

## ORIGINAL ARTICLE

# Fetal macrosomia and adolescence obesity: results from a longitudinal cohort study

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**Objective:** To assess the association between fetal macrosomia and adolescent obesity.

**Design:** Longitudinal cohort study of the association between macrosomia and adolescent obesity.

**Subjects:** Between 1 October 2005 and 1 February 2007, a follow-up study of live-born infants born in 1993–1995 in Wuxi, a suburban area of Shanghai, was conducted. Subjects with birth weight > 4000 g were selected as the exposed. For each exposed subject, one subject with a birth weight of 2500–4000 g, matched by year of birth, sex of infant, and type of institute at birth, was chosen as non-exposed. Clinical data were collected by structured interview and physical examination. Obesity was defined as body mass index (weight (kg)/height (m<sup>2</sup>)) higher than the sex-age-specific criteria by the working group on obesity in China. Distribution of baseline characteristics and adolescent obesity rate between the exposed and non-exposed groups was compared.

**Results:** A total of 1435 pairs of exposed and non-exposed subjects were included in the final analysis. No major difference in baseline characteristics (other than birth weight) was found between the exposed and non-exposed groups. Obesity rate was significantly higher in the exposed group (2.9%) than in the non-exposed group (1.6%). Adolescent obesity rates were 1.4, 1.9, 2.6, and 5.6%, respectively, in study subjects with a birth weight of 2500–3499, 3500–3999, 4000–4499, and ≥4500 g. The association between birth weight and adolescent obesity remained essentially the same when mother's demographic and anthropometric factors, breast feeding, and adolescent life-style factors were adjusted.

**Conclusion:** Compared with infants of normal birth weight, infants with birth weight >4000 g, especially those >4500 g, are at increased risk of adolescent obesity.

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**Keywords:** macrosomia; body mass index; adolescence; birth weight

## Introduction

Obesity has become an epidemic.<sup>1–3</sup> Approximately 250 million people are obese worldwide, and the World Health Organization has estimated that there will be 300 million obese people in 2025.<sup>4</sup> Sixty-one percent of the US population is now above normal weight, including 20% who are obese.<sup>1</sup> About half of the adult population in Europe is

overweight or obese.<sup>5</sup> About half of adult Canadians are overweight and 15% obese.<sup>6</sup> The prevalence of childhood obesity in Canada tripled from 1981 to 1996.<sup>7</sup> Obesity is becoming a problem even in urban or suburban areas of developing countries, especially in those undergoing economic transition.<sup>8</sup>

Secular trends in birth weight have echoed the trends in body weight and obesity in childhood and adulthood, with a substantial increase over the last quarter century in many developed and developing countries.<sup>9–16</sup> In the last two decades, China has also witnessed an increasing trend of macrosomia. Studies reported that macrosomia increased from 5 to 8%<sup>17–19</sup> in several urban areas in China. At the same time, in a large national representative study consisting

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of more than 30 cities with various sizes and locations, Ji *et al.* reported that obesity rates in China increased from 0.1–0.4% in 1985 to 0.9–10.6% in 2000.<sup>20</sup> Studies on the association between fetal macrosomia and obesity in childhood, adolescence, and adulthood, mostly conducted in industrialized countries, have yielded inconsistent findings.<sup>21–27</sup>

The objective of this study was to examine the association between macrosomia at birth and subsequent obesity in adolescence in a rural population in China.

## Materials and methods

The study subjects were live-born infants born in 1993, 1994, and 1995 in Xi Shan, Hui Shan, and Jiangying Districts of Wuxi, a rural area about 200 km from Shanghai, who participated in the US–China collaborative study of periconceptional folic acid supplementation and neural tube defects in the 1990s.<sup>28</sup> We excluded subjects who were stillbirths or died before 12th birth day or had major congenital malformation or moved outside of study area before the scheduled follow-up.

From the original birth cohort of the US–China collaborative study, we selected subjects with fetal macrosomia (birth weight >4000 g) as the exposed group. For each exposed subject, one subject with normal *in utero* growth (birth weight 2500–4000 g), matched by year of birth (same), sex of infant (same), type of institute at birth (township, regional central, and tertiary centre (frequency match)), was chosen as non-exposed.

Perinatal data including maternal age, parity, occupation, educational level, body mass index (BMI, weight (kg)/height (m<sup>2</sup>)) before pregnancy, date of the last menstrual period, pregnancy complications, infant's date of birth, and birth weight were obtained from the records maintained by the local Maternal and Children Health Bureaus. Gestational age was derived from the last menstrual period and date of birth.

Research nurses approached the parents of the eligible study subjects between 1 October 2005 and 1 February 2007. The parents who agreed to participate after full explanation of the purposes and procedures of the study were asked to sign consent and to take their children to local Maternal and Children Health Bureaus for interview and physical examination. Structured questionnaire was used to collect information on current household income, outdoor physical activity, and time spent on television watching.

