groups.

Table 4 presented the rate and odds ratio (OR) for overweight and obesity on current weight by age groups. Overall, HBW group revealed a significantly higher rate of overweight and obesity in HBW group than those in NBW group and the OR was 1.308 (95% *CI*: 1.167-1.467) and 1.791 (95% *CI*: 1.591-2.016) respectively. After adjusting for confounding factors in Model 2 and in Model 3, a slightly

decreased however still significant associations were observed with the AOR of 1.230 (95% *CI*: 1.056-1.432) for overweight and 1.611 (95% *CI*: 1.368-1.897) for obesity. In different age groups, the results were similar, and AOR in age 8-9 group for overweight and in most age groups for obesity remained significant. Results were similar in sensitivity analyses with different thresholds for HBW, which were displayed in Supplementary Table 1.

Discussion

We evaluated the association of high birth weight and overweight and obesity using the cross-sectional survey from 7 provinces in China. In the present study, high birth weight was significantly associated with the increase risk of overweight and obesity among Chinese children and adolescents before and after adjusting for the co-variables. More specifically, we found age 8-9 group with HBW had the highest adjusted risk of 1.508 for overweight than those with NBW, and all age groups except age 16-18 with HBW had a higher risk for obesity.

Birth weight is commonly regarded as an important indicator of depicting development status in intrauterine environments. A meta-analysis gathering 643,902 persons from 66 studies, aged 1 to 75, has proved that low birth weight and high birth weight were followed by opposite long-term effects on overweight compared with NBW, with high birth weight predisposed for overweight in later life with OR of 1.66 (95% CI 1.55-1.77) [27]. Many studies have also verified high level of birth weight as one strong predictor of obesity among children or adolescents [25-26]. However, most studies in China, to our knowledge, were limited to one specific age group or one provincial area, which cannot reveal the overall association among children and adolescents more broadly. In this study, a significantly positive association between high birth weight and overweight and obesity was concluded, which is consisted with the results of previous studies [27-29]. There are some possible explanations for the association. One possible explanation is that hyper-nutrition in pregnancy led to the increase of lean body mass or fat mass in the fetus, which might play an important role in obesity [30-31]. Another explanation is that birth weight might modify the genetic predisposition and thus affected the risk of obesity later in life [32-33]. Even though underlying mechanisms have been raised, there is no systematic explanation for birth weight and obesity. How birth weight affects obesity is a complex process within the life courses and warrants further study.

Weight management during pregnancy was reported to be an effective way to control birth weight [20-21, 34], and evidence had proved that excessive gestational weight gain may lead to high birthweight and large for gestational age infants[35-36]. The Institute of Medicine in US revised the gestational weight gain guidelines in 2009 encouraging health professionals and mothers to manage weight gain by following healthy dietary recommendations and increasing physical activity [36], and noted phone-based interventions can help pregnant women control gestational weight gain by providing guidance, reminders, and educational materials[37]. Other factors such as sedentary time might also influence the risk of obesity in children and adolescents [15]. Some studies focused on the interaction of birth weight and diet and behavioral

factors [27-28], also Ren et al found the synergy effect of high birth weight and unhealthy diet on the high risk of obesity [29]. Thus diet intervention studies on children with HBW are needed in the future.

There are three limitations in this study. Firstly, the information of birth weight was retrospectively obtained from their parents by questionnaire. In this way, there was possibly memory bias. However, we have tried to weaken the bias though collecting information on their certificate or the health clinic card then repeating the survey after six months. Subjects with difference of birth weight in the two investigations over 10% were exclude in the study. Secondly, using dietary recall over last 7 days may be a less accurate method for daily intake of fruits, vegetables and sugar-sweetened beverages consuming, which may also influence the results. Thirdly, some maternal confounders were not adjusted in the study because those factors were not collected in the survey, such as maternal age of pregnancy, and gestational weight gain, which may also influence the results.

Conclusion

This study explored the association of HBW with overweight and obesity among students aged 6-18 years, based on a national cross-sectional survey in China. The results showed that high birth weight was positively associated with overweight and obesity in children. Most younger age groups with HBW were found to have a higher risk of overweight and obesity in childhood, with birth weight remained positively associated with higher BMI z-score even after the adjustment. This study indicates that HBW is a high-risk influence factor of overweight and obesity in children, and thus measures to control birth weight, such as controlling gestational weight gain, should be taken as they may play an important role in the prevention and control of childhood overweight and obesity.

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Contributors

JM, Y Ma and ZZ conceived and designed the project; ZZ collected the data; ZZ and ZY analyzed the data and prepared the manuscript; ZY, XW, DG and YD were involved in writing the article and had a final approval of the submitted and published versions.

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Competing interests None declared.

Patient consent Obtained.

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Table 1. Characteristics of study subjects with normal weight against overweight

Baseline characteristics	NBW group	Normal （3800）	NBW Overweight group （653）	HBW Normal group （3380）	HBW verweight group （760）	P value
Male, n (%)	2190 (57.6)		441 (67.5)	1906 (56.4)	505 (66.4)	<0.001
Age (year) / mean ± SD	11.16 ±0.05		10.76 ±0.13	11.29 ± 0.06	10.83 ± 0.12	<0.001
Urban area, n (%)	2146 (56.5)		388 (59.4)	2144 (63.4)	501 (65.9)	<0.001
Single child, n (%)	2488 (65.5)		479(73.4)	1966 (58.2)	524 (68.9)	<0.001
Birth information						
Birth weight (kg) / mean ± SD	3.22 ± 0.35		3.25 ± 0.36	4.21 ± 0.29	4.21± 0.26	<0.001
Caesarean birth, n (%)	1330 (37.4)		269(43.7)	1424 (43.4)	420 (56.3)	<0.001
Single birth, n (%)	3488 (97.0)		604 (98.1)	3242 (97.9)	739 (98.9)	0.001
Breast feeding, n (%)	3098 (86.0)		536 (86.3)	2887 (86.9)	636 (85.1)	0.552
Anthropometry, mean ± SD						
Height (cm)	146.08 ± 17.36		147.24± 16.49	148.44 ± 17.30	149.16 ± 16.92	<0.001
Weight (kg)	38.18 ± 13.00		48.30 ± 16.23	40.11 ± 13.13	49.80 ± 16.69	<0.001
WC (cm)	61.64 ± 8.09		72.51 ± 9.49	62.70 ±7.83	72.65 ± 9.39	<0.001
Systolic pressure (mmHg)	103.88± 11.51		108.08 ± 12.121	103.98 ± 11.36	107.22 ± 12.17	<0.001
Diastolic pressure (mmHg)	65.71 ± 8.29		67.93 ± 8.99	65.78 ± 8.28	67.04 ± 8.55	<0.001
Body mass index (kg/m^2)	17.26 ± 2.39		21.47 ± 2.74	17.61 ± 2.32	21.58 ± 2.71	<0.001
Diet and physical activity, mean ± SD						
Fruit (serving/day)	1.20 ± 1.03		1.25 ± 0.96	1.27 ± 1.08	1.20 ± 0.95	0.050
Vegetable (serving/day)	1.77 ± 1.40		1.79 ± 1.42	1.78 ± 1.43	1.78 ± 1.43	0.976
Sugar-sweetened beverage (cup/day)	0.42 ± 0.75		0.49 ± 0.92	0.45 ± 0.80	0.46 ± 0.86	0.167
Moderate PA (hour/day)	0.49 ± 0.81		0.46 ± 0.72	0.52 ± 0.82	0.50 ± 0.89	0.196

