# scientific reports



# **OPEN**

# Saturation effects of pre-pregnancy BMI on infant birth weight in Jiangxi Province, China: a retrospective study

Jun Xiong¹, Huan Li²,³, Xiao-Qing Tan²,³, Xiao-Ju He¹™ & Wen-Yan Fu⁴™

There were limited analyses on relationship between body mass index (BMI) pre-pregnancy, as well as birth weight. Research aimed to examine the relation between these two, as well as low birth weight (LBW) risk in Jiangxi Province, China. A total of 1193 pregnant subjects from Jiangxi Province, China were enrolled in the final analysis. Standardized questionnaires were administered to the women during childbirth, newborns' medical information was obtained from hospital records. Pre-pregnancy BMI was categorized into underweight, normal, overweight, and obese groups. Multivariate linear regression models were employed to assess connection between pre-pregnancy BMI, birth weight. We utilized generalized additive model and fitted smoothing curve (penalized spline method) to examine relationship between pre-pregnancy BMI and birth weight, as well as LBW risk. The incidence of LBW was 12.1%, with average pre-pregnancy BMI of 20.9 ± 2.5 kg/m<sup>2</sup>. The smoothing curve revealed an L-shaped association between pre-pregnancy BMI, birth weight and LBW risk. The curve indicated that as pre-pregnancy BMI increased, LBW risk initially decreased and then plateaued, while birth weight initially escalated and then plateaued. The inflection point for pre-pregnancy BMI was identified as 22 kg/m<sup>2</sup>. On the left side of inflection point,  $\beta$  (95% CI) for birth weight was 0.04 (0.02, 0.07), and ORs (95% CIs) for LBW risk were 0.78 (0.69, 0.89), on the right side the corresponding values were - 0.00 (-0.03, 0.03) and 1.02 (0.88, 1.19), respectively. All the outcomes presented to be similar in various subgroups. Within a specific range (BMI<22 kg/m<sup>2</sup>), the correlation between pre-pregnancy BMI and birth weight is statistically significant. This research indicated pre-pregnancy BMI demonstrates a saturation effect on birth weight and LBW risk among Jiangxi Province population.

**Keywords** Pre-pregnancy BMI, Low birth weight, Birth weight, Jiangxi

# Abbreviations

BMI body mass index LBW low birth weight ANC antenatal care units DU delivery units SD standard deviation OR odds ratio

CI confidence interval

In both epidemiological investigations and clinical settings, birth weight serves as a primary indicator of newborn health, owing to its robust correlation with morbidity and mortality in the early stages of life<sup>1,2</sup>. Infants with low or high birth weight face an elevated perinatal death rate and adverse outcomes extending into childhood to adulthood <sup>1,3–5</sup>. The high birth weight of newborns are commonly found in developed countries or regions<sup>3</sup>, while in the case of developing areas, low birth weight (LBW)has always been the key factor to reduce the survival rate of newborns<sup>5,6</sup>.

<sup>1</sup>Department of Obstetrics and Gynecology, The Second Affiliated Hospital of Nanchang University, Nanchang 330006, China. <sup>3</sup>The Second Clinical Medical College of Nanchang University, Nanchang 330006, China. <sup>4</sup>Department of Pharmacy, The Second Affiliated Hospital of Nanchang University, Nanchang 330006, China. <sup>△</sup>Department of Pharmacy, The Second Affiliated Hospital of Nanchang University, Nanchang 330006, China. <sup>△</sup>Department of Pharmacy, The Second Affiliated Hospital of Nanchang University, Nanchang 330006, China. <sup>△</sup>Department of Pharmacy, The Second Affiliated Hospital of Nanchang University, Nanchang 330006, China. <sup>△</sup>Department of Pharmacy, The Second Affiliated Hospital of Nanchang University, Nancha

