Relationship between weight retention at 6 weeks postpartum and the risk of large-for-gestational age birth in a second pregnancy in China: a retrospective cohort study

Jing Liu,1 Guang Song,2 Ge Zhao,1 Tao Meng

ABSTRACT

Objective We aimed to investigate the association between weight retention at 6 weeks postpartum after the first pregnancy and large-for-gestational age (LGA) risk in a subsequent pregnancy.

Study design A retrospective cohort study.

Setting A tertiary hospital of China.

Participants 5950 Chinese singleton pregnancies that delivered their second singletons between 28 and 42 weeks of gestation.

Outcomes measures We calculated the weight retention at 6 weeks postpartum after the first pregnancy (the body mass index (BMI) at 6 weeks after the first birth minus the prepregnant BMI of the first pregnancy) and the gestational weight gain in the second pregnancy. We used the logistic regression to obtain adjusted OR. We determined the relationship between maternal BMI change at 6 weeks after the first pregnancy and LGA risk in the second pregnancy.

Results Relative to other categories of BMI change at 6 weeks postpartum, women who gained ≥3 kg/m² compared with the prepregnancy BMI were at increased LGA risk. The stratified analysis showed that LGA risk was increased in the second pregnancy in underweight and normal weight women who gained ≥3 kg/m² when using remain stable women as the reference group (OR=3.35, 95% CI 1.11 to 10.12 for underweight women; OR=2.23, 95% CI 1.43 to 3.45 for normal weight women) a tertiar and excessive (OR=2.62, 95% CI 1.02 to 6.76) gestational weight in the second pregnancy when using obese women as the reference.

Conclusion Postpartum weight retention at 6 weeks after the first pregnancy provides us a new early window to identify LGA risk in a subsequent pregnancy and allows us to implement primary preventative strategies.

INTRODUCTION

The incidence of maternal obesity is gradually increasing over time. During women’s life course, pregnancy is a critical intervention point for obesity development.1 Compared with the women who have not been pregnant, the women are three times more likely to develop obesity within 5 years following delivery.2 This may increase the risk of adverse outcome during subsequent pregnancies due to the risk of being obese is increased.3 4 Maternal overweight and obesity are related to the risk of long-term health problems in the child including obesity, cardiovascular disease, diabetes and cognitive and behavioural disorders.5 Encouraging women to achieve the appropriate gestational weight gain and lose weight postpartum is crucial to reduce the risk of developing obesity and improving maternal and fetal health over the life span.6 Besides gestational weight gain, postpartum weight retention (PPWR) is also affected by the duration of breastfeeding, food intake and the frequency of physical exercise.7

Strengths and limitations of this study

► This is the first study to assess the relationship between weight retention at 6 weeks postpartum after the first pregnancy and the risk of large-for-gestational age birth in a second pregnancy.

► Prepregnant body mass index before the first pregnancy and gestational weight gain during the second pregnancy were also considered when assess the relationship between weight retention at 6 weeks postpartum and the risk of large-for-gestational age birth in a second pregnancy.

► As a single-centre, retrospective cohort study, the universality of the result may be limited. It should be replicated at other centres and in other patient populations.

► Income, physical activity and breastfeeding duration were not analysed, which was the limitation of this study.
As a marker of the intrauterine environment, birth weight is a related to subsequent health and disease, such as obesity and cardiovascular disease. The incidence of large-for-gestational age (LGA) birth, defined as >90th percentile weight for gestational age, has increased over time in high-income countries, and it is associated with both childhood and adult obesity.

On average, birth weight increases with parity. The physiological conditions associated with nulliparity may induce the lower birthweights in first-born infants. It has been hypothesised that the first pregnancy primes the body and the body is more efficient with each subsequent pregnancy. Many other environmental and maternal factors which affect birth weight also vary across the reproductive lifespan of women. Maternal prepregnancy weight or weight gain during pregnancy is one of them. Changes in maternal body mass index (BMI) between pregnancies could modify the risk of LGA birth in the subsequent pregnancy. Some studies have reported that weight changes across two pregnancies are associated with LGA in the next pregnancy. However, it is too late to reduce the risk for LGA when the women attain a second pregnancy with a BMI of overweight or obese. Therefore, we should identify the high-risk women early and implement appropriate management for prevention.