Vigorous PA (hour/day)	0.47 ± 0.78	0.46 ± 0.65	0.47 ± 0.74	0.49 ± 0.82	0.850
Sedentary time (hour/day)	5.73 ± 3.76	5.75 ± 3.58	5.87 ± 3.73	5.72 ± 3.76	0.442
Socioeconomic status, n (%)					
Parental education level					
none/primary	313 (8.2)	55 (8.9)	313 (9.5)	61 (8.2)	<0.001
secondary	2407(67.3)	374 (60.6)	2207 (67.0)	461 (62.4)	
college and above	876 (24.5)	189 (30.5)	776 (23.5)	217 (29.4)	
Maternal education level					
none/primary	369 (10.4)	57(9.3)	407 (12.4)	73(9.9)	<0.001
secondary	2417 (67.9)	392 (63.5)	2181 (66.3)	467 (63.3)	
college and above	772 (21.7)	168 (27.2)	702 (21.3)	198 (26.8)	
Family history, n (%)					
Parental hypertension	144 (4.1)	27 (4.5)	128 (4.0)	37 (5.1)	0.558
Maternal hypertension	66 (1.9)	17 (2.8)	95(3.0)	25 (3.5)	0.014
Parental diabetes	41 (1.2)	11 (1.9)	39 (1.2)	14 (2.0)	0.251
Maternal diabetes	17 (0.5)	4 (0.7)	31 (1.0)	11 (1.6)	0.017
Parental obesity	176 (5.3)	49(8.5)	159 (5.1)	59(8.6)	<0.001
Maternal obesity	108(3.2)	19 (3.3)	128 (4.1)	42 (6.1)	0.003

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Table 2. Characteristics of study subjects with normal weight against obesity

Baseline characteristics	NBW group	Normal （3800）	NBW Obesity group （528）	HBW Normal group （3380）	HBW Obesity group （841）	P value
Male, n (%)	2190 (57.6)		383 (72.5)	1906 (56.4)	603 (71.7)	<0.001
Age (year) / mean ± SD	11.16 ±0.05		10.14 ±0.13	11.29 ± 0.06	10.23 ± 0.11	<0.001
Urban area, n (%)	2146 (56.5)		315 (59.7)	2144 (63.4)	564 (67.1)	<0.001
Single child, n (%)	2488 (65.5)		410 (77.7)	1966 (58.2)	605 (71.9)	<0.001
Birth information						
Birth weight (kg) / mean ± SD	3.22 ± 0.35		3.31 ± 0.35	4.21 ± 0.29	4.24± 0.32	<0.001
Caesarean birth, n (%)	1330 (37.4)		256 (50.2)	1424 (43.4)	534 (64.3)	<0.001
Single birth, n (%)	3488 (97.0)		502 (97.1)	3242 (97.9)	811 (98.2)	0. 511
Breast feeding, n (%)	3098 (86.0)		413 (79.7)	2887 (86.9)	721(86.7)	0.017
Anthropometry, mean ± SD						
Height (cm)	146.08 ± 17.36		146.62± 15.50	148.44 ± 17.30	148.69 ± 15.87	<0.001
Weight (kg)	38.18 ± 13.00		55.83 ± 19.37	40.11 ± 13.13	58.75 ± 20.96	<0.001
WC (cm)	61.64 ± 8.09		80.27 ± 11.25	62.70 ±7.83	81.67 ± 11.63	<0.001
Systolic pressure (mmHg)	103.88± 11.51		111.92 ± 13.43	103.98 ± 11.36	111.24 ± 13.10	<0.001
Diastolic pressure (mmHg)	65.71 ± 8.29		70.43 ±9.59	65.78 ± 8.28	70.15 ± 8.78	<0.001
Body mass index (kg/m^2)	17.26 ± 2.39		25.09 ± 3.94	17.61 ± 2.32	25.62 ± 4.26	<0.001
Diet and physical activity, mean ± SD						
Fruit (serving/day)	1.20 ± 1.03		1.32 ± 1.03	1.27 ± 1.08	1.36 ± 1.09	<0.001
Vegetable (serving/day)	1.77 ± 1.40		1.90± 1.57	1.78 ± 1.43	1.95 ± 1.49	0.003
Sugar-sweetened beverage (cup/day)	0.42 ± 0.75		0.37 ± 0.59	0.45 ± 0.80	0.40 ± 0.61	0.041

Moderate PA (hour/day)	0.49 ± 0.81	0.51 ± 0.82	0.52 ± 0.82	0.50 ± 0.69	0.375
Vigorous PA (hour/day)	0.47 ± 0.78	0.48 ± 0.45	0.47 ± 0.74	0.47 ± 0.67	0.967
Sedentary time (hour/day)	5.73 ± 3.76	5.87 ± 3.75	5.87 ± 3.73	5.74 ± 3.56	0.431
Socioeconomic status, n (%)					
Parental education level					
none/primary	313 (8.2)	29 (5.7)	313 (9.5)	35 (4.3)	<0.001
secondary	2407(67.3)	319 (62.5)	2207 (67.0)	504 (61.5)	
college and above	876 (24.5)	162 (31.8)	776 (23.5)	281 (34.2)	
Maternal education level					
none/primary	369 (10.4)	31 (6.1)	407 (12.4)	60 (7.3)	<0.001
secondary	2417 (67.9)	346 (67.9)	2181 (66.3)	529 (64.0)	
college and above	772 (21.7)	168 (26.0)	702 (21.3)	198 (28.7)	
Family history, n (%)					
Parental hypertension	144 (4.1)	29 (5.8)	128 (4.0)	49 (6.0)	0.002
Maternal hypertension	66 (1.9)	12 (2.4)	95(3.0)	31 (3.8)	0.067
Parental diabetes	41 (1.2)	9 (1.8)	39 (1.2)	16 (2.1)	0.032
Maternal diabetes	17 (0.5)	6 (1. 2)	31 (1.0)	20 (2.6)	<0.001
Parental obesity	176 (5.3)	59 (12.4)	159 (5.1)	88 (11.5)	<0.001
Maternal obesity	108(3.2)	25 (5.3)	128 (4.1)	65 (8.5)	<0.001

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Table 3. The association between BMI z-score and birth weight in different age groups

	Model 1[a]			Model 2[b]		
	Standardized coefficients	95% *CI*	*P*	*Standardized coefficients*	95% *CI*	*P*
Birth weight	0.117	0.100-0.133	<0.001	0.100	0.079-0.120	<0.001
age 6-7	0.121	0.082-0.160	<0.001	0.145	0.091-0.198	<0.001
age 8-9	0.162	0.126-0.197	<0.001	0.161	0.116-0.205	<0.001
age 10-11	0.134	0.090-0.179	<0.001	0.103	0.048-0.158	<0.001
age 12-13	0.098	0.061-0.135	<0.001	0.091	0.044-0.139	<0.001
age 14-15	0.090	0.045-0.134	<0.001	0.102	0.043-0.161	0.001
age 16-18	0.079	0.032-0.126	0.001	0.076	0.016-0.136	0.013

Note: General linear regression model was used to calculate the association between BMI z-score (dependent variable) and birth weight (independent variable).

