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Relationship between Low Birthweight and Thinness, Severe Obesity in 3 to 12-Year-Old Shanghai Children: A large-scale population-based study

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ABSTRACT

Objectives: Low birthweight (BW) is a general symbol of inadequate intrauterine conditions that elicit abnormal fetal growth and development. The aim of current study is to investigate the relationship between low BW and thinness or severe obesity during maturation.

Design: A large-scale cross-sectional population-based survey.

Setting: 134 kindergartens and 70 elementary schools.

Participants: 70,284 Chinese children aged 3-12 years.

Primary and secondary outcome measures: International Obesity Task Force BMI cut-offs were used to define grade 1, 2, 3 thinness, overweight, obesity and severe obesity. Logistic regression was used to estimate the association.

Results: Total 70,284 children participated in the survey. The percentage of grade 1 thinness and severe obesity in children with low birthweight is significantly higher than that with normal birthweight ($P < 0.05$). Low BW correlated with an increased risk of grade 1 thinness (OR = 1.56, 95%CI = 1.38–1.75), grade 2 thinness (OR = 1.34, 95%CI = 1.10–1.64), grade 3 thinness (OR = 1.99, 95%CI= 1.63–2.42) and severe obesity (OR = 1.27, 95%CI = 1.03–1.55) but did not correlate with overweight.

Conclusions: The relationship between low BW and thinness or severe obesity risk is associated.

Strengths and limitations of this study:

- This study is a large population-based cross-sectional survey, with a representative, multistage proportional cluster sampling.
- Low birthweight was found to be correlated with an increased risk of grade 1 thinness, grade 2 thinness, grade 3 thinness and severe obesity, rather than overweight or obesity.
- Longitudinal studies are still needed to making cause-and-effect inferences and observing continuous age-effects and long-term effects.

INTRODUCTION

Childhood obesity is one of the most serious global public health challenges.[1] Furthermore, obesity in childhood may lead to short-term morbidity and to subsequent adverse consequences across the individual's lifespan and his or her subsequent generation.[1] Growing evidence indicates that perinatal characteristics have been recognized as contributing factors to the obesity epidemic.[2] Birthweight (BW) is frequently used as an indicator of the conditions experienced in utero which contribute to the newborn baby's survival, health, growth, and development.[3 4] Lower BW is a general symbol of inadequate intrauterine conditions that elicit abnormal fetal growth and development.[5] Based on the findings of numerous studies, low BW (birthweight < 2500g) has been shown to trigger various short-term and long-term health issues, especially for birth injuries, delayed motor development, delayed cognitive and social skills, obesity and chronic diseases.[4 6]

A great number of studies have indicated that high BW is associated with an increased risk of childhood obesity.[6-9] Nevertheless, the conclusions drawn by studies evaluating the associations between low BW and obesity appear to be controversial. Some studies suggest that low BW correlates with a significantly elevated risk for obesity.[10 11] while some other studies contradict this result, reporting that low BW is unrelated to or protective against overweight and/or obesity.[6 12 13] However, these studies only assess the effect of BW on childhood overweight or obesity but ignored childhood thinness.

Because of the absence of evidence regarding the relationship between BW and thinness and the inconsistent conclusions regarding the relationship of BW and overweight or obesity, in our large population-based observational study, we aimed to examine the relationship between BW and the risk of obesity and placed extra emphasis on the effect of thinness in 3–12–year-old children from 7 districts of Shanghai.

METHODS

Study design and quality control

Our study was a school-based cross-sectional population study and was part of a governmental population survey of autism spectrum disorders. Multistage, stratified clustered random sampling was conducted in 3 to 12-year-old children in Shanghai, China and related baseline data was collected from 134 kindergartens and 70 elementary schools in June 2014. Details of the sampling and quality control process have been described previously.[14] The 17 districts of Shanghai were stratified into eight urban districts in the central area and nine suburban areas, according to the geographical and social population distributions; people living in urban and suburban districts were defined as urban and suburban residents. EpiData 3.1 (EpiData Association, Odense, Denmark) was used for data inputting and a logical error check was applied. We also repeated data entry by randomly sampling 15% of the questionnaires to ensure consistency. The study was approved by the Institutional Review Boards of the Shanghai Municipal Commission of Health and Family Planning.

Measurements

We used growth questionnaires for collecting information about children's families and social environments. Teachers distributed questionnaires to students, asked students to take the questionnaire home and have their parents fill in the information, then the teachers collected the completed questionnaires and returned them to the investigator. Parents provided the following information about their children: age, sex, weight, height, birthweight, education level, and so on by self–report. Participants with complete birthweight, weight and height data constituted the final sample. BMI was calculated as weight divided by the square of height (kg/m^2) and classified as grade 3 thinness, grade 2 thinness, grade 1 thinness, overweight, obesity and severe obesity, according to the International Obesity Task Force age- and sex-specific cut-off points, of which BMI cut-offs equal to 16.0, 17.0, 18.5, 25.0, 30.0 and 35.0 kg/m^2 at age 18 years, respectively.[15]

Birthweight, was divided into low BW group (neonates weighing $<$ 2500 g at birth, irrespective of gestational age), normal BW group (neonates weighing: 2500–4000 g at birth, irrespective of gestational age) and high BW group (neonates weighing $\geq$4000g at birth, irrespective of gestational age).

Neonatal characteristics including gestational weeks (< 37 weeks, 37–42 weeks and ≥42 weeks), normal delivery (yes or no), single-child family (yes or no), maternal history of abortion (yes or no), asphyxia (lack of oxygen at birth, yes or no), and infant feeding patterns (breast feeding exclusively, formula feeding exclusively, mixed feeding) were considered as potential prenatal confounding factors.[6 16] Moreover, parental socioeconomic characteristics were considered as follows: family income was divided into three categories (low: < 50,000 Chinese Yuan per year; middle: 50,000–200,000 Chinese Yuan per year; high: ≥ 200,000 Chinese Yuan per year) according to the definitions of social science,[17] parental education (low: illiterate, primary school and junior school; middle: high school, technical school and college; high: undergraduate, master and doctor), and residence location (urban districts: Yangpu, Xuhui, and Jing'an; suburban districts: Minhang, Pudong, Fengxian and Chongming).

Statistical analysis

Continuous variables were presented as the mean with standard deviations (SD) and a Student's *t*-test was carried out for group comparisons. Categorical variables were presented as absolute numbers with relative frequencies (%) and inter-subgroup differences were examined using Pearson Chi-square (χ^2) test. Multivariable logistic regression was used to estimate the relationship between BW and the risk of childhood thinness and obesity with normal weight as a reference group. Odds ratio (OR) and 95% confident interval (CI) were obtained by using the multiple models. All statistical analyses were performed with IBM SPSS Statistics Version 22 (SPSS, Chicago, IL, USA). The criterion for statistical significance was 0.05 by two-tailed.

RESULTS

In total, 84,075 questionnaires were distributed and 81,384 completed questionnaires were returned with a response rate of 96.80%. Complete data regarding weight, height, and BW were available for 70,284 children. 3,359 children were born with low BW and 59,356 children were born with normal BW. 32,629 boys (52.03%) and 30,086 girls (47.97%) aged 3 to 12 years. Sex-specific variables such as growth (age, BMI category, and BW), neonatal characteristics (pregnancy term, breast-feeding, normal delivery, children number, abortion and asphyxia) and parental socioeconomic characteristics (residence, family income and parental education) were described in detail in **Table 1**.

The distribution of different BMI categories between low and normal BW was shown in **Figures 1**. For boys, the respective percentage of grade 3 thinness (3.64% vs. 2.23%, $P < 0.05$), grade 2 thinness (3.64% vs. 2.83%, $P < 0.05$), grade 1 thinness (12.95% vs. 9.00%, $P < 0.05$) were higher in the low BW group than those in the normal BW group; in contrast, the respective percentage of overweight (14.00% vs. 16.34%, $P > 0.05$), obesity (4.75% vs. 5.22%, $P > 0.05$) were lower but severe obesity (5.86% vs. 4.36%, $P < 0.05$) was higher in low BW group compared with normal group ($p < 0.05$). Meanwhile, the percentage of severe obesity and grade 3 thinness were relatively higher in low BW group compared with the normal BW group ($P < 0.05$), which shows a U-shape. The pattern is similar in girls; however in boys the percentage of grade 3 thinness (3.64% vs. 5.81%, $P < 0.05$), grade 2 thinness (3.64% vs. 4.78%, $P > 0.05$), grade 1 thinness (12.95% vs. 14.85%, $P > 0.05$) were higher but overweight(14.00% vs. 8.92%, $P < 0.05$), obesity (4.75% vs. 2.82%, $P < 0.05$) and severe obesity (5.86% vs. 4.66%, $P > 0.05$) were lower than that in girls in low BW group.

Multivariable logistic regression was used to further determine the relationship between BW and thinness, overweight and obesity after adjusting for potential confounders. As is shown in **Table 2**, an initial analysis was performed in model 1 adjusting for only age and gender variables. The results showed that low BW is significantly correlated with a higher risk for both thinness (grade 3 thinness: OR = 2.16, 95%CI = 1.82–2.56; grade 2 thinness: OR = 1.43, 95%CI = 1.20–1.70; grade 1 thinness: OR = 1.49, 95%CI = 1.34–1.65) and severe obesity (OR = 1.62, 95%CI: 1.38–1.90). In addition, model 2 is further adjusted for neonatal characteristics based on model 1 and model 3 characterized by additional adjustments for socioeconomic variables based on model 2. Still, low BW children are more likely to have grade 1 thinness (OR = 1.56, 95%CI = 1.38–1.75), grade 2 thinness (OR = 1.34, 95%CI = 1.10–1.64) and especially grade 3 thinness (OR = 1.99, 95%CI = 1.63–2.42); the pattern is consistent in the three models. The low BW remained to be statistically significant predictors of severe obesity (OR = 1.27, 95%CI = 1.03–1.55).

DISCUSSION

In the present study, we reported a bidirectional effect of low BW, increasing the risk of grade 3 thinness and severe obesity.