Obesity was the outcome variable of the study, which was defined as BMI higher than the sex-age-specific criteria set by the working group on obesity in China.<sup>20</sup> We first compared the distribution of socio-demographic and perinatal factors, and current life-style factors and adolescent obesity rates between the exposed and non-exposed groups. Obesity rates were also compared in study subjects after dividing them

into four groups according to birth weight: 2500–3499, 3500–3999, 4000–4499, and ≥4500 g. Trend  $\chi^2$  test was performed to assess possible dose-response effect of birth weight on adolescent obesity. Finally, we performed multiple logistic regression analysis to assess the independent effects of birth weight on adolescent obesity, with adjusted relative risks and 95% confidence intervals as the effect measures. Four sets of confounding factors were adjusted in the regression models: model I included mother's age and education and household income; model II included variables in model I and mother's BMI before pregnancy; model III included variables in model II and breast feeding; and model IV included variables in model III and current outdoor activity time and TV time. Conditional logistic regression analysis was performed in models comparing obesity rates for the matched exposed and non-exposed subjects, whereas non-conditional logistic regression was used in models comparing obesity rates among the four groups divided by birth weight categories. In models with four study groups, the original matches were no longer held and conditional logistic regress method is not applicable. The selection and categorization of confounding factors were determined by literature review and preliminary assessment of data collected by this study. All the data analyses were performed with the SAS package (Version 8.8; SAS Institute, Inc., Cary, North Carolina).

This study was approved by the Ethics committee of Shanghai Institute of Planned Parenthood Research, China.

## Results

A total of 1503 pairs of exposed (macrosomia) and non-exposed (birth weight 2500 to 3999 g) subjects were recruited. Among them, 1435 pairs had completed the follow-up and were included in the final analysis. The age of subjects was between 10 and 14 years (mostly 12 years of age). Nine hundred and twenty subjects were girls, whereas 1950 subjects were boys. Adolescent obesity rate was 2.4% in boys and 2.0% in girls ( $P=0.5$ ).

Table 1 compares demographic characteristics, perinatal, and current life-style risk factors. Aside from birth weight, maternal weight, and mode of delivery, no major difference was found between the exposed and non-exposed groups in these factors.

Table 2 presents the obesity rates between the two study groups. Overall, 2.2% of the participating adolescents were obese. Obesity rate was significantly higher in the exposed group (2.9%) than in the non-exposed group (1.6%). The macrosomia-associated increase in adolescent obesity remained essentially the same when mother's demographic characteristics factors were adjusted for, but the point estimate was decreased marginally (1.8 to 1.8) when mother's BMI before pregnancy was added to the regression model. When infant breast feeding and current life-style

**Table 1** Comparison of baseline characteristics, perinatal factors, and current life-style factors between exposed and non-exposed groups, Wuxi, China, 2005–2007

	Exposed (n = 1435)	Non-exposed (n = 1435 )	P-value
Birth weight in gram, mean (s.d.)	4121.3 ± 202.1	3306.6 ± 325.4	< 0.001
Gestational age in week, mean (s.d.)	40.4 ± 1.5	39.8 ± 1.7	< 0.001
Mother's age in years, mean (s.d.)	23.8 ± 3.0	23.7 ± 2.9	0.15
Mother's occupation, n (%)			
Farmer	1203 (83.8)	1203 (83.9)	0.003
Non-farmer	232 (16.2)	231 (16.1)	
Mother's education, n (%)			
Junior high school or lower	1283 (89.4)	1304 (90.9)	0.043
Senior high school or higher	152 (10.6)	130 (9.1)	
Family income			
< 10 000	268 (19.5)	309 (22.2)	0.27
10 000–15 000	243 (17.7)	242 (17.4)	
15 000–20 000	232 (16.9)	210 (15.1)	
20 000–30 000	381 (27.7)	400 (28.7)	
> 30 000	253 (18.4)	232 (16.7)	
Mother's height in cm, mean (s.d.)	160.5 ± 4.2	159.1 ± 4.5	< 0.001
Mother's weight in kg, mean (s.d.)	54.2 ± 6.2	52.6 ± 5.5	0.0051
Mother's BMI in kg/m <sup>2</sup> , mean (s.d.)	20.8 ± 2.2	20.6 ± 2.1	0.15
Hospital at delivery, n (%)			
City/provincial level	64 (4.5)	64 (4.5)	0.76
County level	339 (23.6)	339 (23.6)	
Township or village	1031 (71.9)	1031 (71.9)	
Model of delivery, n (%)			
Cesarean delivery	381 (26.6)	224 (16.7)	< 0.001
Vaginal—natural	829 (57.9)	1073 (75.00)	
Vaginal—assisted	223 (15.6)	134 (9.4)	
Feeding during infancy, n (%)			
Breast feeding, any	1142 (97.5)	1131 (97.8)	0.67
No breast feeding	29 (2.5)	26 (2.3)	
Current outdoor activity time in hour per day, n (%)			
> 2 h	259 (18.8)	255 (18.1)	0.36
1–2 h	672 (48.7)	687 (48.8)	
10 min–1 h	354 (25.7)	350 (24.8)	
No	95 (6.9)	117 (8.3)	
Current television/computer time in hour per day, n (%)			
< 1 h	536 (37.6)	601 (42.0)	0.06
1–2 h	746 (52.3)	688 (48.1)	
2–3 h	124 (8.7)	122 (8.5)	
> 3 h	21 (1.5)	19 (1.3)	