Birth weightresults from complex interplay of psychological, biological, and socioeconomic factors<sup>7,8</sup>. Biologically, matrilineal nutrition and metabolism status, the functioning of placenta, and the fetal and matrilineal genetic background play significant roles<sup>9-11</sup>. Body mass index (BMI), equaling weight (kg)/height squared (m<sup>2</sup>), stands as a universally recognized measure for evaluating maternal nutritional status<sup>12,13</sup>. Compared with other biochemical and genetic indicators, the pre- pregnancy BMI value is relatively easier to obtain and adjust through diet and exercise<sup>12,14,15</sup>. Therefore, many scholars study the correlation between birth weight as well as BMI in pre-pregnancy, in order to find correlations underneath, for the regulation of birth weight. To date, there has been inconsistency in the findings of studies examining correlation between BMI in pregnancy and both birth weight and LBW risk. For instance, Mohamed et al. 16 reported that a lower BMI in pregnancy was linked to higher likelihood of LBW. Trombe et al. pointed out, despite high BMI in pregnancy results in infants with high birth weight, there is no correlation observed between low BMI in pregnancy and LBW (RR = 1.70; 95% CI: 0.81-3.55). Pre-pregnancy BMI is closely associated with obstetric complications such as gestational diabetes and preeclampsia, which may serve as mediators in the relationship between pre-pregnancy BMI and birthweight<sup>17,18</sup>. These studies were regionally limited to non Asian populations. Furthermore, the majority of studies have primarily explored the linear correlation between BMI in pregnancy and birth weight, and LBW risk, without delving into the nonlinear aspects of this relationship. Jiangxi Province, located in central China, has a certain degree of representativeness in terms of its geography, climate, and population structure, making it a good representation of the fertility and health conditions in vast rural and small-to-medium-sized urban areas of China. Hence, study aims to examine the connection between pre-pregnancy BMI, as well as both birth weight and LBW risk in Jiangxi Province, China, in order to provide support for counseling guidelines aimed at optimizing preconception health and pregnancy outcomes.

### Methods

#### **Ethics statements**

The study obtained ethical approval given by ethics review boards of the Second Affiliated Hospital of Nanchang University. All methods were performed in accordance with the relevant guidelines and regulations. Subjects provided written informed consent to be included in research. In cases where subjects couldn't provide written consent, fingerprinting was utilized as an alternative method. The outlined procedure received approval from ethics committee.

#### Study population

This retrospective study was carried out within the antenatal care units (ANC) and delivery units (DU) of the Second Affiliated Hospital of Nanchang University in Jiangxi Province, China. Pregnant women aged 16 to 50 years, seeking routine care at the ANC or presenting at the DU, were chosen for study. Recruitment and enrollment were conducted between September 2022 and September 2023.

#### **Enrollment process**

Within the DÜ, a total of 1632 pregnant or delivering women underwent referral and screening. Out of this group, 1256 individuals were briefed on the study protocol. Subsequently, the 1256 subjects who chose to participate were verified by experienced technical staff, focusing on collecting data related to obstetric complications during pregnancy, birth weight, and socio-demographic characteristics. Post to the exclusion of individuals who delivered before 28 weeks (n=25), those for whom weight and/or height measurements could not be obtained (n=29), cases of multiple gestations (n=6), and instances of stillbirth (n=3), 1193 participants were finally included (see Fig. 1).

#### Definitions for birth weight and maternal variables

Gestational age was determined based on the last menstruation, with ultrasounds used for ambiguity or doubt regarding fetal positioning and gestational age estimation confirmation. LBW infants were defined as those weighing less than 2500 g at birth. Measurements of weight and height for each subject were directly obtained when admission and delivery, while pre-pregnancy weight was reported for the calculation of pregnancy weight gain and BMI in pregnancy. WHO definitions for Asian populations were employed, categorizing underweight (BMI <  $18.5 \text{ kg/m}^2$ ), normal ( $18.5 \text{ BMI} < 23 \text{ kg/m}^2$ ), and overweight or obese (BMI  $\geq 23 \text{ kg/m}^2$ ).

#### Statistical analysis

Categorical variables in baseline information was presented as mean  $\pm$  SD, for continuous variables, count or percentage. Continuous and categorical variables utilized statistical comparisons, conducted using Student's t-test and  $\chi^2$  analysis, respectively. Correlation between weight during pre-pregnancy and LBW risk was examined through multivariate logistic regression analysis, adjusting for factors such as newborn sex, gestational age of delivery, maternal age, education, gestational weight gain, smoking habits, parity, and the number of antenatal visits. Similarly, we also used multivariate linear regression models for the correlation analysis between BMI in pregnancy and birth weight. Basis for inclusion of covariates in our multivariate analysis: (1) Factors that are statistically significant in univariate analysis; (2) Factors that may clinically influence birth weight; (3) Reference to other literature. To further characterize the relationship between BMI in pregnancy and birth weight, as well as LBW risk, we also applied generalized additive model and fitted smoothing curve (penalized spline method). In the case of detecting nonlinearity, a recursive algorithm was used to identify inflection points. Subsequently, two-segment binary logistic or linear regression model was constructed on both sides of the inflection points. To enhance reliability, we conducted subgroup analyses through stratified multivariate regression. Statistical analyses were conducted by R (http://www.R-project.org, the R Foundation), Empower (R; www.empowerstats.com; X&Y Solutions, Inc, Boston, MA). P-values were two-tailed, statistical significance: P < 0.05.