Some studies have assessed the relationship between low BW and the risk of childhood obesity, but the results were controversial.[6 18-22] In a systematic review and meta-analysis involving eleven studies, pooled estimates for low BW (< 2500g) revealed no correlation with obesity (pooled OR = 0.87, 95%CI = 0.69–1.08) using normal BW (2500–4000 g) as the reference category.[6] Another systematic review and meta-analysis of 30 studies found that low BW was correlated with a reduced risk of childhood obesity (pooled OR = 0.67, 95%CI = 0.59–0.76).[18] With regard to long-term risk of overweight and obesity, two previous papers have suggested a positive correlation with low BW, including a population-based cross-sectional survey among Chinese adults (obesity: OR = 1.99, 95%CI = 1.15–3.43),[11] and an observational study among older women in Sweden (obesity: OR = 1.14, 95%CI = 1.03–1.26).[10] On the contrary, a large full-range BW study reported that children with a BW less than 2,500 g were protected against overweight or obesity from 6 months to 3 years of life, but this correlation disappeared among boys at 2 years of age.[20] Our study highlighted the correlation between low BW and increased risk of severe obesity rather than overweight or obesity among the Chinese children aged between 3 and 12 years. An age-specific effect of low BW on obesity might address some of the primary reasons why previous studies have drawn contrasting conclusions. Another possible explanation was small sample size and low prevalence of obesity in low BW children, which might limit the statistical power in the analyses of associations between low BW and the risk of childhood obesity.[23]

It was difficult to explain the particular pattern between grade 1, 2 and 3 thinness, and various BW groups. In a follow up study in 2 rural Shaanxi counties of Northwest China, low

BW was not related with boys' obesity or thinness rates (adjusted OR = 2.91, 95% CI = 0.95–8.93) but significantly correlated with increased risk of thinness among girls (adjusted OR = 4.41, 95% CI = 1.77–10.97).[24] Our study confirmed the correlation and further demonstrated that low BW is correlated with an increased risk of subsequent grade 3 thinness, followed by grade 1 thinness, and then grade 2 thinness after adjusting for confounding variables. On the other hand, high BW exerted a protective effect on grade 2 thinness, followed by grade 1 thinness, then grade 3 thinness. Most notably, low BW was a risk factor for grade 3 thinness as well as severe obesity. We hypothesized that the relationship between BW and thinness, overweight or obesity risk was not directly linear, whereas the relationship between low BW and BMI was U-shaped. Low BW was an adverse perinatal environment factor which predicts changes to the central regulatory mechanism linked with negative influences on metabolism and BMI.[25] Thus, children with low BW accompanied by poor childhood weight outcomes should receive more public health attention.

Several studies have indicated that abnormal BW was an important risk factor for metabolic disease occurrence, especially for hypertension, type 2 diabetes, abdominal obesity and other chronic diseases later in life,[11 26-28] A proposed explanation for the relationship between BW and postnatal growth was through the concept of 'Developmental Origins of Health and Disease', which stated that environmental cues during critical periods of life lead to predictive adaptive responses that shaped tissue development and metabolic pathways, thereby permanently affecting long-term health and disease risk.[29] Our epidemiological observations might have implications for understanding intrauterine environmental influences during early development and the relationship of BW with later risk of thinness and obesity.

Strengths and Limitations

Our study recruited children from low- to high-income families across seven districts of the Shanghai area by a large, representative, multistage proportional cluster sampling. We were able to assess the relationship between low BW and risk of childhood thinness, obesity or severe obesity using a large sample size (n = 70,284) of children with low BW (4.61%).

What's more, we provided a comprehensive profile of the distribution of overall BMI status including grade 1, grade 2, grade 3 thinness, normal weight, overweight, obesity and severe obesity in low and normal BW groups. As for the potential confounding variables corrected in the multivariable logistic regression, we took a broad range of predictors into consideration, from prenatal to postnatal.

However, there were several limitations in our study. First, the cross-sectional nature precluded us from making cause-and-effect inferences and observing continuous age-effects and long-term effects. Second, the information, including height and weight was collected by questionnaires because of the large sample size, and there was underlying bias of self-reported data. In addition, the BW records might have been wrongly recalled by the parents or guardian, thus the degree and direction of potential bias in the results was unknown. More accurate physical examination would be conducted in future studies.

CONCLUSIONS

In summary, low BW was positively correlated with an increased risk of thinness and severe obesity but not correlated with overweight or obesity. We call for special attention for children with abnormal BW for healthier physical development during growth. We hope the pattern of thinness and obesity in different BW groups may provide valuable insights to direct healthcare policies for improving outcomes and quality in later life.

Authors' contributions

ZJ, YY, FJ and XJ helped perform the study. XJ and SL designed the research; CC drafted the manuscript and performed statistical analyses; SL contributed to the interpretation of results and critically reviewed the manuscript; SL had primary responsibility for final content. All authors read and approved the final manuscript and declared no conflict of interest. We are grateful to all parents and teachers of the children for their assistance and cooperation in this study.

Conflicts of interests

The authors declare no conflict of interest.

Ethics approval and consent to participate

This study was conducted according to the guidelines in the World Medical Association (2000) Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (http://www.wma.net/en/30publications/ 10policies/b3/) and the Guidelines for the Ethical Conduct of Medical Research Involving Children, revised in 2000 by the Royal College of Paediatrics and Child Health: Ethics Advisory Committee (Arch Dis Child 2000, 82, 177–182). All procedures involving human subjects were approved by the Institutional Review Boards of the Shanghai Municipal Commission of Health and Family Planning. Verbal informed consent was obtained from all participants, and witnessed and formally recorded. Parents were given notification and information about the survey at the beginning of the questionnaire, it is difficult to get written consent in large scale population-based cross-sectional study in China.

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Table 1 Characteristics of the study participants

Variables	Number	Boys N (%)	Girls N (%)	χ^2	*P* value
Number	62715	32629 (52.0)	30086 (48.0)		
Age (year)				2.76	0.948
3	2006	1023(3.1)	983(3.3)		
4	8186	4250(13.0)	3936(13.1)		
5	8481	4434(13.6)	4047(13.5)		
6	8237	4286(13.1)	3951(13.3)		
7	8133	4260(13.1)	3873(12.9)		
8	8540	4431(13.6)	4109(13.7)		
9	7494	3876(11.9)	3618(12.0)		
10	6477	3402(10.4)	3075(10.2)		
11	5161	2667(8.2)	2494(8.3)		
Body Mass Index Category				803.87	**<0.001**
Grade 3 Thinness	1637	752(2.3)	885(2.9)		
Grade 2 Thinness	2071	938(2.9)	1133(3.8)		
Grade 1 Thinness	6568	3001(9.2)	3567(11.9)		
Normal	38831	19502(59.8)	19329(64.3)		
Overweight	8614	5292(16.2)	3322(11.0)		
Obesity	2514	1696(5.2)	818(2.7)		
Severe obesity	2480	1448(4.4)	1032(3.4)		
Birthweight Category (g)				19.88	**<0.001**
<2500	3359	1622 (4.3)	1737 (5.3)		
2500-4000	59356	31007 (82.9)	28349 (86.2)		
Neonatal Characteristics					
Pregnancy Term (Weeks)				19.22	**<0.001**
<37	3854	2135(6.6)	1719(5.8)		

37-42	56238	29106(90.1)	27132(91.0)		
≥42	2035	1063(3.3)	972(3.3)		
Feeding Patterns (<4 Month)				4.59	0.101
Breast Feeding	30716	15925(49.1)	14791(49.5)		
Formula Feeding	9959	5119(15.8)	4840(16.2)		
Mixed Feeding	21612	11363(35.1)	10249(34.3)		
Normal Delivery				1.23	0.267
Yes	30054	15563(48.0)	14491(48.5)		
No	32226	16831(52.0)	15395(51.5)		
One-Child Family				34.94	**<0.001**
Yes	43207	22748(74.4)	20459(72.3)		
No	15665	7816(25.6)	7849(27.7)		
Abortion				3.16	0.076
Yes	14849	7818(24.2)	7031(23.5)		
No	47401	24561(75.9)	22840(76.5)		
Asphyxia				45.15	**<0.001**
Yes	2146	1269(3.9)	877(3.1)		
No	59732	30916(96.1)	28816(97.1)		
Socioeconomic Characteristics					
Area				3.20	0.074
Suburban	49231	25709(78.9)	23522(78.3)		
Urban	13371	6866(21.1)	6505(21.7)		
Income				4.92	0.086
Low	16762	8811(27.6)	7951(26.9)		
Middle	34442	17898(56.0)	16544(56.7)		
High	10279	5261(16.5)	5018(17.0)		
Mother's Education Level				48.07	**<0.001**

Low	17541	9485(31.1)	8056(28.4)		
Middle	24365	12435(40.8)	11930(42.1)		
High	16972	8629(32.1)	8343(29.5)		
Father's Education Level				33.79	**<0.001**
Low	15357	8280(27.1)	7077(25.0)		
Middle	24305	12467(40.8)	11838(41.8)		
High	19196	9805(32.1)	9391(33.2)		

BMI, body mass index.

Table 2. Association between low birthweight and thinness, overweight, obesity, severe obesity by multivariate logistic regression models.

Variables	Model 1*		Model 2 #		Model 3 &	
	Adjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Grade 3 Thinness	2.16 (1.82 - 2.56)	<0.001	2.12 (1.74 - 2.59)	<0.001	1.99 (1.63 - 2.42)	**<0.001**
Grade 2 Thinness	1.43 (1.20 - 1.70)	<0.001	1.35 (1.10 - 1.65)	<0.001	1.34 (1.10 - 1.64)	**<0.001**
Grade 1 Thinness	1.49 (1.34 - 1.65)	<0.001	1.52 (1.35 - 1.72)	<0.001	1.56 (1.38 - 1.75)	**<0.001**
Normal	Reference	-	Reference	-	Reference	**-**
Overweight	0.89 (0.80 - 1.00)	0.050	0.88 (0.77 - 1.00)	0.050	0.87 (0.76 - 0.99)	**0.040**
Obesity	1.05 (0.87 - 1.26)	0.620	1.00 (0.81 - 1.25)	0.970	0.85 (0.67 - 1.06)	0.150
Severe Obesity	1.62 (1.38 - 1.90)	<0.001	1.43 (1.18 - 1.75)	<0.001	1.27 (1.03 - 1.55)	**0.020**

OR: odds ratio; CI: confidence interval;

* Model 1 adjusted for age and gender;

Model 2 adjusted for age, gender and neonatal characteristics (pregnant term, feeding pattern, delivery mode, one child, abortion and asphyxia);

& Model 3 adjusted for age, gender, neonatal characteristics (pregnant term, feeding pattern, delivery mode, one child, abortion and asphyxia) and socioeconomic characteristics (urbanicity, parental education and family income);

- data is not available.