[a] Model 1 was unadjusted for any covariates.

[b] Model 2 was adjusted for urban-rural area, single child, delivery, fruit and vegetable intake, sugar-sweetened beverage, moderate and vigorous physical activity, sedentary time, elevated blood pressure.

Table 4. Odds ratio of high birth weight (HBW) group for overweight and obesity in different age groups

	HBW group (n=4981)	NBW group (n=4981)	Model 1[a]		Model 2[b]		Model 3[c]	
	n (%)	n (%)	*OR*[a]	95% *CI*	*AOR*[b]	95% *CI*	*AOR*[c]	95% *CI*
Overweight	760 (15.3)*	653 (13.1)	1.308*	1.167-1.467	1.242*	1.077-1.433	1.230*	1.056-1.432
age 6-7	138 (15.8)	132 (15.2)	1.155	0.887-1.505	1.163	0.806-1.677	1.244	0.847-1.828
age 8-9	177 (15.4) *	148 (12.9)	1.422*	1.118-1.808	1.492*	1.111-2.005	1.508*	1.102-2.062
age 10-11	116 (18.2) *	88 (13.8)	1.566*	1.151-2.132	1.441	0.978-2.124	1.354	0.895-2.049
age 12-13	160 (15.7) *	135 (13.3)	1.318*	1.026-1.693	1.123	0.823-1.534	1.043	0.739-1.471
age 14-15	80 (12.3)	68 (10.4)	1.269	0.899-1.793	1.139	0.726-1.787	1.292	0.788-2.118
age 16-18	89 (13.5)	82 (12.5)	1.160	0.839-1.604	1.155	0.779-1.711	1.078	0.700-1.659
Obestiy	841 (16.9) *	528 (10.6)	1.791*	1.591-2.016	1.673*	1.436-1.949	1.611*	1.368-1.897
age 6-7	162 (18.6) *	108 (12.4)	1.658*	1.276-2.168	1.692*	1.158-2.470	1.741*	1.167-2.596
age 8-9	266 (23.2) *	162 (14.1)	1.952*	1.567-2.431	1.954*	1.456-2.622	1.844*	1.343-2.531
age 10-11	134 (21.0) *	89 (13.9)	1.789*	1.325-2.415	1.867*	1.270-2.744	1.813*	1.203-2.730
age 12-13	141 (13.9) *	86 (8.5)	1.823*	1.369-2.428	1.628*	1.116-2.373	1.641*	1.078-2.496
age 14-15	65 (10.0) *	37 (5.7)	1.896*	1.244-2.889	1.837*	1.070-3.153	1.986*	1.097-3.597
age 16-18	73 (11.1) *	46 (7.0)	1.696*	1.150-2.502	1.546	0.922-2.593	1.256	0.705-2.238

Note: Odds ratios of high birth weight (HBW) group for overweight and obesity were assessed by multivariate logistic regression with the dependent variable (overweight or obesity) and independent variable (birthweight)

[a] Model 1 was unadjusted for any covariates.

[b] Adjusted for urban-rural area, single child, delivery, fruit and vegetable intake, sugar-sweetened beverage, moderate and vigorous physical activity, sedentary time, elevated blood pressure.

[c] Further adjusted for paternal and maternal education level, hypertension, diabetes and obesity.

* $P<0.05$

Supplementary Table 1. Odds ratio of high birth weight group for overweight and obesity in different age groups

	HBWgroup	NBW group	Model 1		Model 2		Model 3	
	n (%)	n (%)	OR[a]	95% *CI*	AOR[b]	95% *CI*	AOR[c]	95% *CI*
Sample number								
HBW defined over 3.5kg	6455	3507	-	-	-		-	-
HBW defined over 4.0kg	4981	4981	-	-	-		-	-
HBW defined over 4.5kg	689	9273	-	-	-		-	-
HBW defined over 5.0kg	176	9786	-	-	-		-	-
Overweight								
HBW defined over 3.5kg	965 (14.9)	448 (12.8)	1.336*	1.183-1.509	1.319*	1.138-1.538	1.334*	1.133-1.571
HBW defined over 4.0kg	760 (15.3)	653 (13.1)	1.308*	1.167-1.467	1.242*	1.077-1.433	1.230*	1.056-1.432
HBW defined over 4.5kg	112 (16.3)	1301 (14.0)	1.322*	1.065-1.640	1.277	0.927-1.678	0.911	0.775-1.070
HBW defined over 5.0kg	27 (15.3)	1386 (14.1)	1.186	0.777-1.810	0.854*	0.736-0.992	0.899	0.766-1.055
Obesity								
HBW defined over 3.5kg	1059 (16.4)	310 (8.8)	2.119*	1.851-2.426	1.905*	1.603-2.264	1.940*	1.612-2.335
HBW defined over 4.0kg	841 (16.9)	528 (10.6)	1.791*	1.591-2.016	1.673*	1.436-1.949	1.611*	1.368-1.897
HBW defined over 4.5kg	138 (20.0)	1231 (13.3)	1.721*	1.408-2.104	1.762*	1.454-2.293	1.820*	1.377-2.407
HBW defined over 5.0kg	33 (18.8)	1336 (13.7)	1.504*	1.017-2.224	0.796*	0.680-0.931	0.857	0.721-1.018

[a] Unadjusted for any covariates.

[b] Adjusted for urban-rural area, single child, delivery, fruit and vegetable intake, sugar-sweetened beverage, moderate and vigorous physical activity, sedentary time, elevated blood pressure.