In our previous study, we have demonstrated that PPWR at 6 weeks after the first pregnancy was associated with an increased risk of higher BMI in a subsequent pregnancy. In the present study, we aimed to estimate whether PPWR at 6 weeks after the first pregnancy could be the predictor of LGA risk in the subsequent pregnancy. We also use stratified analyses by category of prepregnant BMI before the first pregnancy and gestational weight gain in the second pregnancy to obtain a more carefully designed intervention to reduce the risk of LGA in the future pregnancy.

METHODS
The study is a retrospective cohort study that was carried out between January 2012 and June 2019. This was conducted among Chinese women who gave birth to their second singleton between 28 and 42 weeks of gestation at the department of obstetrics of a tertiary hospital in the Northeast of China. Exclusion criteria included: (1) women who experienced LGA in the first pregnancy, which is a risk factor for LGA; (2) women who could not provide their prenatal records for their first and second births. All participants provided written informed consent. LGA was defined as >90th percentile, of sex-specific and gestational age-specific birth weight based on the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) standards. We excluded women who experienced LGA in the first pregnancy to evaluate the first-time occurrence of LGA in the second pregnancy.

Data collection
Maternal weight in kilograms was routinely measured at the first antenatal visit of each pregnancy and it was recorded in the maternal prenatal record, which is usually taken place before 14 weeks of gestation (mean gestational age was 12.3 weeks, range from 10 weeks to 14 weeks in the first pregnancy; mean gestational age was 12.1 weeks, range from 10 weeks to 14 weeks in the second pregnancy). Maternal BMI measured at the first antenatal visit was used as the prepregnancy BMI. Maternal weight was recorded either during the last prenatal visit or before delivery. The weight at 6 weeks postpartum was also recorded in their records (mean days were 44 days, range from 40 days to 50 days after the first pregnancy; mean days were 46 days, range from 41 days to 50 days after the second pregnancy). BMI was calculated as weight (in kilograms) divided by height (in metres) squared. The weight retention at 6 weeks postpartum after the first pregnancy was defined as the BMI at 6 weeks after the first birth minus the prepregnant BMI of the first pregnancy.

BMI at the start of each pregnancy was categorised as underweight (BMI<18.5 kg/m²), normal weight (18.5 kg/m²≤BMI<24.0 kg/m²), overweight (24.0 kg/m²≤BMI<28.0 kg/m²) and obese (≥28.0 kg/m²), according to the 2016 China consensus statement on the management of overweight/obesity. The categorisation has been used in some relevant publications. We used Institute of Medicine guidelines to assess gestational weight gain in the second pregnancy because this is the most clinically relevant categorisation of weight gain and is simply classified as inadequate, adequate or excessive. Adequate weight gain was defined using gestational age-based guidelines rather than the total expected weight gain to account for the shorter time interval for weight gain in the event of preterm delivery. Adequate gestational weight gain was based on BMI class in the second and third trimesters as follows: underweight 1.0–1.3 pound/week, normal weight 0.8–1.0 pound/week, overweight 0.5–0.7 pound/week and obese 0.4–0.6 pound/week.

Interpregnancy interval was calculated as the number of complete months between the birth of the first child and the estimated date of conception of the second child. Birth weight was measured by professionals at birth as part of routine care.

Statistical analysis
First, the association between the change in BMI at 6-week postpartum and LGA in the second pregnancy was explored. Then, analyses were stratified by prepregnant BMI before the first pregnancy and gestational weight gain during the second pregnancy, respectively. At last, analyses were focused on the women who gained more than 3 BMI units to explore the high-risk people for LGA in the second pregnancy. Continuous variables were expressed as the mean±SD. Differences of continuous parameters (maternal age, prepregnant BMI before the first pregnancy and interpregnancy interval)
among four groups (BMI changes as less than −1 to −1 to less than 1, 1 to less than 3, and 3 or more BMI units, table 1) were analysed using the analysis of variance test. Univariable comparisons were carried out using the χ² test for categorical variables. Logistic regression was used to examine the association between the prepregnant BMI before the first pregnancy with the risk of LGA in the second pregnancy in table 4. Separate models for each category of gestational weight gain during the second pregnancy were run (table 4). When calculated the OR and 95% CIs, the regression was adjusted for maternal age, prepregnant BMI before the first pregnancy, gestational diabetes mellitus in the second pregnancy and interpregnancy interval. We used a stable BMI change (±1.0) at 6 weeks postpartum after the first pregnancy as a reference group in tables 2 and 3, and the prepregnant BMI category obese before