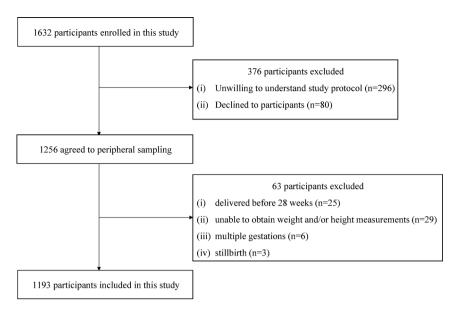


Fig. 1. Flow chart of study participants.

### **Results**

#### **Basic characteristics**

Table 1 presents data from 1193 subjects comprised within current analysis. The participants had a mean (SD) age of 28.7(4.6) years. Overall incidence of LBW was 12.1%, with the LBW incidence increasing to 22.2% in the underweight group. When compared to pregnant women with low BMI in pregnancy, those with higher BMI in pregnancy exhibited a greater likelihood of longer gestation duration, lower gestational weight gain, and older age (all P < 0.05). There was no significant difference among the 3 BMI groups on newborn sex, education levels, parity, antenatal visits, and maternal smoking habits (all P > 0.05).

#### Correlation between BMI in pregnancy, birth weight and LBW risk

Table 2 shows that all the adjusted models (models 1–3) in terms of potential confounders showed positive correlations of BMI in pre-pregnancy and birth weight. If BMI in pre-pregnancy was evaluated to be tertiles, the adjusted  $\beta$  of BMI in pre-pregnancy within final adjusted model (model 3) on birth weight regarding subjects in tertiles 2 and 3 reached 0.16 (95% CI: 0.07, 0.25) and 0.20 (95% CI: 0.09, 0.31), separately, in comparison to the data in tertile 1 (P for trend < 0.001). In Table 2, in comparison to subjects in the tertile 1, the adjusted ORs of BMI in pre-pregnancy on LBW regarding subjects in the tertiles 2 and 3 reached 0.37 (95% CI: 0.24, 0.59) and 0.36 (95% CI: 0.20, 0.65), separately.

# Saturation effect analysis of BMI in pre-pregnancy on LBW risk and birth weight

We employed a generalized additive model and the penalized spline method to explore the nonlinear relationship between BMI in pre-pregnancy, LBW risk and birth weight (Fig. 2a and b). The fully adjusted smoothing curve exhibited non-linear correlation between BMI in pre-pregnancy and both LBW risk and birth weight. As BMI in pre-pregnancy escalated, the LBW risk declined initially and then stabilized, while birth weight exhibited an initial increase followed by a plateau. A visual examination of the curve suggested an inflection point at approximately 22 kg/m². Subsequently, we fitted the association between BMI in pre-pregnancy, LBW risk, and birth weight, using a two-piecewise binary logistic and linear regression model (Table 3). Identified inflection point for BMI in pre-pregnancy was 22 kg/m². On the inflection point left side (BMI in pre-pregnancy  $\leq$  22 kg/m²), the  $\beta$  (95% CI) for birth weight was 0.04 (0.02, 0.07), while on the right side, it was -0.00 (-0.03, 0.03). The odds ratios (ORs) (95% CIs) for LBW risk were 0.78 (0.69, 0.89) on the left side, and 1.02 (0.88, 1.19) on the right side. These findings indicated that the association between increased birth weight and a reduced LBW risk with BMI in pre-pregnancy levels was evident on inflection point left side (BMI in pre-pregnancy  $\leq$  22 kg/m²).

# Potential effect modifiers stratified analyses

Stratified analyses were carried out for influence evaluation exerted by BMI in pre-pregnancy on birth weight within a range of subgroups (Fig. 3). Subgroup analysis indicated the absence of significant interactions across various subgroups, encompassing maternal age (<25, 25-34,  $\ge 35$  years old), education (no formal education, primary, secondary/university+), smoking habit (no vs. yes), newborn sex (male vs. female), gestational age of delivery (28-33, 34-36,  $\ge 37$  weeks), parity (0, 1-2,  $\ge 3$ ), and antenatal visits (0-4 vs.  $\ge 5$ ) in 2 cohorts (all P for interactions > 0.05).