Abbreviations: BMI, body mass index; s.d., standard deviation.

**Table 2** Association between fetal macrosomia and adolescent obesity, Wuxi, China, 2005–2007

Macrosomia	# obese	Rate obese (%)	Crude RR (95% CI)	aRR <sup>+</sup> (95% CI)	aRR <sup>++</sup> (95% CI)	aRR <sup>+++</sup> (95% CI)	aRR <sup>++++</sup> (95% CI)
Yes (n = 1435)	41	2.9	1.8 (1.1–3.0)	1.8 (1.1–3.0)	1.8 (1.1–2.9)	1.8 (1.1–2.9)	1.7 (1.0–2.8)
No (n = 1435)	23	1.6	Reference	Reference	Reference	Reference	Reference

Abbreviations: CI, confidence interval; RR, relative risks. Adjusted RR<sup>+</sup>: adjusted for mother's age, mother's education, family income. Adjusted RR<sup>++</sup>: adjusted for mother's age, mother's education, family income, mother's body mass index before pregnancy. Adjusted RR<sup>+++</sup>: adjusted for mother's age, mother's education, family income, mother's body mass index before pregnancy, feed method after birth. Adjusted RR<sup>++++</sup>: adjusted for mother's age, mother's education, family income, mother's body mass index before pregnancy, feed method after birth, current outdoor activity time in hour per day, current TV time in hour per day.

**Table 3** Association between birth weight and adolescent obesity, Wuxi, China, 2005–2007

Birth weight	# obese	Rate obese (%)	Crude RR (95% CI)	aRR <sup>+</sup> (95% CI)	aRR <sup>++</sup> (95% CI)	aRR <sup>+++</sup> (95% CI)	aRR <sup>++++</sup> (95% CI)
2500–3499 ( <i>n</i> = 814)	11	1.4	Reference	Reference	Reference	Reference	Reference
3500–3999 ( <i>n</i> = 621)	12	1.9	1.7 (0.9–3.4)	1.5 (0.7–3.4)	1.5 (0.6–3.3)	1.5 (0.6–3.3)	1.4 (0.6–3.3)
4000–4499 ( <i>n</i> = 1293)	33	2.6	1.9 (1.0–3.7)	1.9 (0.9–3.7)	1.8 (0.9–3.7)	1.8 (0.9–3.7)	1.8 (0.9–3.6)
≥4500 ( <i>n</i> = 142)	8	5.6	4.2 (1.7–10.4)	4.5 (1.8–11.5)	4.3 (1.7–11.2)	4.4 (1.7–11.2)	3.7 (1.4–10.0)

Abbreviations: CI, confidence interval; RR, relative risks. Adjusted RR<sup>+</sup>: Adjusted for mother's age, mother's education, family income. Adjusted RR<sup>++</sup>: adjusted for mother's age, mother's education, family income, mother's body mass index before pregnancy. Adjusted RR<sup>+++</sup>: adjusted for mother's age, mother's education, family income, mother's body mass index before pregnancy, feed method after birth. Adjusted RR<sup>++++</sup>: adjusted for mother's age, mother's education, family income, mother's body mass index before pregnancy, feed method after birth, current outdoor activity time in hour per day, current TV time in hour per day.

factors were added to the regression models, the point estimates dropped further to 1.7, but remained statistically significant (Table 2).

Adolescent obesity rates were 1.4, 1.9, 2.6, and 5.6%, respectively, in study subjects with a birth weight of 2500–3499, 3500–3999, 4000–4499, and ≥4500 g. Although there was a overall trend of increasing obesity rates with increased birth weight ( $P < 0.01$  for  $\chi^2$  for trend), close scrutiny of the data revealed that only in the group with a birth weight ≥4500 g, the increased risk of adolescent obesity was both clinically and statistically significant (Table 3).