<table>
<thead>
<tr>
<th>Maternal BMI change at 6 weeks after the first pregnancy</th>
<th>Lost 1.0 or more</th>
<th>Remain stable (±1.0)</th>
<th>Gained 1.0–2.9</th>
<th>Gained 3.0 or more</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>21</td>
<td>209</td>
<td>3414</td>
<td>2306</td>
<td>–</td>
</tr>
<tr>
<td>Maternal age (years)</td>
<td>31.8±3.4</td>
<td>30.2±4.8</td>
<td>32.9±4.0</td>
<td>33.5±4.4</td>
<td>&lt;0.001</td>
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<td>Prepregnant BMI before the first pregnancy, kg/m²**</td>
<td>21.5±3.21</td>
<td>21.93±3.14</td>
<td>21.39±3.21</td>
<td>22.45±3.25</td>
<td>&lt;0.001</td>
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<tr>
<td>Prepregnant BMI before the first pregnancy (n)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Underweight (BMI &lt;18.5)</td>
<td>2 (9.5%)</td>
<td>29 (13.9%)</td>
<td>557 (16.3%)</td>
<td>272 (11.8%)</td>
<td></td>
</tr>
<tr>
<td>Normal weight (18.5≤BMI&lt;24.0)</td>
<td>13 (61.9%)</td>
<td>147 (70.3%)</td>
<td>2401 (70.3%)</td>
<td>1589 (68.9%)</td>
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</tr>
<tr>
<td>Overweight (24.0≤BMI&lt;28)</td>
<td>4 (19.0%)</td>
<td>28 (13.4%)</td>
<td>383 (11.2%)</td>
<td>359 (15.6%)</td>
<td></td>
</tr>
<tr>
<td>Obese (BMI ≥28)</td>
<td>2 (9.5%)</td>
<td>5 (2.4%)</td>
<td>73 (2.1%)</td>
<td>86 (3.7%)</td>
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<tr>
<td>Prepregnant BMI before the second pregnancy (n)†</td>
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<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>Underweight (BMI &lt;18.5)</td>
<td>3 (14.3%)</td>
<td>20 (9.6%)</td>
<td>313 (9.2%)</td>
<td>159 (6.9%)</td>
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<tr>
<td>Normal weight (18.5≤BMI&lt;24.0)</td>
<td>12 (57.1%)</td>
<td>152 (72.7%)</td>
<td>1918 (56.2%)</td>
<td>724 (31.4%)</td>
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<tr>
<td>Overweight (24.0≤BMI&lt;28)</td>
<td>4 (19.0%)</td>
<td>30 (14.4%)</td>
<td>1044 (30.6%)</td>
<td>1272 (55.2%)</td>
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<tr>
<td>Obese (BMI ≥28)</td>
<td>2 (9.5%)</td>
<td>7 (3.3%)</td>
<td>139 (4.1%)</td>
<td>151 (6.5%)</td>
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<tr>
<td>Interpregnancy interval (months)</td>
<td>48.3±19.3</td>
<td>48.6±28.5</td>
<td>43.3±26.1</td>
<td>44.0±28.2</td>
<td>0.036</td>
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<td>Gestational weight gain during the second pregnancy (n);‡</td>
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<td>&lt;0.001</td>
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<td>Inadequate</td>
<td>3 (14.3%)</td>
<td>31 (14.8%)</td>
<td>444 (13.0%)</td>
<td>184 (8.0%)</td>
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<tr>
<td>Adequate</td>
<td>9 (42.9%)</td>
<td>86 (41.1%)</td>
<td>1331 (39.0%)</td>
<td>830 (36.0%)</td>
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<tr>
<td>Excessive</td>
<td>9 (42.9%)</td>
<td>92 (44.0%)</td>
<td>1639 (48.0%)</td>
<td>1292 (56.0%)</td>
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<tr>
<td>Gestational diabetes mellitus in the second pregnancy (n)§</td>
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<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
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<td>Yes</td>
<td>4 (19.0%)</td>
<td>23 (11.0%)</td>
<td>410 (12.0%)</td>
<td>577 (25.0%)</td>
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<tr>
<td>No</td>
<td>17 (81.0%)</td>
<td>186 (89.0%)</td>
<td>3004 (88.0%)</td>
<td>1729 (75.0%)</td>
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</tr>
<tr>
<td>LGA (n)¶</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>4 (19.0%)</td>
<td>33 (15.8%)</td>
<td>547 (16.0%)</td>
<td>550 (24.0%)</td>
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<tr>
<td>No</td>
<td>17 (81.0%)</td>
<td>176 (84.2%)</td>
<td>2867 (84.0%)</td>
<td>1751 (76.0%)</td>
<td></td>
</tr>
</tbody>
</table>