| Characteristics                          | Total        | pre-pregnancy BMI (kg/m²)                      |             |                                |          |
|--|--------------|--|-------------|--------------------------------|----------|
|  |              | Underweight, T1 (<18.5)   Normal, T2(18.5-<23) |             | Overweight and obese, T3 (≥23) | P- value |
| N  | 1193         | 176  | 808         | 209                            |          |
| Gestational weight gain (kg)             | 12.6 ± 3.8   | 12.9 ± 3.6                                     | 12.8 ± 3.9  | 11.5±3.7                       | < 0.001  |
| Maternal age (year), n (%)               |              |  |             |                                | 0.163    |
| <25                                      | 293 (24.1%)  | 53 (30.1%)                                     | 189 (23.4%) | 44 (21.1%)                     |          |
| 25–34                                    | 785 (64.7%)  | 110 (62.5%)                                    | 526 (65.1%) | 139 (66.5%)                    |          |
| ≥ 35                                     | 136 (11.2%)  | 13 (7.4%)                                      | 93 (11.5%)  | 26 (12.4%)                     |          |
| Education                                |              |  |             |                                | 0.915    |
| No formal education                      | 217 (17.9%)  | 31 (17.6%)                                     | 144 (17.8%) | 41 (19.6%)                     |          |
| Primary                                  | 549 (45.2%)  | 83 (47.2%)                                     | 366 (45.3%) | 89 (42.6%)                     |          |
| Secondary/University+                    | 448 (36.9%)  | 62 (35.2%)                                     | 298 (36.9%) | 79 (37.8%)                     |          |
| Gestation age at delivery (weeks), n (%) |              |  |             |                                | < 0.001  |
| 28-33+6                                  | 43 (3.5%)    | 14 (8.0%)                                      | 21 (2.6%)   | 7 (3.3%)                       |          |
| 34-36+6                                  | 99 (8.2%)    | 23 (13.1%)                                     | 50 (6.2%)   | 25 (12.0%)                     |          |
| ≥ 37                                     | 1072 (88.3%) | 139 (79.0%)                                    | 737 (91.2%) | 177 (84.7%)                    |          |
| Sex of the newborn, n (%)                |              |  |             |                                | 0.819    |
| Male                                     | 673 (55.4%)  | 95 (54.0%)                                     | 443 (54.8%) | 119 (56.9%)                    |          |
| Female                                   | 541 (44.6%)  | 81 (46.0%)                                     | 365 (45.2%) | 90 (43.1%)                     |          |
| Parity                                   |              |  |             |                                | 0.08     |
| 0  | 573 (47.2%)  | 74 (42.0%)                                     | 394 (48.8%) | 93 (44.5%)                     |          |
| 1-2                                      | 595 (49.0%)  | 95 (54.0%)                                     | 389 (48.1%) | 102 (48.8%)                    |          |
| ≥3                                       | 46 (3.8%)    | 7 (4.0%)                                       | 25 (3.1%)   | 14 (6.7%)                      |          |
| Smoking habit, n (%)                     |              |  |             |                                | 0.358    |
| Yes                                      | 51 (4.2%)    | 9 (5.1%)                                       | 34 (4.2%)   | 5 (2.4%)                       |          |
| No                                       | 1163 (95.8%) | 167 (94.9%)                                    | 774 (95.8%) | 204 (97.6%)                    |          |
| Antenatal visits, n (%)                  |              |  |             |                                | 0.198    |
| 0-4                                      | 122 (10.0%)  | 21 (11.9%)                                     | 81 (10.0%)  | 14 (6.7%)                      |          |
| ≥5                                       | 1092 (90.0%) | 155 (88.1%)                                    | 727 (90.0%) | 195 (93.3%)                    |          |
| LBW, n (%)                               |              |  |             |                                | < 0.001  |
| No                                       | 1067 (87.9%) | 137 (77.8%)                                    | 729 (90.2%) | 184 (88.0%)                    |          |
| Yes                                      | 147 (12.1%)  | 39 (22.2%)                                     | 79 (9.8%)   | 25 (12.0%)                     |          |

**Table 1**. Baseline characteristics of study participants data are presented as N (percentage), mean  $\pm$  standard deviation.

#### Discussion

Within our retrospective research, we identified a nonlinear, dose-response correlation between BMI in prepregnancy and both birth weight and LBW risk, with an inflection point at 22 kg/m². On the left side, as BMI in pre-pregnancy increased, there was a corresponding escalation within birth weight and a decrease in LBW risk. Conversely, on the right side, no discernible relationship was observed between BMI in pre-pregnancy and birth weight or LBW risk. This observation suggests that BMI in pre-pregnancy exhibits a saturation effect on LBW risk and birth weight.