## Discussion

Obesity rate observed in this study was much lower than the rates reported in recent literature from various non-Chinese adolescent populations<sup>29–31</sup> and the rates reported in a national survey of Chinese cities in children aged 7 to 18 years in 2000.<sup>20</sup> As we used the same criterion to define obesity as the Chinese national survey, the lower rate observed in our study could not be explained by differences in definition. The study population was from rural areas, which may explain, at least in part, why a lower rate was observed here. On the other hand, we found that macrosomia was a risk factor for adolescent obesity, independent of major maternal demographic and anthropometric factors, breast feeding, and life-style factors of the adolescents. Furthermore, in-depth analysis by grouping study subjects into refined birth weight categories revealed that obesity risk in adolescents increased abruptly when birth weight surpassed 4500 g.

Our study took the advantage of the well designed and well implemented birth cohort created by the US–China collaborative study on folic acid supplementation and neural tube defects.<sup>28</sup> The original US–China collaborative study has collected detailed information on maternal demographic factors, prenatal care, labor and delivery, and infants' birth weight, and gestational age. Such rich information on perinatal events not only allowed a meaningful assessment of the comparability of the study groups and control for confounding by matching and regression analysis, but also reduced biases arising from recall and misclassification as well.

Obesity is known to track from the fetal period and infancy into childhood and adult life in Caucasians.<sup>32–35</sup> In a recent birth cohort study of 2135 men and 2380 women who were born at Helsinki University Central Hospital between 1934 and 1944, who attended child welfare clinics and were still resident in Finland in the year 2000, Eriksson *et al.* found that the incidence of obesity (based on lifetime maximum BMI ascertained from a postal questionnaire and defined as a BMI ≥30 kg/m<sup>2</sup>) rose linearly with increasing body size at birth.<sup>32</sup> This study also found that the mean weight and BMI of people who later became obese exceeded the average and remained above average at a statistically significant level at all ages from 6 months to 12 years.<sup>32</sup> Also, a higher maternal BMI in pregnancy was associated with a more rapid childhood growth and an increased risk of becoming obese in adult life, whereas higher socioeconomic status and better educational attainment were associated with a lower prevalence of obesity.<sup>32</sup>

Birth weight as a predictor of health in later life showed a U-shaped curve, with both low birth weight and macrosomia associated with increased risks.<sup>36,37</sup> The slow growth- and accelerated growth-related adverse health outcomes in later life may represent different disease mechanisms, and both may be modified by growth during infancy and childhood.<sup>32,35,38</sup> Therefore, the significance of macrosomia is not just for its relationship with short-term outcomes such as prolonged labor, cesarean section, and birth injury. The possibility of increased risk on long-term health outcomes, such as obesity, in childhood and adulthood of macrosomia should be considered as well.

Macrosomia ratio (975:460) was much higher in boys than in girls in our data. Although we did not calculate sex-specific macrosomia rate, the sex ratio of macrosomia cases found in our study could well represent the sex-specific macrosomia rate, as we have a quite complete ascertainment of macrosomia cases of the study communities (>90%). The phenomenon that birth weight is higher in males than in females has been consistently observed.<sup>39,40</sup> For example, in birth weight by gestational age curve based on more than 1.6 millions of infants in Norway, birth weight was higher in males than in females in every week of gestation, and for term births the difference was 115 to 170 g. Whether genetic or endocrinological factors have played a role in the sex-related difference in birth weight deserves further investigation.

Higher obesity rates in boys have been observed in some Chinese adolescent populations. For example, according to a survey conducted in 2000, the prevalence of obesity in boys aged 7–18 years was 6.5, 4.9, 4.5, and 2.0%, respectively, in Beijing, Shanghai, coastal big cities, and coastal medium/small-sized cities, whereas the prevalence of obesity in girls of the same age group was 3.7, 2.6, 2.8, and 1.7%, respectively, in these cities.<sup>20</sup> However, adolescent obesity rate in our sample was not higher in boys in our sample (2.41% versus 1.96%,  $P=0.45$ ). Of notice is that in the calculation of these rates, definition of childhood/adolescent obesity has been stratified by gender: BMI of 22.5, 23.6, 24.7, 25.7, and 26.4, respectively, for boys aged 10, 11, 12, 13, and 14 years, and 22.1, 23.3, 24.2, 25.6, and 26.3, respectively, for girls. Higher obesity rates in boys than in girls have also been reported in countries outside China,<sup>29,30</sup> but not in other studies.<sup>31,41,42</sup> Cultural and life-style factors during early childhood and adolescence could be the explanations for the differences in sex–obesity relationship reported in different populations.

In summary, our large cohort study in a rural area in China showed that macrosomia, especially birth weight >4500 g, was an independent risk factor for adolescent obesity. As interventions at population level need to balance the needs for preventing low birth weight and macrosomia simultaneously, and as our data found that a birth weight >4500 g was the critical cutoff in terms of obesity risk, a refined definition of macrosomia with 4500 g as the cutoff could be considered.

## Conflict of interest

The authors declare no conflict of interest.

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