[c] Further adjusted for paternal and maternal education level, hypertension, diabetes and obesity

* $P<0.05$

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1#
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1#
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2#
Objectives	3	State specific objectives, including any prespecified hypotheses	2#
Methods			
Study design	4	Present key elements of study design early in the paper	3#
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3# 4#
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4#
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4# 5#
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4# 5#
Bias	9	Describe any efforts to address potential sources of bias	4#
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5#
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5#
		(*b*) Describe any methods used to examine subgroups and interactions	5#
		(*c*) Explain how missing data were addressed	5#
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5#
		(*e*) Describe any sensitivity analyses	6#
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6#
		(b) Give reasons for non-participation at each stage	6#
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6#
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6#
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6#
		(*b*) Report category boundaries when continuous variables were categorized	6#
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6#
Discussion			
Key results	18	Summarise key results with reference to study objectives	6#
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7#
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7#
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	8#

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The association of high birth weight with overweight and obesity in Chinese students aged 6 to 18 years: a national cross-sectional study in China.

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The association of high birth weight with overweight and obesity in Chinese students aged 6 to 18 years: a national cross-sectional study in China

Zhiyong Zou, Zhongping Yang, Zhaogeng Yang, Xijie Wang, Di Gao, Yanhui Dong, Jun Ma△, Yinghua Ma△

Author affiliations
Institute of Child and Adolescent Health, School of Public Health, Peking University, Beijing, 100191, China

△JM and YM are co-corresponding authors.
Corresponding authors: Jun Ma, Ph.D., Professor; Yinghua Ma, Ph.D., Professor; Institute of Child and Adolescent Health, School of Public Health, Peking University Health Science Center, No. 38 Xueyuan Road, Haidian District, Beijing, 100191, China. Tel: +86-10-82801624, Fax: +86-10-82801178, Email: majunt@bjmu.edu.cn; yinghuama@bjmu.edu.cn

Abstract

Background: Childhood overweight and obesity prevalence in China has drastically increased 57 times over the past 30 years, and to control birth weight is an effective way to reduce the risk of overweight and obesity across the life course.

Objectives: This paper aimed to evaluate the association of high birth weight (HBW) with overweight and obesity in Chinese students aged 6-18 years.

Methods: All the students with HBW (n=4981) aged 6-18 years were selected from a cross-sectional survey from 7 provinces of China, and other 4981 students with normal birth weight (NBW) were randomly sampled with matched gender, age and province. Anthropometric parameters were measured and characteristics were collected by questionnaires. Multiple logistic regression was used to estimate the odds ratio (OR) of overweight and obesity with HBW in unadjusted and adjusted for confounding factors.

Results: Participants with HBW revealed higher body mass index (BMI) in childhood. The prevalence of overweight and obesity were significantly higher in HBW group than NBW group (overweight 15.3% versus 13.1%, $p<0.05$; obesity 16.9% versus 10.6%, $p<0.05$), and results were similar in all age groups except age 6-7, age 14-15 and age 16-18 for overweight. Additionally, HBW was positively associated with overweight (OR=1.230; 95%CI: 1.056-1.432) and obesity (OR=1.611; 95%CI: 1.368-1.897) after adjustment for covariates.

Conclusions: HBW leads to an increased risk of overweight and obesity in childhood, thus measures to control birth weight, such as controlling gestational weight gain, should be taken from the earliest beginning of life.

Key Words: high birth weight; body mass index; overweight; obesity

Trial registration: January 22, 2015; Registration number: NCT02343588

Strength and limitation of this study

- This study used a national multi-centered sample covering all-age children and adolescents in school.
- The 1:1 matching of gender, age and province between high birth weight (HBW) group and normal birth weight (NBW) group was used to enhance the study.
- Some maternal information such as maternal age of pregnancy, and gestational weight gain, were not collected in the survey, which may influence the results.
- 70.9% of birth weight was reported based on the health clinic card or birth certificate, with the other 29.1% recalled by their parents twice during six months which may have recall bias.

Introduction

Overweight and obesity in childhood has become a critical health issue with the continuous increase of prevalence worldwide,[1] especially in China.[2,3] The prevalence of obesity in Chinese students aged 7-18 years has increased from 0.13% in 1985 to 7.26% in 2014,[4] while the prevalence of overweight increased from 6.3% in 1991 to 17.1% in 2011.[5] Overweight and obesity are considered high-risk factors of cardiovascular and metabolic complications,[6-8] and students with overweight and obesity are more likely to suffer physical and psychosocial problems in adulthood.[9-11] Previous studies have shown that an improvement to physical activity or dietary intake could produce stronger effects than those without it, while the number of health behaviors was inversely related to the intervention effects for obesity,[12,13] and the difficulty in preventing obesity is that obesity is the result of many factors, including genetics, unhealthy lifestyles, the family environment as well as heavy marketing of unhealthy food products.[13,14]

The hypothesis of Developmental Origins of Health and Disease (DOHaD) postulates that adverse influence in intrauterine life can lead to permanent readjustments in physiology and metabolism, which further causes increased risk of diseases in later life. Thus, focusing on the early developmental phase of life, offers a new way to the mechanism of overweight and obesity.[15] In childhood and puberty, the association between birth weight and obesity has been continually observed in cross-sectional,[16,17] longitudinal [18] and cohort [19] studies. Most studies have found that HBW was related to elevated risk of obesity in children or adolescents,[16-19] and healthy lifestyle intervention before and during pregnancy could be effective to reduce the risk of HBW, which meant a balanced diet with low glycemic load, light to moderate intensity physical activity, and moderate weight gain during pregnancy.[20,21] However, very few studies have focused on Chinese school-age children, nor they have accounted for regional difference and provincial disparities, thus a multi-centered study is needed to clarify the associations.

Using the baseline survey data from 7 provinces in China, the present study aimed to evaluate the association of HBW with overweight and obesity among school children aged 6-18 years, and also to investigate the strength of association between HBW and BMI z-score.

Methods

Sample and Participants

The sampling was based on a cross-sectional baseline survey from 7 provinces in China (Liaoning, Tianjin, Ningxia, Shanghai, Chongqing, Hunan, and Guangdong) prior to the commencement of a national multi-centered intervention trial, and these provinces covered all seven geographical areas of China. The protocol of the cluster randomized controlled trial was previously published.[22] This study was approved by

the medical ethical committee of the Peking University (IRB00001052-13034), and written informed consent was given by all students and their guardians before the baseline survey commence.

Using the common criteria of HBW,[16,18,19] all the students aged 6-18 years with birth weight over 4.0 kg (n=4981) were selected from the baseline survey in 65 347 students, and other 4 981 students with normal birth weight (NBW, 2.5 kg ≤ birth weight < 4.0 kg) were randomly sampled with matched age, gender and province. Finally, 9 962 students including 4 981 students in HBW group and 4 981 students in NBW group were enrolled in the present study, and were further divided into six subgroups in Table 1 and Table 2: NBW Normal weight group (n=3800), NBW Overweight group (n=653), NBW Obesity group (n=528)， HBW Normal weight group (n=3380), HBW Overweight group (n=760) and HBW Obesity group (n=841), while overweight and obesity were defined using the cut-offs references developed by the Working Group on Obesity in China (WGOC).[23]

Birth weight data

Birth weight was collected using a standard parent questionnaire. Parents were required to record their children's birth weight based on the record of birth certificate or health clinic. If they did not have, parents were asked to recall the birth weight based on their own measurements. About 70.9% of parents record the information of their children's birth weight based on the health clinic card or birth certificate, and the proportions in the HBW group and NBW group were 73.4% (3655/4981) and 68.4% (3406/4981), respectively. To ensure the reliability of birth weight data, parents were asked to repeat the same process of questionnaire survey six months later. The error in birth weight values between the baseline and six months later was lower than 10% and participants with the error over 10% were eliminated in this study.