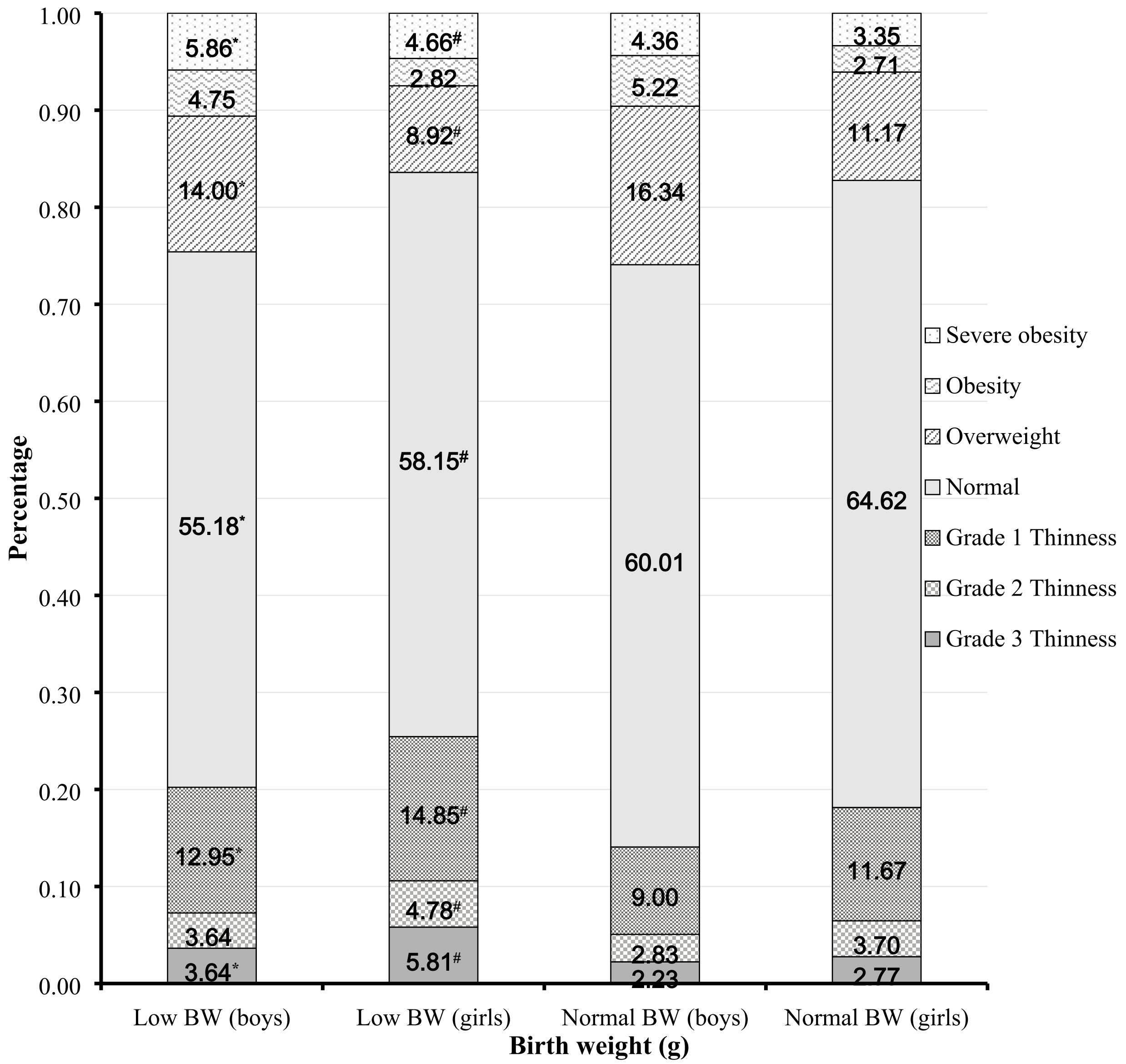

Figure 1 Percentage of thinness, overweight, obesity and severe obesity between low and normal birthweight

* Statistically significant difference between low and normal BW in boys (χ2 test, P < 0·05);

Statistically significant difference between low and normal BW in girls (χ2 test, 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	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			-
Study design	4	Present key elements of study design early in the paper	3, 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	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	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
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	-
		(*e*) Describe any sensitivity analyses	-
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	5, 6
		(b) Give reasons for non-participation at each stage	5
		(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	5,6,13,14,15
		(b) Indicate number of participants with missing data for each variable of interest	5,6,13,14,15
Outcome data	15*	Report numbers of outcome events or summary measures	5,6,13,14,15
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	5,6,13,14,15,16
		(*b*) Report category boundaries when continuous variables were categorized	5,6,13,14,15,16
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5,6,13,14,15
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5, 6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
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	8,9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8
Generalisability	21	Discuss the generalisability (external validity) of the study results	7,8,9
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	10

*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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Association of Low Birthweight with Thinness and Severe Obesity in 3 to 12-Year-Old Children: A large-scale population-based cross-sectional study in Shanghai, China.

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Keywords:	Birthweight, Obesity, Thinness, Children

Association of Low Birthweight with Thinness and Severe Obesity in 3 to 12-Year-Old Children: A large-scale population-based cross-sectional study in Shanghai, China.

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Keywords: Severe Obesity, Thinness, low Birthweight, Children

Running title:Association of Low Birthweight with Thinness and Severe Obesity

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ABSTRACT

Objectives: Low birthweight (BW) is a general symbol of inadequate intrauterine conditions that elicit abnormal fetal growth and development. The aim of current study is to investigate the relationship between low BW and thinness or severe obesity during maturation.

Design: A large-scale cross-sectional population-based survey.

Setting: 134 kindergartens and 70 elementary schools.

Participants: 70,284 Chinese children aged 3-12 years.

Primary and secondary outcome measures: International Obesity Task Force BMI cut-offs were used to define grade 1, 2, 3 thinness, overweight, obesity and severe obesity. Logistic regression was used to estimate the association between birthweight and BMI category.

Results: Total 70,284 children participated in the survey. The percentage of grade 1 thinness and severe obesity in children with low birthweight is significantly higher than that with normal birthweight ($P < 0.05$). Low BW correlated with an increased risk of grade 1 thinness (OR = 1.56, 95%CI = 1.38–1.75), grade 2 thinness (OR = 1.34, 95%CI = 1.10–1.64), grade 3 thinness (OR = 1.99, 95%CI= 1.63–2.42) and severe obesity (OR = 1.27, 95%CI = 1.03–1.55) but did not correlate with overweight.

Conclusions: The relationship between low BW and thinness or severe obesity risk is associated.

Strengths and limitations of this study:

- This study is a large population-based cross-sectional survey, with a representative, multistage proportional cluster sampling.
- Low birthweight was found to be correlated with an increased risk of grade 1 thinness, grade 2 thinness, grade 3 thinness and severe obesity, rather than overweight or obesity.
- Height/weight and birthweight was collected by self-reported questionnaires in a cross-sectional study.

INTRODUCTION

Childhood obesity is one of the most serious global public health challenges.[1] Furthermore, obesity in childhood may lead to short-term morbidity and to subsequent adverse consequences across the individual's lifespan and his or her subsequent generation.[1] Growing evidence indicates that perinatal characteristics have been recognized as contributing factors to the obesity epidemic.[2] Birthweight (BW) is frequently used as an indicator of the conditions experienced in utero which contribute to the newborn baby's survival, health, growth, and development.[3 4] Lower BW is a general symbol of inadequate intrauterine conditions that elicit abnormal fetal growth and development.[5] Based on the findings of numerous studies, low BW (birthweight < 2500g) has been shown to trigger various short-term and long-term health issues, especially for birth injuries, delayed motor development, delayed cognitive and social skills, obesity and chronic diseases.[4 6]

A great number of studies have indicated that high BW is associated with an increased risk of childhood obesity.[6-9] Nevertheless, the conclusions drawn by studies evaluating the associations between low BW and obesity appear to be controversial. Some studies suggest that low BW correlates with a significantly elevated risk for obesity.[10 11] while some other studies contradict this result, reporting that low BW is unrelated to or protective against overweight and/or obesity.[6 12 13] However, these studies only assess the effect of BW on childhood overweight or obesity but ignored childhood thinness.

Because of the absence of evidence regarding the relationship between BW and thinness and the inconsistent conclusions regarding the relationship of BW and overweight or obesity, in our large population-based observational study, we aimed to examine the relationship between BW and the risk of obesity and placed extra emphasis on the effect of thinness in 3–12–year-old children from 7 districts of Shanghai.

METHODS

Study design and quality control

Our study was a school-based cross-sectional population study and was part of a governmental population survey of autism spectrum disorders. Multistage, stratified clustered random sampling was conducted in 3 to 12-year-old children in Shanghai, China and related baseline data was collected from 134 kindergartens and 70 elementary schools in June 2014. Details of the sample size, sampling and quality control process have been described previously.[14 15] The 17 districts of Shanghai were stratified into eight urban districts in the central area and nine suburban areas, according to the geographical and social population distributions; people living in urban and suburban districts were defined as urban and suburban residents. EpiData 3.1 (EpiData Association, Odense, Denmark) was used for data inputting and a logical error check was applied. We also repeated data entry by randomly sampling 15% of the questionnaires to ensure consistency. The study was approved by the Institutional Review Boards of the Shanghai Municipal Commission of Health and Family Planning.

Measurements

We used growth questionnaires for collecting information about children's families and social environments. Teachers distributed questionnaires to students, asked students to take the questionnaire home and have their parents fill in the information, then the teachers collected the completed questionnaires and returned them to the investigator. Parents provided the following information about their children: age, sex, weight, height, birthweight, education level, and so on by self–report. Participants with complete birthweight, weight and height data constituted the final sample. BMI was calculated as weight divided by the square of height (kg/m^2) and classified as grade 3 thinness, grade 2 thinness, grade 1 thinness, overweight, obesity and severe obesity, according to the International Obesity Task Force age- and sex-specific cut-off points, of which BMI cut-offs equal to 16.0, 17.0, 18.5, 25.0, 30.0 and 35.0 kg/m^2 at age 18 years, respectively.[16]

Birthweight, was divided into low BW group (neonates weighing < 2500 g at birth, irrespective of gestational age), normal BW group (neonates weighing: 2500–4000 g at birth, irrespective of gestational age) and high BW group (neonates weighing ≥4000g at birth, irrespective of gestational age).