*Measured at the first antenatal visit of the first pregnancy, which is usually taken place before 14 weeks.
†Measured at the first antenatal visit of the second pregnancy, which is usually taken place before 14 weeks.
‡Measured at the time of delivery of the second pregnancy.
§Measured between 24 and 28 gestational weeks of the second pregnancy. Gestational diabetes mellitus was defined according to the International Association of Diabetes and Pregnancy Study Groups; a diagnosis of gestational diabetes mellitus was made when one or more of the test parameters equalled or exceeded the following cut points: fasting 5.1 mmol/L, 1 hour 10.0 mmol/L or 2 hours 8.5 mmol/L.
¶Measured at the birth of the second pregnancy.
BMI, body mass index; LGA, large-for-gestational age.
the first pregnancy as a reference group in table 4. A two-tailed p<0.05 was used to define statistical significance. Statistical analysis was performed using STATA V.16.0 software.

Patient and public involvement
Patients or the public were not involved in the design, or conduct, or reporting or dissemination plans of our research.

RESULTS
The study population of 5950 women consisted of 21 women (0.4%) who lost 1 BMI unit at 6 weeks postpartum after the first pregnancy, 209 women (3.5%) who maintained their BMI at 6 weeks postpartum after the first pregnancy (gain or loss, 1 BMI units), 3414 women (57.4%) who gained 1-2.9 BMI units at 6 weeks postpartum after the first pregnancy and 2306 women (38.8%) who gained more than 3 BMI units at 6 weeks postpartum after the first pregnancy. In the entire study population, the prevalence LGA of during a second pregnancy was 19.1% (1134/5950). Compared with other categories of BMI change at 6 weeks postpartum after the first pregnancy, women who gained ≥3.0 kg/m² were at increased risk of LGA births (table 1).

There was an increased risk of LGA birth in the second pregnancy in underweight and normal weight women who gained ≥3.0 kg/m² when using remain stable women (BMI change <1.0) as the reference group (OR=3.35, 95% CI 1.11 to 10.12 for underweight women; OR=2.23, 95% CI 1.43 to 3.45 for normal weight women) at 6 weeks postpartum after the first pregnancy (table 2). No association was observed between the risk of LGA in the second pregnancy and the weight change at 6 weeks postpartum after the first pregnancy in overweight/obese women (table 2).

The same study population was assessed stratified by gestational weight gain in the second pregnancy.
in table 3. The risk of LGA birth was increased in the second pregnancy in women who gained ≥3 kg/m² at 6 weeks postpartum after the first pregnancy and with an adequate or excessive weight gain when using remain stable women (BMI change <1.0) as the reference group (OR=1.72, 95% CI 1.01 to 2.93 for adequate women; OR=2.14, 95% CI 1.22 to 3.75 for excessive women).

For the women who gained ≥3 kg/m² at 6 weeks postpartum after the first pregnancy, the risk of LGA birth was increased in normal weight women with an adequate (OR=3.21, 95% CI 1.10 to 9.33) and excessive (OR=2.62, 95% CI 1.02 to 6.76) gestational weight in the second pregnancy when using obese women as the reference group (table 4). The risk of LGA birth was also increased in underweight women with excessive (OR=3.18, 95% CI 1.17 to 8.66) gestational weight in the second pregnancy (table 4).

**DISCUSSION**

In the present study, we found that the proportion of LGA births was higher in women who gained more than 3 BMI units at 6 weeks postpartum (550/2306, 24.1%) compared with women who remained weight stable (33/209, 15.8%) (table 1). Both underweight and normal weight women who gained ≥3 kg/m² at 6 weeks postpartum had an increased risk of LGA birth in their second pregnancy compared with women who remained weight stable (table 2). Since larger weight gain is associated with a greater LGA risk, the goal of weight monitoring and managements should be to identify the women with a rollercoaster-type pattern of weight changes as the high-risk group who need a close follow-up. The risk assessment at 6 weeks postpartum is a new opportunity to detect women at risk for large weight gain and LGA more effectively. Underweight and normal weight women are prone to have larger weight gain than obese women; thus, they might be at the highest risk for subsequent BMI gain and the related adverse pregnancy outcomes. For women who were obese at the beginning of their first pregnancy, weight change was not associated with the subsequent pregnancy in the present study. The reason would be that the risk of LGA births is already increased in obese women, and the BMI change in obese group was not large enough to lead to a further increased risk. Getahun et al31 found that compared with women with normal BMI in both pregnancies, any increase or decrease in prepregnancy BMI between normal and obese is associated with increased risk of LGA birth, but prepregnancy BMI category changed from underweight towards normal from first to second pregnancy is not associated with increased risk of LGA. This study is different from ours in that it focused on the BMI category between two pregnancies while we investigated the change in maternal BMI in the second pregnancy regardless of whether BMI category has changed or not. The BMI changed between two pregnancies may not cause the alteration of BMI category, but it still could increase the risk of LGA.