Adverse perinatal complications may arise from both excessively high or low BMI in pre-pregnancy. Similarly, macrosomia and LBW rate is also influenced by BMI in pre-pregnancy. In a study by Vince et al.<sup>21</sup>, involving 32,051 pregnant women in Croatia, it was observed that low BMI in pre-pregnancy increased LBW risk, while obese pregnant women faced an elevated macrosomia risk. Similarly, a descriptive-analytical study involving Iranian pregnant women at 28-36 weeks of gestation revealed positive correlation between maternal BMI in pre-pregnancy and birth weight  $(P=0.02)^{22}$ . However, conflicting conclusions have been reported in some studies regarding correlation between BMI in pre-pregnancy and birth weight<sup>23-25</sup>. For instance, a prospective study involving 34,104 pregnant women in Central China<sup>26</sup> revealed diverse BMI categories: 14.4% underweight (n=4,920), 70.2% normal weight (n=23,925), 12.7% overweight (n=4,334), and 2.7% obese (n=925). This study underscored the correlation between maternal pre-pregnancy overweight and obesity, and an elevated LBW risk (overweight: OR = 1.720, 95%  $CI = 1.533 \sim 1.930$ ; obesity: OR = 1.710, 95%  $CI = 1.360 \sim 2.151$ ). Interestingly, it also revealed that underweight was similarly correlated with escalated LBW risk (OR=1.438, 95% CI=1.294~1.599). Similarly, a prospective cross-sectional study in Pakistan found that compared with normal weight cohort, underweight subjects had elevated LBW risk (P<0.01) and decreased macrosomia risk  $(P < 0.01)^{27}$ . Nevertheless, overweight and obese subjects showed no significant differences from normal-weight cohort in deliver of macrosomic neonates (P=0.89 and P=0.66, respectively). Nakanishi et al.<sup>28</sup> emphasized that, dose-response correlation between low BMI in pre-pregnancy severity and LBW was evident only within low BMI range. Our study contributes additional evidence, when pre-pregnancy BMI <22 kg/m<sup>2</sup>, the correlation

| pre-pregnancy BMI (kg/m2)        | Event (%) | Model 1           | Model 2           | Model 3           |  |  |  |
|----------------------------------|-----------|-------------------|-------------------|-------------------|--|--|--|
|                                  |           | β(95% CI)         | β(95% CI)         | β(95% CI)         |  |  |  |
| Birth weight                     |           |                   |                   |                   |  |  |  |
| Per 1 kg/m <sup>2</sup> increase |           | 0.02(0.01, 0.03)  | 0.02 (0.01, 0.03) | 0.02 (0.01, 0.04) |  |  |  |
| Tertiles                         |           |                   |                   |                   |  |  |  |
| Underweight, T1 (<18.5)          | 39(22.2)  | 0.00              | 0.00              | 0.00              |  |  |  |
| Normal, T2 (18.5-< 23)           | 79(9.8)   | 0.16 (0.07, 0.25) | 0.16 (0.07, 0.25) | 0.16 (0.07, 0.25) |  |  |  |
| Overweight and obese, T3 (≥23)   | 25(12.0)  | 0.18 (0.07, 0.29) | 0.17 (0.06, 0.29) | 0.20 (0.09, 0.31) |  |  |  |
| P for trend                      |           | < 0.001           | < 0.001           | < 0.001           |  |  |  |
|                                  | Event (%) | OR(95% CI)        | OR(95% CI)        | OR(95% CI)        |  |  |  |
| LBW                              |           |                   |                   |                   |  |  |  |
| Per 1 kg/m <sup>2</sup> increase |           | 0.90 (0.84, 0.98) | 0.90 (0.83, 0.98) | 0.88 (0.81, 0.95) |  |  |  |
| Tertiles                         |           |                   |                   |                   |  |  |  |
| Underweight, T1 (<18.5)          | 39(22.2)  | 1                 | 1                 | 1                 |  |  |  |
| Normal, T2 (18.5-< 23)           | 79(9.8)   | 0.38 (0.25, 0.58) | 0.38 (0.25, 0.58) | 0.37 (0.24, 0.59) |  |  |  |
| Overweight and obese, T3 (≥23)   | 25(12.0)  | 0.48 (0.28, 0.83) | 0.47 (0.27, 0.83) | 0.36 (0.20, 0.65) |  |  |  |
| P for trend                      |           | < 0.001           | < 0.001           | < 0.001           |  |  |  |

**Table 2**. Association of pre-pregnancy BMI with birth weight and LBW in different models. Model 1: adjusted none. Model 2: adjusted maternal age, education. Model 3: adjusted smoking habit, antenatal visits, sex of the newborn, education, gestational weight gain, maternal age, parity and gestation age at delivery.