Neonatal characteristics including gestational weeks (< 37 weeks, 37–42 weeks and ≥42 weeks), normal delivery (yes or no), single-child family (yes or no), maternal history of abortion (yes or no), asphyxia (lack of oxygen at birth, yes or no), and infant feeding patterns (breast feeding exclusively, formula feeding exclusively, mixed feeding) were considered as potential prenatal confounding factors.[6 17] Moreover, parental socioeconomic characteristics were considered as follows: family income was divided into three categories (low: < 50,000 Chinese Yuan per year; middle: 50,000–200,000 Chinese Yuan per year; high: ≥ 200,000 Chinese Yuan per year) according to the definitions of social science,[18] parental education (low: illiterate, primary school and junior school; middle: high school, technical school and college; high: undergraduate, master and doctor), and residence location (urban districts: Yangpu, Xuhui, and Jing'an; suburban districts: Minhang, Pudong, Fengxian and Chongming).

Statistical analysis

Continuous variables were presented as the mean with standard deviations (SD) and a Student's *t*-test was carried out for group comparisons. Categorical variables were presented as absolute numbers with relative frequencies (%) and inter-subgroup differences were examined using Pearson Chi-square (χ^2) test. Multinomial logistic regression was used to estimate the relationship between BW and the risk of childhood thinness and obesity with normal weight as a reference group. Model 1 adjusted for the basic characteristics, age and gender, which were all influence factors of BMI category. Also, neonatal characteristics were reported to be associated with both birthweight and BMI category, thus were adjusted as a confounder in model 2. Socioeconomic characteristics could reflect the environment and nutritional status to some extent and were further adjusted in model 3. All confounding variables enter into the multivariate regression model. Odds ratio (OR) and 95% confident interval (CI) were obtained by using the multiple models. All statistical analyses were performed with IBM SPSS Statistics Version 22 (SPSS, Chicago, IL, USA). The criterion for statistical significance was 0.05 by two-tailed.

RESULTS

In total, 84,075 questionnaires were distributed and 81,384 completed questionnaires were returned with a response rate of 96.80%. Complete data regarding weight, height, and BW were available for 70,284 children. 3,359 children were born with low BW and 59,356 children were born with normal BW. 32,629 boys (52.03%) and 30,086 girls (47.97%) aged 3 to 12 years. Sex-specific variables such as growth (age, BMI category, and BW), neonatal characteristics (pregnancy term, breast-feeding, normal delivery, children number, abortion and asphyxia) and parental socioeconomic characteristics (residence, family income and parental education) were described in detail in **Table 1**.

The distribution of different BMI categories between low and normal BW was shown in **Figures 1**. Linear-by-linear trend test was performed and the chi-square tests value was 36.98 (P<0.001). For boys, the respective percentage of grade 3 thinness (3.64%, 95%CI 3.55-3.73%, vs. 2.23%, 95%CI 2.21-2.25%, P < 0.05), grade 2 thinness (3.64%, 95%CI 3.55-3.73%, vs. 2.83%, 95%CI 2.81-2.85%, P < 0.05), grade 1 thinness (12.95%, 95%CI 12.79-13.11%, vs. 9.00%, 95%CI 8.97-9.03%, P < 0.05) were higher in the low BW group than those in the normal BW group; in contrast, the respective percentage of overweight (14.00%, 95%CI 13.83-14.17%, vs. 16.34%, 95%CI 16.30-16.38%, P > 0.05), obesity (4.75%, 95%CI 4.65-4.85%, vs. 5.22% 95%CI 5.20-5.24%, P > 0.05) were lower but severe obesity (5.86%, 95%CI 5.75-5.97%, vs. 4.36%, 95%CI 4.34-4.38%, P < 0.05) was higher in low BW group compared with normal group (p < 0.05). Meanwhile, the percentage of severe obesity and grade 3 thinness were relatively higher in low BW group compared with the normal BW group (P < 0.05), which shows a U-shape. The pattern is similar in girls; the percentage of grade 3 thinness (5.81%, 95%CI 5.70-5.92% vs. 2.77% 95%CI 2.75-2.79%, P < 0.05), grade 2 thinness (4.78%, 95%CI 4.68-4.88% vs. 3.70%, 95%CI 3.68-3.72%, P < 0.05), grade 1 thinness (14.85%, 95%CI 14.68-15.02% vs. 11.67%, 95%CI 11.63-11.71%, P < 0.05) were higher but overweight (8.92%, 95%CI 8.79-9.05%, vs. 11.17%, 95%CI 11.13-11.21%, P < 0.05), obesity (2.82%, 95%CI 2.74-2.90%, vs. 2.71%, 95%CI 2.69-2.73,

$P > 0.05$) and severe obesity (4.66%, 95%CI 4.56-4.76% vs. 3.35%, 95%CI 3.33-3.37, $P < 0.05$) were lower in low BW group.

Multivariable logistic regression was used to further determine the relationship between BW and thinness, overweight and obesity after adjusting for potential confounders. As is shown in **Table 2**, an initial analysis was performed in model 1 adjusting for only age and gender variables. The results showed that low BW is significantly correlated with a higher risk for both thinness (grade 3 thinness: OR = 2.16, 95%CI = 1.82–2.56; grade 2 thinness: OR = 1.43, 95%CI = 1.20–1.70; grade 1 thinness: OR = 1.49, 95%CI = 1.34–1.65) and severe obesity (OR = 1.62, 95%CI: 1.38–1.90). In addition, model 2 is further adjusted for neonatal characteristics based on model 1 and model 3 characterized by additional adjustments for socioeconomic variables based on model 2. Still, low BW children are more likely to have grade 1 thinness (OR = 1.56, 95%CI = 1.38–1.75), grade 2 thinness (OR = 1.34, 95%CI = 1.10–1.64) and especially grade 3 thinness (OR = 1.99, 95%CI = 1.63–2.42); the pattern is consistent in the three models. The low BW remained to be statistically significant predictors of severe obesity (OR = 1.27, 95%CI = 1.03–1.55).

DISCUSSION

In the present study, we reported a bidirectional effect of low BW, increasing the risk of grade 3 thinness and severe obesity.

Some studies have assessed the relationship between low BW and the risk of childhood obesity, but the results were controversial.[6 19-23] In a systematic review and meta-analysis involving eleven studies, pooled estimates for low BW (< 2500g) revealed no correlation with obesity (pooled OR = 0.87, 95%CI = 0.69–1.08) using normal BW (2500–4000 g) as the reference category.[6] Another systematic review and meta-analysis of 30 studies found that low BW was correlated with a reduced risk of childhood obesity (pooled OR = 0.67, 95%CI = 0.59–0.76).[19] With regard to long-term risk of overweight and obesity, two previous papers have suggested a positive correlation with low BW, including a population-based cross-sectional survey among Chinese adults (obesity: OR = 1.99, 95%CI = 1.15–3.43),[11] and an observational study among older women in Sweden (obesity: OR = 1.14, 95%CI = 1.03–1.26).[10] On the contrary, a large full-range BW study reported that children with a BW less than 2,500 g were protected against overweight or obesity from 6 months to 3 years of life, but this correlation disappeared among boys at 2 years of age.[21] Our study highlighted the correlation between low BW and increased risk of severe obesity rather than overweight or obesity among the Chinese children aged between 3 and 12 years. An age-specific effect of low BW on obesity might address some of the primary reasons why previous studies have drawn contrasting conclusions. In a Swedish cohort with 285 marginally low BW (2000-2500g) and 95 normal birthweight children, no increased risk of overweight or obesity was observed by up to 7 years (BMI 0.47 kg/m^2 (95% CI 0.17-0.76) lower compared with controls). [24] Another possible explanation might be the potential of growth have not been fully developed among those low birthweight children. Not all low birthweight children undergo catch-up growth, and different growth pattern might exist. Special attention should be payed among those low birthweight children in future cohort study.

It was difficult to explain the particular pattern between grade 1, 2 and 3 thinness, and various BW groups. In a follow up study in 2 rural Shaanxi counties of Northwest China, low BW was not related with boys' obesity or thinness rates (adjusted OR = 2.91, 95% CI = 0.95–8.93) but significantly correlated with increased risk of thinness among girls (adjusted OR = 4.41, 95% CI = 1.77–10.97).[25] Our study confirmed the correlation and further demonstrated that low BW is correlated with an increased risk of subsequent grade 3 thinness, followed by grade 1 thinness, and then grade 2 thinness after adjusting for confounding variables. On the other hand, high BW exerted a protective effect on grade 2 thinness, followed by grade 1 thinness, then grade 3 thinness. Most notably, low BW was a risk factor for grade 3 thinness as well as severe obesity. We hypothesized that the relationship between BW and thinness, overweight or obesity risk was not directly linear, whereas the relationship between low BW and BMI was U-shaped. Low BW was an adverse perinatal environment factor which predicts changes to the central regulatory mechanism linked with negative influences on metabolism and BMI.[26] Thus, children with low BW accompanied by poor childhood weight outcomes should receive more public health attention.

Several studies have indicated that abnormal BW was an important risk factor for metabolic disease occurrence, especially for hypertension, type 2 diabetes, abdominal obesity and other chronic diseases later in life,[11 27-29] A proposed explanation for the relationship between BW and postnatal growth was through the concept of 'Developmental Origins of Health and Disease', which stated that environmental cues during critical periods of life lead to predictive adaptive responses that shaped tissue development and metabolic pathways, thereby permanently affecting long-term health and disease risk.[30] Our epidemiological observations might have implications for understanding intrauterine environmental influences during early development and the relationship of BW with later risk of thinness and obesity.

Strengths and Limitations

Our study recruited children from low- to high-income families across seven districts of the Shanghai area by a large, representative, multistage proportional cluster sampling. We were able to assess the relationship between low BW and risk of childhood thinness, obesity or severe obesity using a large sample size (n = 70,284) of children with low BW (4.61%). What's more, we provided a comprehensive profile of the distribution of overall BMI status including grade 1, grade 2, grade 3 thinness, normal weight, overweight, obesity and severe obesity in low and normal BW groups. As for the potential confounding variables corrected in the multivariable logistic regression, we took a broad range of predictors into consideration, from prenatal to postnatal.