BMI and blood pressure

Height and weight were measured by trained project members and experienced research nurses and doctors according the standardized procedure. To record these measurements, students were asked to stand straight in light clothing and without shoes. A portable stadiometer and a lever type weight scale were validated and then used to measure height and weight, twice respectively. The mean value for both height and weight measurements was calculated using the duplicate measures. Height was measured to the nearest 0.1 cm and weight was measured to the nearest 0.1 kg. In rechecking 5% of students, the error was less than 3% or if higher all students were re-measured according to the protocol. Body mass index (BMI) was calculated as body weight divided by height (m) squared (kg/m^2),

Blood pressure was measured using a standardized mercury sphygmomanometer (model XJ1ID) recommended by National High Blood Pressure Education Program (NHBPEP) Working Group in children and adolescents. The cuff size was selected according to the NHBPEP working group, and placed approximately 2 cm above the crease of the elbow. The first reading was taken after students had sat at ease for at least 5 minutes, with the students asked to keep quiet through the whole measurement. Systolic blood pressure (SBP) was determined by onset of the first Korotkoff sound and diastolic blood pressure (DBP) was defined by the fifth Korotkoff sound. This

was performed twice, with the average recorded and used in this study. Elevated blood pressure in children and adolescents was defined as SBP or DBP or both are higher than the corresponding cut-offs. The cut-offs were age-, gender- and height-percentile-specific was recommended by NHBPEP Working Group in 2004.[24]

Questionnaires

The research team developed self-reported questionnaires for children and parents to collect information of obesity-related factors. Child-reported questionnaires were filled by students in the classroom with the interpretation by trained research staff, with the exception that children at the third grade or under in primary school completed questionnaires at home with guardians' assistance. Parent-reported questionnaires were all finished by students' guardians.

Child-reported questionnaires contained diet intake (fruit, vegetable and sugar-sweetened beverage), moderate physical activity (PA), vigorous PA, sedentary time of students. For diet intake, students were asked how many days they eat fruits, vegetables or drink sugar-sweetened beverages and how many servings or cups of these for each day in the past 7 days. The average intake was calculated: (days × servings/cups for each day)/7. One serving of fruits or vegetables was defined as the size of an adult's fist, while one cup of sugar-sweetened beverage as almost 250 ml. Moderate and vigorous PA (MVPA) were collected by asking how many days students do moderate or vigorous PA and how many hours for each day over the past 7 days. The average PA followed the calculation of (days × hours for each day)/7. Moderate PA included light activities (e.g. walking) while vigorous PA included high-load activities on musculoskeletal tissues in the body (e.g. sports and games).[25] Sedentary time, consisting of doing homework, watching TV and using a computer, asked how many days and how many hours for the three separate activities over the past 7 days. Following the calculation of (days × hours for each day)/7 for each activity, the average sedentary time was the sum of homework, TV and computer time.

Parent-reported questionnaire collected the child's birth information (delivery, single birth or not and breast-feeding), single child or not, socioeconomic status (parents' education levels) and family history (hypertension, diabetes, obesity). Delivery mode included spontaneous delivery and cesarean delivery. Breast-feeding was categorized as ≥6 month and <6 month. Socioeconomic status was defined as education levels of children's parents, involving 3 levels: primary school or below, secondary school, and college or above. In this study, family history covered father's and mother's history of hypertension, diabetes and obesity. This was established through a diagnoses of hypertension or diabetes according to their medical history, while BMI was calculated by weight/height^2 (kg/m^2) for height and weight values provided in the questionnaire. Adult obesity was defined as BMI ≥28 kg/m^2 in the Chinese guideline for adult obesity.[26]

Patient and Public Involvement

Students and their parents were not involved in setting the research question or outcome measures, nor they involved in the recruitment and conduct of the study.

School doctors and class teachers help us to organize and maintain order of the physical examination by class held in the school.

Statistical Analyses

EpiData Software Version 3.02 was used to do data entry, and all the analyses were performed by IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY, USA). Age, birth weight, height, weight, BMI, DBP, SBP, sweet drinks, MVPA were recorded as the mean value (SD). Gender, delivery, single birth, breast feeding, elevated blood pressure, parental education, and family history were displayed as categorical variables (the number and percentage). T-test was conducted for the P value of BMI between HBW group and normal group by gender and age group and Chi-square test was verified for the percentage of overweight and obesity. Multivariate logistic regression was used to calculate the odds ratios (*OR*) and 95% confidence intervals (*CI*) of different birth weight groups for overweight and obesity by age group. This was further adjusted for urban-rural area, single child, delivery, food intake and physical activity, sedentary time, elevated blood pressure in Model 2, and adjusted for paternal and maternal education level, family history such as hypertension, diabetes and obesity in Model 3. Sensitivity analyses were conducted with different thresholds for HBW compared with NBW, which were displayed in Supplementary Table 1. The criterion for statistical significance was *P* value <0.05.

Results

A total of 9962 children and adolescents aged 6-18 years were recruited in this study, and the distribution of characteristics in all groups was presented separately in Table 1 and Table 2. As presented in Table 1, the mean value of birth weight was 3.22±0.35 kg, 3.25±0.36kg, 4.21±0.29 kg and 4.21±0.26 kg respectively for NBW Normal weight group, NBW Overweight group, HBW Normal group and HBW Overweight group. Compared with other three groups, students in HBW overweight group were observed with significantly higher rate of caesarean birth, urban area, single child, single birth, maternal hypertension, diabetes, obesity and parental obesity (*P*<0.05). Results in Table 2 were similar between HBW obesity group and other three groups, except with the rate of parental hypertension and parental diabetes significant higher (*P*<0.05).

The associations between BMI z-score and birth weight in different age groups were documented in Table 3. All age groups were observed with significant positive associations between BMI z-score and birth weight, highest in age 8-9 group. When adjusted for urban-rural area, single child, fruit and vegetable intake, sugar-sweetened beverage, moderate and vigorous physical activity, sedentary time, elevated blood pressure in Model 2, the associations remained significant in overall as well as different age groups.