We further found that the women who gained adequate weight in the second pregnancy still have an increased risk of LGA if their BMI change was ≥3 kg/m² at 6 weeks postpartum (table 3). Some studies suggested that a new policy regarding the need for parity-specific gestational weight gain recommendations should be discussed.33 34 The data in the present study provided support for the specific recommendations for gestational weight gain, which advise the women who had larger weight retention after the first pregnancy should have stricter weight control during the second pregnancy. In the stratified analysis, we showed even gaining adequate gestational weight in the second pregnancy, the women with a normal BMI in the first pregnancy but BMI change was ≥3 kg/m² at 6 weeks postpartum were at increased risk of LGA births (table 4), which in line with the suggestion for specific gestational weight gain recommendations. Nohr et al35 also suggested that multiparas may benefit from lower weight gain than currently recommended to avoid PPWR.

Maternal parity is a well-recognised predictor of infant birth weight, with the hypothesis that the first pregnancy...
primes the body and the body is more efficient with each subsequent pregnancy. Other factors, like maternal prepregnancy weight or weight gain during pregnancy, are also associated with birth weight. There is evidence that women who do not lose pregnancy weight at 1-year postpartum are more likely to retain weight longer term. PPWR reflects the lifestyle and nutrition habit after delivery and it increases the prepregnancy BMI of subsequent pregnancy that are factors for LGA. Furthermore, the large PPWR could induce inflammatory disorders related to reduction in insulin sensitivity, which may contribute to macrosomia through regulation of fetal nutrition. It is difficult to identify all women who are planning a pregnancy but as the inter-conception period is also the preconception period for the next pregnancy, it is important to engage with women during this period to optimize their and their children's health. Rather, behavioural changes during the postpartum period that impact lifestyle factors may have established new habits that contributed to a greater gestational weight gain in their second pregnancy. Some studies have demonstrated that the interpregnancy weight retention is associated with adverse perinatal outcomes in the subsequent pregnancy, including LGA. Our previous study showed that PPWR at 6 weeks after the first pregnancy is a good predictor for interpregnancy weight change. The relationship between PPWR at 6 weeks and the risk of LGA in the second pregnancy would provide us new evidence in support to encourage women to achieve postpartum weight loss.

Since the announcement that China’s one-child policy was to be replaced by a universal two-child policy effective from 2016, it allowed approximately 90 million primiparous women of childbearing age to have the option of a second pregnancy. The appearance of multiparas leads to women of childbearing age to have the option of a new early time point for the next pregnancy, including LGA. As far as we know, this is the first large-scale study to investigate the association between PPWR at 6 weeks and LGA risk in the subsequent pregnancy in China. Our study had several limitations. The generalisability of the findings of this retrospective study is limited by one centre, the demographic characteristics of the sample are not representative of the national population. Furthermore, participants in the present study were all Chinese women; thus, the effect of lifestyle and dietary habits on PPWR and LGA might be different from other races. Another important limitation was the lack of information on breastfeeding duration, which is the potential confounder related to interpregnancy weight gain and LGA birth. Meantime, the confounders such as education, income, physical activity and postterm pregnancy were also not analysed in this study.

CONCLUSION
A large weight retention at 6 weeks postpartum after the first pregnancy was associated with LGA risk in the second pregnancy, even for the women with a normal BMI in the first pregnancy gaining adequate gestational weight in the second pregnancy. PPWR at 6 weeks after the first pregnancy provides us a new early time point to identify LGA risk in the second pregnancy and allows clinicians to implement primary strategies for prevention. Diet control and physical exercise should be suggested to the women who retained large weight at 6 weeks postpartum. Parity-specific individual gestational weight gain recommendations also should be taken into consideration for multiparas according to PPWR at 6 weeks after the first pregnancy.
REFERENCES