However, there were several limitations in our study. First, the cross-sectional nature precluded us from making cause-and-effect inferences and observing continuous age-effects and long-term effects. Because etiology of thinness and obesity could not be drawn, cohort studies are still needed to track growth trajectory of low birthweight children. Second, the information, including height and weight was collected by questionnaires because of the large sample size, and there was underlying bias of self-reported data. Also, misunderstandings of the questions on neonatal outcome is another underlying risk. In addition, the BW records might have been wrongly recalled by the parents or guardian, thus the degree and direction of potential bias in the results was unknown. Our results suggest a need for carefully designed longitudinal studies with precise physical examination and indicators to document thinness and obesity among low birthweight children.

CONCLUSIONS

In summary, low BW was positively correlated with an increased risk of thinness and severe obesity but not correlated with overweight or obesity. We call for special attention for children with abnormal BW for healthier physical development during growth, and their mothers by creating a favorable environment with recommendation on physical activity and nutrition and limitation of their alcohol and tobacco consumption to lower the risk of low BW. We hope the pattern of thinness and obesity in different BW groups may provide valuable insights to direct healthcare policies for improving outcomes and quality in later life.

Patient and Public Involvement

Parents were informed about question and data of survey before filling in the questionnaires, they didn't involve the design, recruitment and conduct of the study, the results will be disseminated to participants as required.

Authors' contributions

ZJ, YY, FJ, HH and XJ helped perform the study. XJ and SL designed the research; CC drafted the manuscript and performed statistical analyses; SL and HH contributed to the interpretation of results and critically reviewed the manuscript; SL had primary responsibility for final content. All authors read and approved the final manuscript and declared no conflict of interest. We are grateful to all parents and teachers of the children for their assistance and cooperation in this study.

Conflicts of interests

The authors declare no conflict of interest.

Ethics approval and consent to participate

This study was conducted according to the guidelines in the World Medical Association (2000) Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (http://www.wma.net/en/30publications/ 10policies/b3/) and the Guidelines for the Ethical Conduct of Medical Research Involving Children, revised in 2000 by the Royal College of Paediatrics and Child Health: Ethics Advisory Committee (Arch Dis Child 2000, 82, 177–182). All procedures involving human subjects were approved by the Institutional Review Boards of the Shanghai Municipal Commission of Health and Family Planning. Verbal informed consent was obtained from all participants, and witnessed and formally recorded. Parents were given notification and information about the survey at the beginning of the questionnaire, it is difficult to get written consent in large scale population-based cross-sectional study in China.

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Data sharing statement: All data relevant to the study are included in the article.

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Table 1 Characteristics of the study participants

Variables	Number	Boys N (%)	Girls N (%)	χ^2	*P* value
Number	62715	32629 (52.0)	30086 (48.0)		
Age (year)				2.76	0.948
3-	2006	1023(3.1)	983(3.3)		
4-	8186	4250(13.0)	3936(13.1)		
5-	8481	4434(13.6)	4047(13.5)		
6-	8237	4286(13.1)	3951(13.3)		
7-	8133	4260(13.1)	3873(12.9)		
8-	8540	4431(13.6)	4109(13.7)		
9-	7494	3876(11.9)	3618(12.0)		
10-	6477	3402(10.4)	3075(10.2)		
11-	5161	2667(8.2)	2494(8.3)		
Body Mass Index Category				803.87	**<0.001**
Grade 3 Thinness	1637	752(2.3)	885(2.9)		

Grade 2 Thinness	2071	938(2.9)	1133(3.8)		
Grade 1 Thinness	6568	3001(9.2)	3567(11.9)		
Normal	38831	19502(59.8)	19329(64.3)		
Overweight	8614	5292(16.2)	3322(11.0)		
Obesity	2514	1696(5.2)	818(2.7)		
Severe obesity	2480	1448(4.4)	1032(3.4)		
Birthweight Category (g)				19.88	**<0.001**
<2500	3359	1622 (5.0)	1737 (5.8)		
2500-4000	59356	31007 (95.0)	28349 (94.2)		
Neonatal Characteristics					
Pregnancy Term (Weeks)				19.22	**<0.001**
<37	3854	2135(6.5)	1719(5.7)		
37-42	56238	29106(89.2)	27132(90.2)		
≥42	2035	1063(3.3)	972(3.2)		
Missing	588	325(1.0)	263(0.9)		

Feeding Patterns (<4 Month)				4.59	0.101
Breast Feeding	30716	15925(48.8)	14791(49.2)		
Formula Feeding	9959	5119(15.7)	4840(16.1)		
Mixed Feeding	21612	11363(34.8)	10249(34.1)		
Missing	428	222(0.7)	206(0.7)		
Normal Delivery				1.23	0.267
Yes	30054	15563(47.7)	14491(48.2)		
No	32226	16831(51.6)	15395(51.2)		
Missing	435	235(0.7)	200(0.7)		
One-Child Family				34.94	**<0.001**
Yes	43207	22748(69.7)	20459(68.0)		
No	15665	7816(24.0)	7849(21.6)		
Missing	3843	2065(6.3)	1778(5.9)		
Abortion				3.16	0.076
Yes	14849	7818(24.0)	7031(23.4)		

No	47401	24561(75.3)	22840(75.9)		
Missing	465	250(0.8)	215(0.7)		
Asphyxia				45.15	**<0.001**
Yes	2146	1269(3.9)	877(2.9)		
No	59732	30916(94.8)	28816(95.8)		
Missing	837	444(1.4)	393(1.3)		
Socioeconomic Characteristics					
Area				3.20	0.074
Suburban	49231	25709(78.8)	23522(78.2)		
Urban	13371	6866(21.0)	6505(21.6)		
Missing	113	54(0.2)	59(0.2)		
Income				4.92	0.086
Low	16762	8811(27.0)	7951(26.4)		
Middle	34442	17898(54.9)	16544(55.0)		
High	10279	5261(16.1)	5018(16.7)		

Missing	1232	659(2.0)	573(1.9)		
Mother's Education Level				48.07	**<0.001**
Low	17541	9485(29.1)	8056(26.8)		
Middle	24365	12435(38.1)	11930(39.7)		
High	16972	8629(26.4)	8343(27.7)		
Missing	3837	2080(6.4)	1757(5.8)		
Father's Education Level				33.79	**<0.001**
Low	15357	8280(25.4)	7077(23.5)		
Middle	24305	12467(38.2)	11838(39.3)		
High	19196	9805(30.0)	9391(31.2)		
Missing	3857	2077(6.4)	1780(5.9)		

BMI, body mass index.

Table 2. Association between low birthweight and thinness, overweight, obesity, severe obesity by multivariate logistic regression models.

	N	Grade 3 Thinness	Grade 2 Thinness	Grade 1 Thinness	Overweight	Obesity	Severe Obesity
Model 1	62,715	2.16 (1.82 - 2.56)	1.43 (1.20 - 1.70)	1.49 (1.34 - 1.65)	0.89 (0.80 - 1.00)	1.05 (0.87 - 1.26)	1.62 (1.38 - 1.90)
Model 2	56,909	2.12 (1.74 - 2.59)	1.35 (1.10 - 1.65)	1.52 (1.35 - 1.72)	0.88 (0.77 - 1.00)	1.00 (0.81 - 1.25)	1.43 (1.18 - 1.75)
Model 3	55,600	1.99 (1.63 - 2.42)	1.34 (1.10 - 1.64)	1.56 (1.38 - 1.75)	0.87 (0.76 - 0.99)	0.85 (0.67 - 1.06)	1.27 (1.03 - 1.55)

OR: odds ratio; CI: confidence interval;

Normal BMI as the reference group.

[*] *P* value <0.05.

Model 1: adjusted for age and gender;

Model 2: adjusted for age, gender and neonatal characteristics (pregnant term, feeding pattern, delivery mode, one child, abortion and asphyxia);

Model 3: adjusted for age, gender, neonatal characteristics (pregnant term, feeding pattern, delivery mode, one child, abortion and asphyxia) and socioeconomic characteristics (urbanicity, parental education and family income);

Figure Legend

Figure 1 Percentage of thinness, overweight, obesity and severe obesity between low and normal birthweight

* Statistically significant difference between low and normal BW in boys ($\chi 2$ test, $P < 0.05$);

[#] Statistically significant difference between low and normal BW in girls ($\chi 2$ test, $P < 0.05$).