Table 4 presented the rate and odds ratio (OR) for overweight and obesity on current weight by age groups. Overall, HBW group revealed a significantly higher rate of overweight and obesity in HBW group than those in NBW group and the OR was 1.308 (95% *CI*: 1.167-1.467) and 1.791 (95% *CI*: 1.591-2.016) respectively. After adjusting for confounding factors in Model 2 and in Model 3, a slightly

decreased however still significant associations were observed with the AOR of 1.230 (95% *CI*: 1.056-1.432) for overweight and 1.611 (95% *CI*: 1.368-1.897) for obesity. In different age groups, the results were similar, and AOR in age 8-9 group for overweight and in most age groups for obesity remained significant. Results were similar in sensitivity analyses with different thresholds for HBW, which were displayed in Supplementary Table 1.

Discussion

We evaluated the associations of HBW and overweight and obesity using the cross-sectional survey from 7 provinces in China. In the present study, HBW was significantly associated with the increase risk of overweight and obesity among Chinese children and adolescents before and after adjusting for the co-variables. More specifically, we found age 8-9 group with HBW had the highest adjusted risk of 1.508 for overweight, and all age groups except age 16-18 with HBW had a higher risk for obesity.

Birth weight is commonly regarded as an important indicator of depicting development status in intrauterine environments. A meta-analysis gathering 643,902 persons from 66 studies, aged 1 to 75, has proved that low birth weight and HBW were followed by opposite long-term effects on overweight compared with NBW, with HBW predisposed for overweight in later life with OR of 1.66 (95% CI 1.55-1.77).[27] Many studies have also verified high level of birth weight as one strong predictor of obesity among children or adolescents.[25,26] However, most studies in China, to our knowledge, were limited to one specific age group or one provincial area, which cannot reveal the overall association among children and adolescents more broadly. In this study, a significantly positive association between HBW and overweight and obesity was concluded, which is consisted with the results of previous studies.[27-29] There are some possible explanations for the association. One possible explanation is that hyper-nutrition in pregnancy led to the increase of lean body mass or fat mass in the fetus, which might play an important role in obesity.[30,31] Another explanation is that birth weight might modify the genetic predisposition and thus affects the risk of obesity later in life.[32,33] Even though underlying mechanisms have been raised, there is no systematic explanation for birth weight and obesity. How birth weight affects obesity is a complex process within the life courses and warrants further study.

Weight management during pregnancy was reported to be an effective way to control birth weight,[20,21,34] and evidence had proved that excessive gestational weight gain may lead to high birthweight and large for gestational age infants.[35,36] The Institute of Medicine in US revised the gestational weight gain guidelines in 2009 encouraging health professionals and mothers to manage weight gain by following healthy dietary recommendations and increasing physical activity,[36] and noted phone-based interventions can help pregnant women control gestational weight gain by providing guidance, reminders, and educational materials.[37] Other factors such as sedentary time might also influence the risk of obesity in children and adolescents.[15] Some studies focused on the interactions of birth weight and diet and behavioral

factors,[27,28] and Ren et al also found the synergy effects of HBW and unhealthy diet on increased risk of obesity.[29] Thus diet intervention studies on children with HBW are needed in the future.

There are three limitations in this study. Firstly, the information of birth weight was retrospectively obtained from their parents by questionnaire. In this way, there was possibly memory bias. However, we have tried to weaken the bias though collecting information on their certificate or the health clinic card then repeating the survey after six months. Subjects with difference of birth weight in the two investigations over 10% were exclude in the study. Secondly, using dietary recall over last 7 days may be a less accurate method for daily intake of fruits, vegetables and sugar-sweetened beverages consuming, which may also influence the results. Thirdly, some maternal confounders were not adjusted in the study because those factors were not collected in the survey, such as maternal age of pregnancy, and gestational weight gain, which may also influence the results.

Conclusion

This study explored the association of HBW with overweight and obesity among students aged 6-18 years, based on a national cross-sectional survey in China. The results showed that HBW was positively associated with overweight and obesity in children. Most younger age groups with HBW were found to have a higher risk of overweight and obesity in childhood, with birth weight remained positively associated with higher BMI z-score even after the adjustment. This study indicated that HBW is a high-risk influence factor of overweight and obesity in children, and thus measures to control birth weight, such as controlling gestational weight gain, should be taken as they may play an important role in the prevention and control of childhood overweight and obesity.

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Contributors

JM, YM and ZZ conceived and designed the project; ZZ collected the data; ZZ and ZY analyzed the data and prepared the manuscript; ZY, XW, DG and YD were involved in writing the article and had a final approval of the submitted and published versions.

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Competing interests None declared.

Patient consent Obtained.

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Table 1. Characteristics of study subjects with normal weight against overweight

Baseline characteristics	NBW Normal group (3800)	NBW Overweight group (653)	HBW Normal group (3380)	HBW Overweight group (760)	P value
Male, n (%)	2190 (57.6)	441 (67.5)	1906 (56.4)	505 (66.4)	<0.001
Age (year) / mean ± SD	11.16 ±0.05	10.76 ±0.13	11.29 ± 0.06	10.83 ± 0.12	<0.001
Urban area, n (%)	2146 (56.5)	388 (59.4)	2144 (63.4)	501 (65.9)	<0.001
Single child, n (%)	2488 (65.5)	479(73.4)	1966 (58.2)	524 (68.9)	<0.001
Birth information					
Birth weight (kg) / mean ± SD	3.22 ± 0.35	3.25 ± 0.36	4.21 ± 0.29	4.21± 0.26	<0.001
Caesarean birth, n (%)	1330 (37.4)	269(43.7)	1424 (43.4)	420 (56.3)	<0.001
Single birth, n (%)	3488 (97.0)	604 (98.1)	3242 (97.9)	739 (98.9)	0.001
Breast feeding, n (%)	3098 (86.0)	536 (86.3)	2887 (86.9)	636 (85.1)	0.552
Anthropometry, mean ± SD					
Height (cm)	146.08 ± 17.36	147.24± 16.49	148.44 ± 17.30	149.16 ± 16.92	<0.001
Weight (kg)	38.18 ± 13.00	48.30 ± 16.23	40.11 ± 13.13	49.80 ± 16.69	<0.001
WC (cm)	61.64 ± 8.09	72.51 ± 9.49	62.70 ±7.83	72.65 ± 9.39	<0.001
Systolic pressure (mmHg)	103.88± 11.51	108.08 ± 12.121	103.98 ± 11.36	107.22 ± 12.17	<0.001
Diastolic pressure (mmHg)	65.71 ± 8.29	67.93 ± 8.99	65.78 ± 8.28	67.04 ± 8.55	<0.001
Body mass index (kg/m^2)	17.26 ± 2.39	21.47 ± 2.74	17.61 ± 2.32	21.58 ± 2.71	<0.001
Diet and physical activity, mean ± SD					
Fruit (serving/day)	1.20 ± 1.03	1.25 ± 0.96	1.27 ± 1.08	1.20 ± 0.95	0.050
Vegetable (serving/day)	1.77 ± 1.40	1.79 ± 1.42	1.78 ± 1.43	1.78 ± 1.43	0.976
Sugar-sweetened beverage (cup/day)	0.42 ± 0.75	0.49 ± 0.92	0.45 ± 0.80	0.46 ± 0.86	0.167
Moderate PA (hour/day)	0.49 ± 0.81	0.46 ± 0.72	0.52 ± 0.82	0.50 ± 0.89	0.196
Vigorous PA (hour/day)	0.47 ± 0.78	0.46 ± 0.65	0.47 ± 0.74	0.49 ± 0.82	0.850