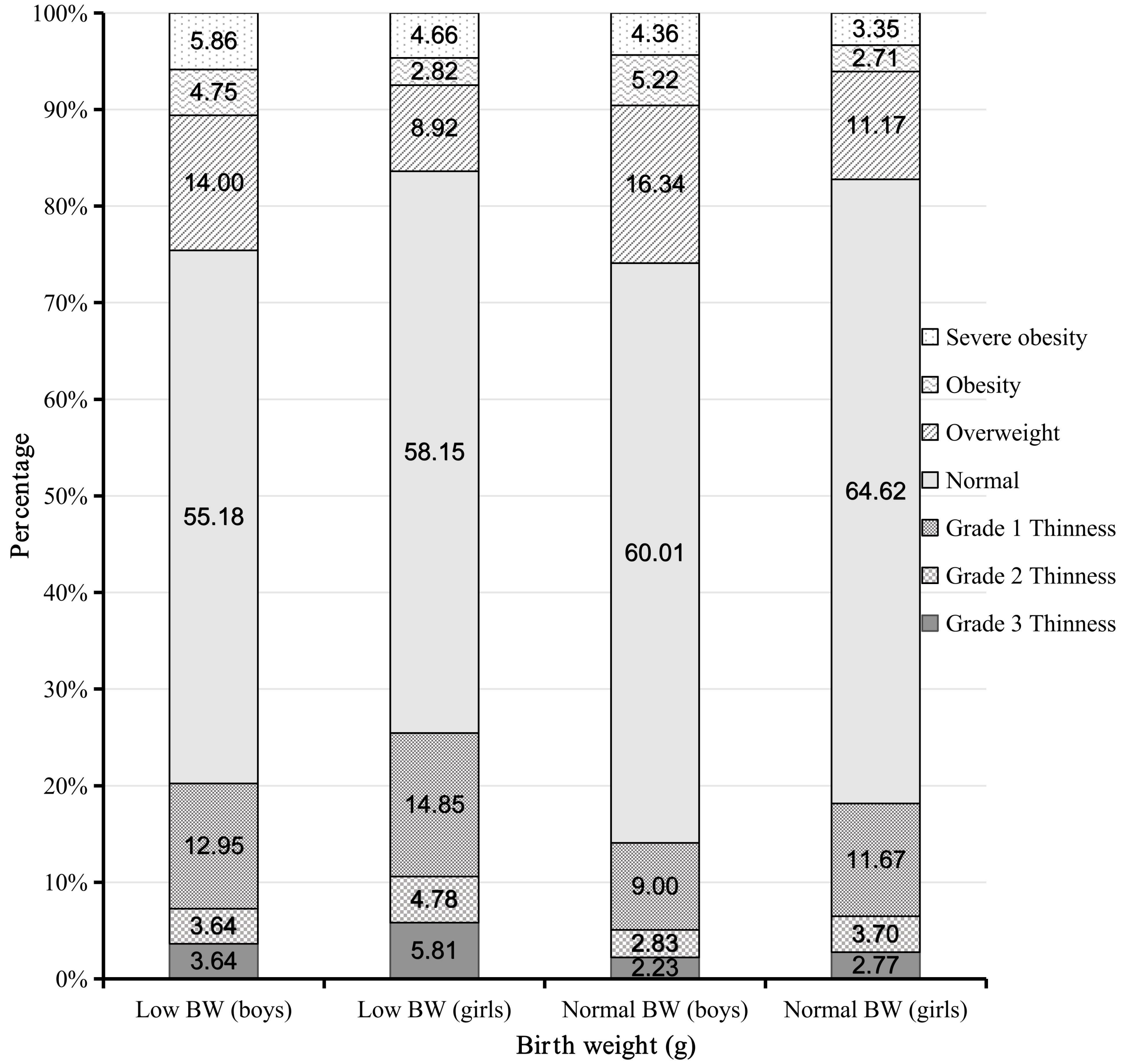

Figure 1 Percentage of thinness, overweight, obesity and severe obesity between low and normal birthweight

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	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			-
Study design	4	Present key elements of study design early in the paper	3, 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	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	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
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	-
		(*e*) Describe any sensitivity analyses	-
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	5, 6
		(b) Give reasons for non-participation at each stage	5
		(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	5,6,13,14,15
		(b) Indicate number of participants with missing data for each variable of interest	5,6,13,14,15
Outcome data	15*	Report numbers of outcome events or summary measures	5,6,13,14,15
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	5,6,13,14,15,16
		(*b*) Report category boundaries when continuous variables were categorized	5,6,13,14,15,16
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5,6,13,14,15
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5, 6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
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	8,9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8
Generalisability	21	Discuss the generalisability (external validity) of the study results	7,8,9
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	10

*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.

Association of Low Birthweight with Thinness and Severe Obesity in 3 to 12-Year-Old Children: A large-scale population-based cross-sectional study in Shanghai, China.

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Association of Low Birthweight with Thinness and Severe Obesity in 3 to 12-Year-Old Children: A large-scale population-based cross-sectional study in Shanghai, China.

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ABSTRACT

Objectives Low birthweight (BW) is a general symbol of inadequate intrauterine conditions that elicit abnormal fetal growth and development. The aim of current study is to investigate the relationship between low BW and thinness or severe obesity during maturation.

Design A large-scale cross-sectional population-based survey.

Setting 134 kindergartens and 70 elementary schools.

Participants 70,284 Chinese children aged 3-12 years.

Outcome measures International Obesity Task Force BMI cut-offs were used to define grade 1, 2, 3 thinness, overweight, obesity and severe obesity. Multinomial logistic regression was used to estimate the association between birthweight and BMI category.

Results Total 70,284 children participated in the survey. The percentage of grade 1 thinness and severe obesity in children with low birthweight is significantly higher than that with normal birthweight ($P < 0.05$). Low BW associated with an increased risk of grade 1 thinness (OR = 1.56, 95%CI = 1.38–1.75), grade 2 thinness (OR = 1.34, 95%CI = 1.10–1.64), grade 3 thinness (OR = 1.99, 95%CI= 1.63–2.42) and severe obesity (OR = 1.27, 95%CI = 1.03–1.55) but did not associate with obesity (OR = 0.85, 95%CI = 0.67–1.06).

Conclusion The relationship between low BW and thinness or severe obesity risk is associated.

Strengths and limitations of this study

- This study is a large population-based cross-sectional survey, with a representative, multistage proportional cluster sampling.
- Low birthweight was found to be associated with an increased risk of grade 1 thinness, grade 2 thinness, grade 3 thinness and severe obesity, rather than overweight or obesity.
- Height/weight and birthweight was collected by self-reported questionnaires in a cross-sectional study.

INTRODUCTION

Childhood obesity is one of the most serious global public health challenges.[1] Furthermore, obesity in childhood may lead to short-term morbidity and to subsequent adverse consequences across the individual's lifespan and his or her subsequent generation.[1] Growing evidence indicates that perinatal characteristics have been recognized as contributing factors to the obesity epidemic.[2] Birthweight (BW) is frequently used as an indicator of the conditions experienced in utero which contribute to the newborn baby's survival, health, growth, and development.[3 4] Lower BW is a general symbol of inadequate intrauterine conditions that elicit abnormal fetal growth and development.[5] Based on the findings of numerous studies, low BW (birthweight < 2500g) has been shown to trigger various short-term and long-term health issues, especially for birth injuries, delayed motor development, delayed cognitive and social skills, obesity and chronic diseases.[4 6]

A great number of studies have indicated that high BW is associated with an increased risk of childhood obesity.[6-9] Nevertheless, the conclusions drawn by studies evaluating the associations between low BW and obesity appear to be controversial. Some studies suggest that low BW correlates with a significantly elevated risk for obesity.[10 11] while some other studies contradict this result, reporting that low BW is unrelated to or protective against overweight and/or obesity.[6 12 13] However, these studies only assess the effect of BW on childhood overweight or obesity but ignored childhood thinness.

Because of the absence of evidence regarding the relationship between BW and thinness and the inconsistent conclusions regarding the relationship of BW and overweight or obesity, in our large population-based observational study, we aimed to examine the relationship between BW and the risk of obesity and placed extra emphasis on the effect of thinness in 3–12–year-old children from 7 districts of Shanghai.

METHODS

Study design and quality control

Our study was a school-based cross-sectional population study and was part of a governmental population survey of autism spectrum disorders. Multistage, stratified clustered random sampling was conducted in 3 to 12-year-old children in Shanghai, China and related baseline data was collected from 134 kindergartens and 70 elementary schools in June 2014. Details of the sample size, sampling and quality control process have been described previously.[14 15] The 17 districts of Shanghai were stratified into eight urban districts in the central area and nine suburban areas, according to the geographical and social population distributions; people living in urban and suburban districts were defined as urban and suburban residents. EpiData 3.1 (EpiData Association, Odense, Denmark) was used for data inputting and a logical error check was applied. We also repeated data entry by randomly sampling 15% of the questionnaires to ensure consistency. The study was approved by the Institutional Review Boards of the Shanghai Municipal Commission of Health and Family Planning.

Measurements

We used growth questionnaires for collecting information about children's families and social environments. Teachers distributed questionnaires to students, asked students to take the questionnaire home and have their parents fill in the information, then the teachers collected the completed questionnaires and returned them to the investigator. Parents provided the following information about their children: age, sex, weight, height, birthweight, education level, and so on by self–report. Participants with complete birthweight, weight and height data constituted the final sample. BMI was calculated as weight divided by the square of height (kg/m^2) and classified as grade 3 thinness, grade 2 thinness, grade 1 thinness, overweight, obesity and severe obesity, according to the International Obesity Task Force age- and sex-specific cut-off points, of which BMI cut-offs equal to 16.0, 17.0, 18.5, 25.0, 30.0 and 35.0 kg/m^2 at age 18 years, respectively.[16]

Birthweight, was divided into low BW group (neonates weighing < 2500 g at birth, irrespective of gestational age), normal BW group (neonates weighing: 2500–4000 g at birth, irrespective of gestational age) and high BW group (neonates weighing ≥4000g at birth, irrespective of gestational age).

Neonatal characteristics including gestational weeks (< 37 weeks, 37–42 weeks and ≥42 weeks), normal delivery (yes or no), single-child family (yes or no), maternal history of abortion (yes or no), asphyxia (lack of oxygen at birth, yes or no), and infant feeding patterns (breast feeding exclusively, formula feeding exclusively, mixed feeding) were considered as potential prenatal confounding factors.[6 17] Moreover, parental socioeconomic characteristics were considered as follows: family income was divided into three categories (low: < 50,000 Chinese Yuan per year; middle: 50,000–200,000 Chinese Yuan per year; high: ≥ 200,000 Chinese Yuan per year) according to the definitions of social science,[18] parental education (low: illiterate, primary school and junior school; middle: high school, technical school and college; high: undergraduate, master and doctor), and residence location (urban districts: Yangpu, Xuhui, and Jing'an; suburban districts: Minhang, Pudong, Fengxian and Chongming).

Statistical analysis

Continuous variables were presented as the mean with standard deviations (SD) and a Student's *t*-test was carried out for group comparisons. Categorical variables were presented as absolute numbers with relative frequencies (%). The linear-by-linear trend test were performed to detect the distribution of different BMI categories between low and normal BW and inter-subgroup differences were examined using Pearson Chi-square (χ^2) test. Multinomial logistic regression was used to estimate the relationship between BW and the risk of childhood thinness and obesity with normal weight as a reference group. Model 1 adjusted for the basic characteristics, age and gender, which were all influence factors of BMI category. Also, neonatal characteristics were reported to be associated with both birthweight and BMI category, thus were adjusted as a confounder in model 2. Socioeconomic characteristics could reflect the environment and nutritional status to some extent and were further adjusted in model 3. All confounding variables enter into the multinomial regression model. Odds ratio (OR) and 95% confident interval (CI) were obtained by using the multiple models. All statistical analyses were performed with IBM SPSS Statistics Version 22 (SPSS, Chicago, IL, USA). The criterion for statistical significance was 0.05 by two-tailed.

Patient and Public Involvement

Parents were informed about question and data of survey before filling in the questionnaires, they didn't involve the design, recruitment and conduct of the study, the results will be disseminated to participants as required.

RESULTS

In total, 84,075 questionnaires were distributed and 81,384 completed questionnaires were returned with a response rate of 96.80%. Complete data regarding weight, height, and BW were available for 70,284 children. 3,359 children were born with low BW and 59,356 children were born with normal BW. 32,629 boys (52.03%) and 30,086 girls (47.97%) aged 3 to 12 years. Sex-specific variables such as growth (age, BMI category, and BW), neonatal characteristics (pregnancy term, breast-feeding, normal delivery, children number, abortion and asphyxia) and parental socioeconomic characteristics (residence, family income and parental education) were described in detail in **Table 1**.