Sedentary time (hour/day)	5.73 ± 3.76	5.75 ± 3.58	5.87 ± 3.73	5.72 ± 3.76	0.442
Socioeconomic status, n (%)					
Parental education level					
none/primary	313 (8.2)	55 (8.9)	313 (9.5)	61 (8.2)	<0.001
secondary	2407(67.3)	374 (60.6)	2207 (67.0)	461 (62.4)	
college and above	876 (24.5)	189 (30.5)	776 (23.5)	217 (29.4)	
Maternal education level					
none/primary	369 (10.4)	57(9.3)	407 (12.4)	73(9.9)	<0.001
secondary	2417 (67.9)	392 (63.5)	2181 (66.3)	467 (63.3)	
college and above	772 (21.7)	168 (27.2)	702 (21.3)	198 (26.8)	
Family history, n (%)					
Parental hypertension	144 (4.1)	27 (4.5)	128 (4.0)	37 (5.1)	0.558
Maternal hypertension	66 (1.9)	17 (2.8)	95(3.0)	25 (3.5)	0.014
Parental diabetes	41 (1.2)	11 (1.9)	39 (1.2)	14 (2.0)	0.251
Maternal diabetes	17 (0.5)	4 (0.7)	31 (1.0)	11 (1.6)	0.017
Parental obesity	176 (5.3)	49 (8.5)	159 (5.1)	59 (8.6)	<0.001
Maternal obesity	108 (3.2)	19 (3.3)	128 (4.1)	42 (6.1)	0.003

Table 2. Characteristics of study subjects with normal weight against obesity

Baseline characteristics	NBW Normal group (3800)	NBW Obesity group (528)	HBW Normal group (3380)	HBW Obesity group (841)	P value
Male, n (%)	2190 (57.6)	383 (72.5)	1906 (56.4)	603 (71.7)	<0.001
Age (year) / mean ± SD	11.16 ±0.05	10.14 ±0.13	11.29 ± 0.06	10.23 ± 0.11	<0.001
Urban area, n (%)	2146 (56.5)	315 (59.7)	2144 (63.4)	564 (67.1)	<0.001
Single child, n (%)	2488 (65.5)	410 (77.7)	1966 (58.2)	605 (71.9)	<0.001
Birth information					
Birth weight (kg) / mean ± SD	3.22 ± 0.35	3.31 ± 0.35	4.21 ± 0.29	4.24± 0.32	<0.001
Caesarean birth, n (%)	1330 (37.4)	256 (50.2)	1424 (43.4)	534 (64.3)	<0.001
Single birth, n (%)	3488 (97.0)	502 (97.1)	3242 (97.9)	811 (98.2)	0. 511
Breast feeding, n (%)	3098 (86.0)	413 (79.7)	2887 (86.9)	721(86.7)	0.017
Anthropometry, mean ± SD					
Height (cm)	146.08 ± 17.36	146.62± 15.50	148.44 ± 17.30	148.69 ± 15.87	<0.001
Weight (kg)	38.18 ± 13.00	55.83 ± 19.37	40.11 ± 13.13	58.75 ± 20.96	<0.001
WC (cm)	61.64 ± 8.09	80.27 ± 11.25	62.70 ±7.83	81.67 ± 11.63	<0.001
Systolic pressure (mmHg)	103.88± 11.51	111.92 ± 13.43	103.98 ± 11.36	111.24 ± 13.10	<0.001
Diastolic pressure (mmHg)	65.71 ± 8.29	70.43 ±9.59	65.78 ± 8.28	70.15 ± 8.78	<0.001
Body mass index (kg/m^2)	17.26 ± 2.39	25.09 ± 3.94	17.61 ± 2.32	25.62 ± 4.26	<0.001
Diet and physical activity, mean ± SD					
Fruit (serving/day)	1.20 ± 1.03	1.32 ± 1.03	1.27 ± 1.08	1.36 ± 1.09	<0.001
Vegetable (serving/day)	1.77 ± 1.40	1.90± 1.57	1.78 ± 1.43	1.95 ± 1.49	0.003
Sugar-sweetened beverage (cup/day)	0.42 ± 0.75	0.37 ± 0.59	0.45 ± 0.80	0.40 ± 0.61	0.041
Moderate PA (hour/day)	0.49 ± 0.81	0.51 ± 0.82	0.52 ± 0.82	0.50 ± 0.69	0.375
Vigorous PA (hour/day)	0.47 ± 0.78	0.48 ± 0.45	0.47 ± 0.74	0.47 ± 0.67	0.967

Sedentary time (hour/day)	5.73 ± 3.76	5.87 ± 3.75	5.87 ± 3.73	5.74 ± 3.56	0.431
Socioeconomic status, n (%)					
Parental education level					
none/primary	313 (8.2)	29 (5.7)	313 (9.5)	35 (4.3)	<0.001
secondary	2407(67.3)	319 (62.5)	2207 (67.0)	504 (61.5)	
college and above	876 (24.5)	162 (31.8)	776 (23.5)	281 (34.2)	
Maternal education level					
none/primary	369 (10.4)	31 (6.1)	407 (12.4)	60 (7.3)	<0.001
secondary	2417 (67.9)	346 (67.9)	2181 (66.3)	529 (64.0)	
college and above	772 (21.7)	168 (26.0)	702 (21.3)	198 (28.7)	
Family history, n (%)					
Parental hypertension	144 (4.1)	29 (5.8)	128 (4.0)	49 (6.0)	0.002
Maternal hypertension	66 (1.9)	12 (2.4)	95(3.0)	31 (3.8)	0.067
Parental diabetes	41 (1.2)	9 (1.8)	39 (1.2)	16 (2.1)	0.032
Maternal diabetes	17 (0.5)	6 (1. 2)	31 (1.0)	20 (2.6)	<0.001
Parental obesity	176 (5.3)	59 (12.4)	159 (5.1)	88 (11.5)	<0.001
Maternal obesity	108 (3.2)	25 (5.3)	128 (4.1)	65 (8.5)	<0.001

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Table 3. The association between BMI z-score and birth weight in different age groups

	Model 1[a]			Model 2[b]		
	Standardized coefficients	*95% CI*	*P*	*Standardized coefficients*	*95% CI*	*P*
Birth weight	0.117	0.100-0.133	<0.001	0.100	0.079-0.120	<0.001
age 6-7	0.121	0.082-0.160	<0.001	0.145	0.091-0.198	<0.001
age 8-9	0.162	0.126-0.197	<0.001	0.161	0.116-0.205	<0.001
age 10-11	0.134	0.090-0.179	<0.001	0.103	0.048-0.158	<0.001
age 12-13	0.098	0.061-0.135	<0.001	0.091	0.044-0.139	<0.001
age 14-15	0.090	0.045-0.134	<0.001	0.102	0.043-0.161	0.001
age 16-18	0.079	0.032-0.126	0.001	0.076	0.016-0.136	0.013

Note: General linear regression model was used to calculate the association between BMI z-score (dependent variable) and birth weight (independent variable).