The distribution of different BMI categories between low and normal BW was examined by linear-by-linear trend test and the chi-square tests value was 36.98 (P<0.001). Detailed information was shown in **Figure 1**. For boys, the respective percentage of grade 3 thinness (3.64%, 95%CI 3.55-3.73%, vs. 2.23%, 95%CI 2.21-2.25%, P < 0.05), grade 2 thinness (3.64%, 95%CI 3.55-3.73%, vs. 2.83%, 95%CI 2.81-2.85%, P < 0.05), grade 1 thinness (12.95%, 95%CI 12.79-13.11%, vs. 9.00%, 95%CI 8.97-9.03%, P < 0.05) were higher in the low BW group than those in the normal BW group; in contrast, the respective percentage of overweight (14.00%, 95%CI 13.83-14.17%, vs. 16.34%, 95%CI 16.30-16.38%, P > 0.05), obesity (4.75%, 95%CI 4.65-4.85%, vs. 5.22% 95%CI 5.20-5.24%, P > 0.05) were not statistically significant but severe obesity (5.86%, 95%CI 5.75-5.97%, vs. 4.36%, 95%CI 4.34-4.38%, P < 0.05) was higher in low BW group compared with normal group (P < 0.05). Meanwhile, the percentage of severe obesity and grade 3 thinness were relatively higher in low BW group compared with the normal BW group (P < 0.05), which shows a U-shape. The pattern is similar in girls; the percentage of grade 3 thinness (5.81%, 95%CI 5.70-5.92% vs. 2.77% 95%CI 2.75-2.79%, P < 0.05), grade 2 thinness (4.78%, 95%CI 4.68-4.88% vs. 3.70%, 95%CI 3.68-3.72%, P < 0.05), grade 1 thinness (14.85%, 95%CI 14.68-15.02% vs. 11.67%, 95%CI 11.63-11.71%, P < 0.05) were higher but severe obesity (4.66%, 95%CI 4.56-4.76% vs. 3.35%, 95%CI 3.33-3.37, P < 0.05) were lower in low BW group. However, overweight (8.92%, 95%CI 8.79-9.05%, vs. 11.17%, 95%CI 11.13-11.21%, P < 0.05) and obesity (2.82%, 95%CI 2.74-2.90%, vs. 2.71%, 95%CI 2.69-2.73, P > 0.05) showed no statistical difference between the groups.

Multinomial logistic regression was used to further determine the relationship between BW and thinness, overweight and obesity after adjusting for potential confounders. As is shown in **Table 2**, an initial analysis was performed in model 1 adjusting for only age and gender variables. The results showed that low BW is significantly associated with a higher risk for both thinness (grade 3 thinness: OR = 2.16, 95%CI = 1.82–2.56; grade 2 thinness: OR = 1.43, 95%CI = 1.20–1.70; grade 1 thinness: OR = 1.49, 95%CI = 1.34–1.65) and severe obesity (OR = 1.62, 95%CI: 1.38–1.90), but did not associate with overweight (OR = 0.89, 95%CI = 0.80–1.00) or obesity (OR = 1.05, 95%CI = 0.87–1.26). In addition, model 2 is further adjusted for neonatal characteristics based on model 1 and model 3 characterized by additional adjustments for socioeconomic variables based on model 2. Still, low BW children are more likely to have grade 1 thinness (OR = 1.56, 95%CI = 1.38–1.75), grade 2 thinness (OR = 1.34, 95%CI = 1.10–1.64) and especially grade 3 thinness (OR = 1.99, 95%CI = 1.63–2.42); the pattern is consistent in the three models. The low BW remained to be statistically significant predictors of severe obesity (OR = 1.27, 95%CI = 1.03–1.55), but not associated with obesity (OR = 0.85, 95%CI = 0.67–1.06).

DISCUSSION

In the present study, we reported a bidirectional effect of low BW, increasing the risk of grade 3 thinness and severe obesity.

Some studies have assessed the relationship between low BW and the risk of childhood obesity, but the results were controversial.[6 19-23] In a systematic review and meta-analysis involving eleven studies, pooled estimates for low BW (< 2500g) revealed no association with obesity (pooled OR = 0.87, 95%CI = 0.69–1.08) using normal BW (2500–4000 g) as the reference category.[6] Another systematic review and meta-analysis of 30 studies found that low BW was associated with a reduced risk of childhood obesity (pooled OR = 0.67, 95%CI = 0.59–0.76).[19] With regard to long-term risk of overweight and obesity, two previous papers have suggested a positive association with low BW, including a population-based cross-sectional survey among Chinese adults (obesity: OR = 1.99, 95%CI = 1.15–3.43),[11] and an observational study among older women in Sweden (obesity: OR = 1.14, 95%CI = 1.03–1.26).[10] On the contrary, a large full-range BW study reported that children with a BW less than 2,500 g were protected against overweight or obesity from 6 months to 3 years of life, but this association disappeared among boys at 2 years of age.[21] Our study highlighted the association between low BW and increased risk of severe obesity rather than overweight or obesity among the Chinese children aged between 3 and 12 years. An age-specific effect of low BW on obesity might address some of the primary reasons why previous studies have drawn contrasting conclusions. In a Swedish cohort with 285 marginally low BW (2000-2500g) and 95 normal birthweight children, no increased risk of overweight or obesity was observed by up to 7 years (BMI 0.47 kg/m^2 (95% CI 0.17-0.76) lower compared with controls). [24] Another possible explanation might be the potential of growth have not been fully developed among those low birthweight children. Not all low birthweight children undergo catch-up growth, and different growth pattern might exist. Special attention should be payed among those low birthweight children in future cohort study.

It was difficult to explain the particular pattern between grade 1, 2 and 3 thinness, and various BW groups. In a follow up study in 2 rural Shaanxi counties of Northwest China, low BW was not related with boys' obesity or thinness rates (adjusted OR = 2.91, 95% CI = 0.95–8.93) but significantly correlated with increased risk of thinness among girls (adjusted OR = 4.41, 95% CI = 1.77–10.97).[25] Our study confirmed the association and further demonstrated that low BW is associated with an increased risk of subsequent grade 3 thinness, followed by grade 1 thinness, and then grade 2 thinness after adjusting for confounding variables. On the other hand, high BW exerted a protective effect on grade 2 thinness, followed by grade 1 thinness, then grade 3 thinness. Most notably, low BW was a risk factor for grade 3 thinness as well as severe obesity. We hypothesized that the relationship between BW and thinness, overweight or obesity risk was not directly linear, whereas the relationship between low BW and BMI was U-shaped. Low BW was an adverse perinatal environment factor which predicts changes to the central regulatory mechanism linked with negative influences on metabolism and BMI.[26] Thus, children with low BW accompanied by poor childhood weight outcomes should receive more public health attention.

Several studies have indicated that abnormal BW was an important risk factor for metabolic disease occurrence, especially for hypertension, type 2 diabetes, abdominal obesity and other chronic diseases later in life,[11 27-29] A proposed explanation for the relationship between BW and postnatal growth was through the concept of 'Developmental Origins of Health and Disease', which stated that environmental cues during critical periods of life lead to predictive adaptive responses that shaped tissue development and metabolic pathways, thereby permanently affecting long-term health and disease risk.[30] Our epidemiological observations might have implications for understanding intrauterine environmental influences during early development and the relationship of BW with later risk of thinness and obesity.

Strengths and Limitations

Our study recruited children from low- to high-income families across seven districts of the Shanghai area by a large, representative, multistage proportional cluster sampling. We were able to assess the relationship between low BW and risk of childhood thinness, obesity or severe obesity using a large sample size (n = 70,284) of children with low BW (4.61%). What's more, we provided a comprehensive profile of the distribution of overall BMI status including grade 1, grade 2, grade 3 thinness, normal weight, overweight, obesity and severe obesity in low and normal BW groups. As for the potential confounding variables associated in the multinomial logistic regression, we took a broad range of predictors into consideration, from prenatal to postnatal.

However, there were several limitations in our study. First, the cross-sectional nature precluded us from making cause-and-effect inferences and observing continuous age-effects and long-term effects. Because etiology of thinness and obesity could not be drawn, cohort studies are still needed to track growth trajectory of low birthweight children. Second, the information, including height and weight was collected by questionnaires because of the large sample size, and there was underlying bias of self-reported data. Also, misunderstandings of the questions on neonatal outcome is another underlying risk. In addition, the BW records might have been wrongly recalled by the parents or guardian, thus the degree and direction of potential bias in the results was unknown. Our results suggest a need for carefully designed longitudinal studies with precise physical examination and indicators to document thinness and obesity among low birthweight children.

CONCLUSIONS

In summary, low BW was positively associated with an increased risk of thinness and severe obesity but not associated with obesity. We call for special attention for children with abnormal

BW for healthier physical development during growth, and their mothers by creating a favorable environment with recommendation on physical activity and nutrition and limitation of their alcohol and tobacco consumption to lower the risk of low BW. We hope the pattern of thinness and obesity in different BW groups may provide valuable insights to direct healthcare policies for improving outcomes and quality in later life.

Contributors ZJ, YY, FJ, HH and XJ helped perform the study. XJ and SL designed the research; CC drafted the manuscript and performed statistical analyses; SL and HH contributed to the interpretation of results and critically reviewed the manuscript; SL had primary responsibility for final content. All authors read and approved the final manuscript and declared no conflict of interest. We are grateful to all parents and teachers of the children for their assistance and cooperation in this study.

Competing interests The authors declare no conflict of interest.

Ethics approval This study was conducted according to the guidelines in the World Medical Association (2000) Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (http://www.wma.net/en/30publications/ 10policies/b3/) and the Guidelines for the Ethical Conduct of Medical Research Involving Children, revised in 2000 by the Royal College of Paediatrics and Child Health: Ethics Advisory Committee (Arch Dis Child 2000, 82, 177–182). All procedures involving human subjects were approved by the Institutional Review Boards of the Shanghai Municipal Commission of Health and Family Planning. Verbal informed consent was obtained from all participants, and witnessed and formally recorded. Parents were given notification and information about the survey at the beginning of the questionnaire, it is difficult to get written consent in large scale population-based cross-sectional study in China.

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Data sharing statement All data relevant to the study are included in the article.

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Table 1 Characteristics of the study participants					
Variables	Number	Boys N (%)	Girls N (%)	χ^2	*P* value
Number	62715	32629 (52.0)	30086 (48.0)		
Age (year)				**2.76**	**0.948**
3-	2006	1023(3.1)	983(3.3)		
4-	8186	4250(13.0)	3936(13.1)		
5-	8481	4434(13.6)	4047(13.5)		
6-	8237	4286(13.1)	3951(13.3)		
7-	8133	4260(13.1)	3873(12.9)		
8-	8540	4431(13.6)	4109(13.7)		
9-	7494	3876(11.9)	3618(12.0)		
10-	6477	3402(10.4)	3075(10.2)		
11-	5161	2667(8.2)	2494(8.3)		
Body Mass Index Category				803.87	**<0.001**
Grade 3 Thinness	1637	752(2.3)	885(2.9)		
Grade 2 Thinness	2071	938(2.9)	1133(3.8)		
Grade 1 Thinness	6568	3001(9.2)	3567(11.9)		
Normal	38831	19502(59.8)	19329(64.3)		
Overweight	8614	5292(16.2)	3322(11.0)		
Obesity	2514	1696(5.2)	818(2.7)		
Severe obesity	2480	1448(4.4)	1032(3.4)		
Birthweight Category (g)				19.88	**<0.001**
<2500	3359	1622 (5.0)	1737 (5.8)		
2500-4000	59356	31007 (95.0)	28349 (94.2)		
Neonatal Characteristics					
Pregnancy Term (Weeks)				19.22	**<0.001**
<37	3854	2135(6.5)	1719(5.7)		

37-42	56238	29106(89.2)	27132(90.2)		
≥42	2035	1063(3.3)	972(3.2)		
Missing	588	325(1.0)	263(0.9)		
Feeding Patterns (<4 Month)				4.59	0.101
Breast Feeding	30716	15925(48.8)	14791(49.2)		
Formula Feeding	9959	5119(15.7)	4840(16.1)		
Mixed Feeding	21612	11363(34.8)	10249(34.1)		
Missing	428	222(0.7)	206(0.7)		
Normal Delivery				1.23	0.267
Yes	30054	15563(47.7)	14491(48.2)		
No	32226	16831(51.6)	15395(51.2)		
Missing	435	235(0.7)	200(0.7)		
One-Child Family				34.94	**<0.001**
Yes	43207	22748(69.7)	20459(68.0)		
No	15665	7816(24.0)	7849(21.6)		
Missing	3843	2065(6.3)	1778(5.9)		
Abortion				3.16	0.076
Yes	14849	7818(24.0)	7031(23.4)		
No	47401	24561(75.3)	22840(75.9)		
Missing	465	250(0.8)	215(0.7)		
Asphyxia				45.15	**<0.001**
Yes	2146	1269(3.9)	877(2.9)		
No	59732	30916(94.8)	28816(95.8)		
Missing	837	444(1.4)	393(1.3)		
Socioeconomic Characteristics					
Area				3.20	0.074
Suburban	49231	25709(78.8)	23522(78.2)		

Urban	13371	6866(21.0)	6505(21.6)		
Missing	113	54(0.2)	59(0.2)		
Income				4.92	0.086
Low	16762	8811(27.0)	7951(26.4)		
Middle	34442	17898(54.9)	16544(55.0)		
High	10279	5261(16.1)	5018(16.7)		
Missing	1232	659(2.0)	573(1.9)		
Mother's Education Level				48.07	**<0.001**
Low	17541	9485(29.1)	8056(26.8)		
Middle	24365	12435(38.1)	11930(39.7)		
High	16972	8629(26.4)	8343(27.7)		
Missing	3837	2080(6.4)	1757(5.8)		
Father's Education Level				33.79	**<0.001**
Low	15357	8280(25.4)	7077(23.5)		
Middle	24305	12467(38.2)	11838(39.3)		
High	19196	9805(30.0)	9391(31.2)		
Missing	3857	2077(6.4)	1780(5.9)		

BMI, body mass index.

Table 2. Association between low birthweight and thinness, overweight, obesity, severe obesity by multinomial logistic regression models.

	N	Grade 3 Thinness	Grade 2 Thinness	Grade 1 Thinness	Overweight	Obesity	Severe Obesity
Model 1	62,715	2.16 (1.82 - 2.56)	1.43 (1.20 - 1.70)	1.49 (1.34 - 1.65)	0.89 (0.80 - 1.00)	1.05 (0.87 - 1.26)	1.62 (1.38 - 1.90)
Model 2	56,909	2.12 (1.74 - 2.59)	1.35 (1.10 - 1.65)	1.52 (1.35 - 1.72)	0.88 (0.77 - 1.00)	1.00 (0.81 - 1.25)	1.43 (1.18 - 1.75)
Model 3	55,600	1.99 (1.63 - 2.42)	1.34 (1.10 - 1.64)	1.56 (1.38 - 1.75)	0.87 (0.76 - 0.99)	0.85 (0.67 - 1.06)	1.27 (1.03 - 1.55)

OR: odds ratio; CI: confidence interval;

Normal BMI as the reference group.

* P value <0.05.

Model 1: adjusted for age and gender;

Model 2: adjusted for age, gender and neonatal characteristics (pregnant term, feeding pattern, delivery mode, one child, abortion and asphyxia);

Model 3: adjusted for age, gender, neonatal characteristics (pregnant term, feeding pattern, delivery mode, one child, abortion and asphyxia) and socioeconomic characteristics (urbanicity, parental education and family income);

Figure Legend

Figure 1 Percentage of thinness, overweight, obesity and severe obesity between low and normal birthweight

* Statistically significant difference between low and normal BW in boys ($\chi 2$ test, $P < 0.05$);

Statistically significant difference between low and normal BW in girls ($\chi 2$ test, $P < 0.05$).

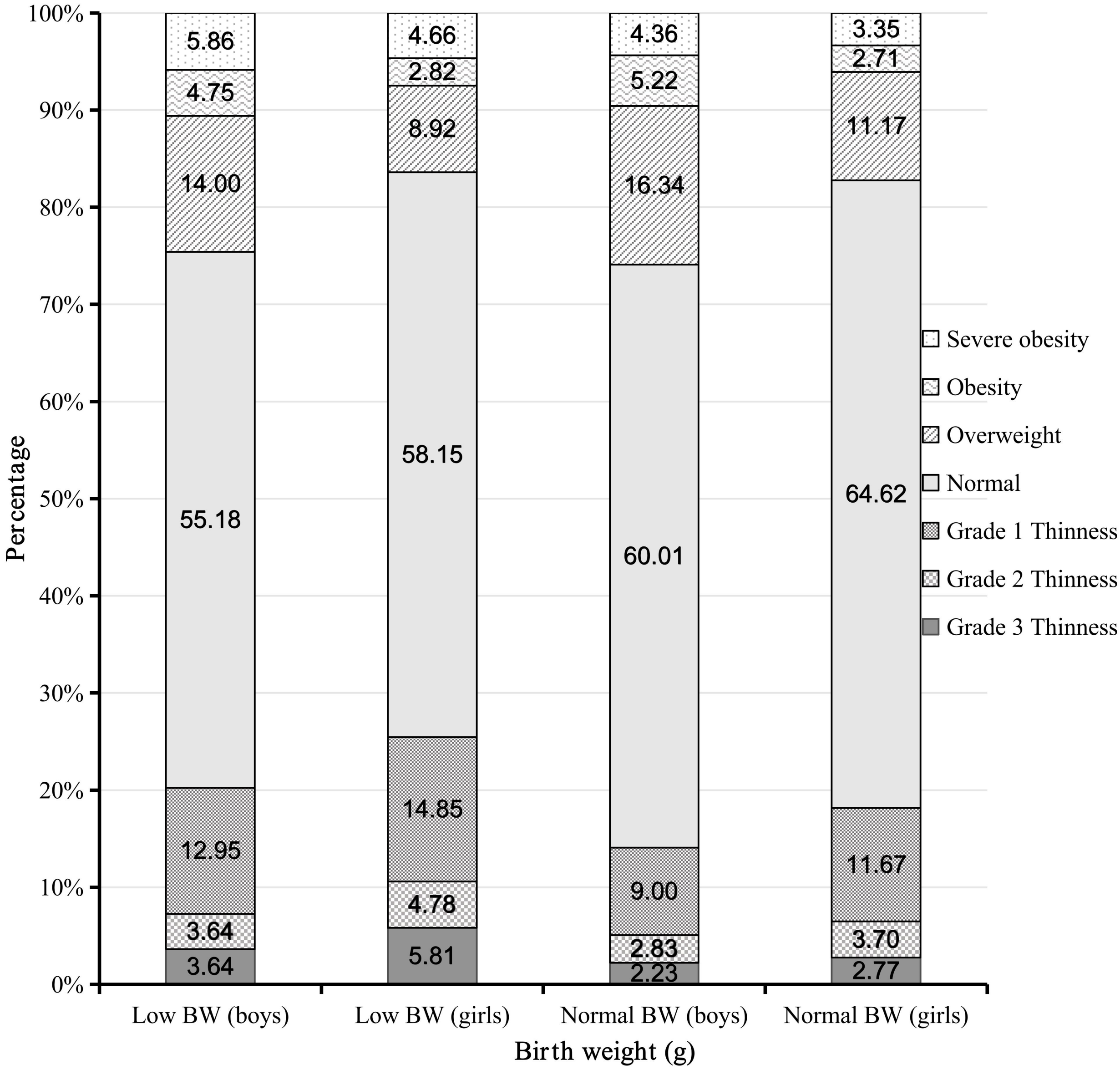

Figure 1 Percentage of thinness, overweight, obesity and severe obesity between low and normal birthweight

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	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			-
Study design	4	Present key elements of study design early in the paper	3, 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	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	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
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	-
		(*e*) Describe any sensitivity analyses	-
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	5, 6
		(b) Give reasons for non-participation at each stage	5
		(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	5,6,13,14,15
		(b) Indicate number of participants with missing data for each variable of interest	5,6,13,14,15
Outcome data	15*	Report numbers of outcome events or summary measures	5,6,13,14,15
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	5,6,13,14,15,16
		(*b*) Report category boundaries when continuous variables were categorized	5,6,13,14,15,16
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5,6,13,14,15
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5, 6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
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	8,9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8
Generalisability	21	Discuss the generalisability (external validity) of the study results	7,8,9
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	10

*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.