[a] Model 1 was unadjusted for any covariates.

[b] Model 2 was adjusted for urban-rural area, single child, delivery, fruit and vegetable intake, sugar-sweetened beverage, moderate and vigorous physical activity, sedentary time, elevated blood pressure.

Table 4. Odds ratio of high birth weight (HBW) group for overweight and obesity in different age groups

	HBW group (n=4981)	NBW group (n=4981)	Model 1[a]		Model 2[b]		Model 3[c]	
	n (%)	n (%)	*OR*[a]	95% *CI*	*AOR*[b]	95% *CI*	*AOR*[c]	95% *CI*
Overweight	760 (15.3)*	653 (13.1)	1.308*	1.167-1.467	1.242*	1.077-1.433	1.230*	1.056-1.432
age 6-7	138 (15.8)	132 (15.2)	1.155	0.887-1.505	1.163	0.806-1.677	1.244	0.847-1.828
age 8-9	177 (15.4) *	148 (12.9)	1.422*	1.118-1.808	1.492*	1.111-2.005	1.508*	1.102-2.062
age 10-11	116 (18.2) *	88 (13.8)	1.566*	1.151-2.132	1.441	0.978-2.124	1.354	0.895-2.049
age 12-13	160 (15.7) *	135 (13.3)	1.318*	1.026-1.693	1.123	0.823-1.534	1.043	0.739-1.471
age 14-15	80 (12.3)	68 (10.4)	1.269	0.899-1.793	1.139	0.726-1.787	1.292	0.788-2.118
age 16-18	89 (13.5)	82 (12.5)	1.160	0.839-1.604	1.155	0.779-1.711	1.078	0.700-1.659
Obesity	841 (16.9) *	528 (10.6)	1.791*	1.591-2.016	1.673*	1.436-1.949	1.611*	1.368-1.897
age 6-7	162 (18.6) *	108 (12.4)	1.658*	1.276-2.168	1.692*	1.158-2.470	1.741*	1.167-2.596
age 8-9	266 (23.2) *	162 (14.1)	1.952*	1.567-2.431	1.954*	1.456-2.622	1.844*	1.343-2.531
age 10-11	134 (21.0) *	89 (13.9)	1.789*	1.325-2.415	1.867*	1.270-2.744	1.813*	1.203-2.730
age 12-13	141 (13.9) *	86 (8.5)	1.823*	1.369-2.428	1.628*	1.116-2.373	1.641*	1.078-2.496
age 14-15	65 (10.0) *	37 (5.7)	1.896*	1.244-2.889	1.837*	1.070-3.153	1.986*	1.097-3.597
age 16-18	73 (11.1) *	46 (7.0)	1.696*	1.150-2.502	1.546	0.922-2.593	1.256	0.705-2.238

Note: Odds ratios of HBW group for overweight and obesity were assessed by multivariate logistic regression with the dependent variable (overweight or obesity) and independent variable (birthweight)

[a] Model 1 was unadjusted for any covariates.

[b] Adjusted for urban-rural area, single child, delivery, fruit and vegetable intake, sugar-sweetened beverage, moderate and vigorous physical activity, sedentary time, elevated blood pressure.

[c] Further adjusted for paternal and maternal education level, hypertension, diabetes and obesity.

* $P<0.05$

Supplementary Table 1. Odds ratio of high birth weight group for overweight and obesity in different age groups

	HBWgroup	NBW group	Model 1		Model 2		Model 3	
	n (%)	n (%)	OR[a]	95% *CI*	AOR[b]	95% *CI*	AOR[c]	95% *CI*
Sample number								
HBW defined over 3.5kg	6455	3507	-	-	-		-	-
HBW defined over 4.0kg	4981	4981	-	-	-		-	-
HBW defined over 4.5kg	689	9273	-	-	-		-	-
HBW defined over 5.0kg	176	9786	-	-	-		-	-
Overweight								
HBW defined over 3.5kg	965 (14.9)	448 (12.8)	1.336*	1.183-1.509	1.319*	1.138-1.538	1.334*	1.133-1.571
HBW defined over 4.0kg	760 (15.3)	653 (13.1)	1.308*	1.167-1.467	1.242*	1.077-1.433	1.230*	1.056-1.432
HBW defined over 4.5kg	112 (16.3)	1301 (14.0)	1.322*	1.065-1.640	1.277	0.977-1.678	0.911	0.775-1.070
HBW defined over 5.0kg	27 (15.3)	1386 (14.1)	1.186	0.777-1.810	0.854*	0.736-0.992	0.899	0.766-1.055
Obesity								
HBW defined over 3.5kg	1059 (16.4)	310 (8.8)	2.119*	1.851-2.426	1.905*	1.603-2.264	1.940*	1.612-2.335
HBW defined over 4.0kg	841 (16.9)	528 (10.6)	1.791*	1.591-2.016	1.673*	1.436-1.949	1.611*	1.368-1.897
HBW defined over 4.5kg	138 (20.0)	1231 (13.3)	1.721*	1.408-2.104	1.762*	1.454-2.293	1.820*	1.377-2.407
HBW defined over 5.0kg	33 (18.8)	1336 (13.7)	1.504*	1.017-2.224	0.796*	0.680-0.931	0.857	0.721-1.018

[a] Unadjusted for any covariates.

[b] Adjusted for urban-rural area, single child, delivery, fruit and vegetable intake, sugar-sweetened beverage, moderate and vigorous physical activity, sedentary time, elevated blood pressure.

[c] Further adjusted for paternal and maternal education level, hypertension, diabetes and obesity

* $P<0.05$

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1#
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1#
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2#
Objectives	3	State specific objectives, including any prespecified hypotheses	2#
Methods			
Study design	4	Present key elements of study design early in the paper	3#
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3# 4#
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4#
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4# 5#
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4# 5#
Bias	9	Describe any efforts to address potential sources of bias	4#
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5#
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5#
		(*b*) Describe any methods used to examine subgroups and interactions	5#
		(*c*) Explain how missing data were addressed	5#
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5#
		(*e*) Describe any sensitivity analyses	6#
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6#
		(b) Give reasons for non-participation at each stage	6#
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6#
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6#
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6#
		(*b*) Report category boundaries when continuous variables were categorized	6#
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6#
Discussion			
Key results	18	Summarise key results with reference to study objectives	6#
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7#
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7#
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	8#

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.