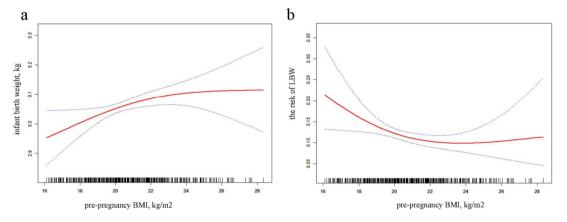


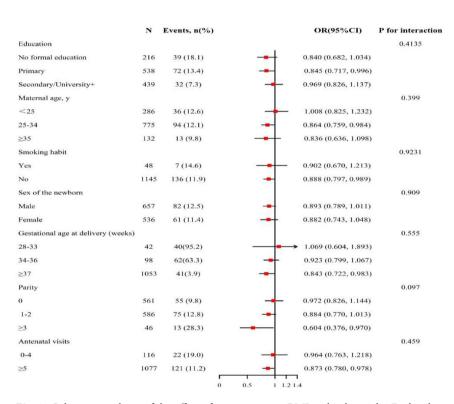
Fig. 2. Association between the pre-pregnancy BMl and birth weight (a) and the risk of LBW (b). A saturation, nonlinear association between the pre-pregnancy BMl and birth weight was found (p < 0.05). The solid line and dashed line represent the estimated values and their comesponding 9\$% confidence interval. Adjustment factors included smoking habit, antenatal visits, sex of the newborn, education, gestational weight gain, maternal age, parity and ges lation age at delivery.

between pre-pregnancy BMI and birthweight is statistically significant. This aligns with the findings of previous studies, collectively suggesting that BMI in pre-pregnancy primarily affects birth weight. The reason may be that, the maternal and fetal health status are directly coupled. Maternal well-being and appropriate nutritional status intricately control fetal metabolic signaling pathways, guiding the process of "fetal programming"<sup>29–31</sup>. When a mother has a low BMI before pregnancy, it could be a result of persistent inadequate energy intake and malnutrition. This condition may lead to reduced fat stores and a compromise in visceral and somatic cell protein status<sup>32</sup>. Additionally, a prolonged period of having a low BMI before pregnancy might increase the energy demands during pregnancy<sup>32</sup>, resulting in an energy deficit throughout the entire gestational period. This deficit might be insufficient to provide the necessary substrates for supporting the growth of fetal tissues. Gestational age is a critical determinant of birth weight. Low pre-pregnancy BMI increases the risk of preterm birth<sup>17</sup>, thereby limiting fetal nutrient acquisition and impairing intrauterine growth, ultimately affecting birth weight.

In this study, we delved into the nonlinear relationship between BMI in pre-pregnancy, birth weight, and LBW risk. Our findings revealed inconsistent trends in correlation between BMI in pre-pregnancy and both birth weight and LBW risk on both sides of the identified inflection point (22 kg/m²). Specifically, on the left side (BMI < 22 kg/m²), the  $\beta$  (95% CIs) for birth weight was 0.04 (0.02, 0.07), and the ORs (95% CI) for LBW risk were 0.78 (0.69, 0.89). Conversely, on the right side (BMI ≥ 22 kg/m²), the  $\beta$  (95% CIs) for birth weight

|                                  |            | Model 1             |         | Model 2             |         | Model 3             |         |
|----------------------------------|------------|---------------------|---------|---------------------|---------|---------------------|---------|
| pre-pregnancy BMI (kg/m2)        | Event (%)  | β(95% CI)           | P       | β(95% CI)           | P       | β(95% CI)           | P       |
| Birth weight                     |            |                     |         |                     |         |                     |         |
| Per 1 kg/m <sup>2</sup> increase |            | 0.02 (0.01,0.03)    | 0.004   | 0.02 (0.01, 0.03)   | < 0.001 | 0.02 (0.01, 0.04)   | < 0.001 |
| Inflection point                 |            |                     |         |                     |         |                     |         |
| <22                              | 104 (12.1) | 0.04 (0.02, 0.07)   | < 0.001 | 0.04 (0.02, 0.06)   | < 0.001 | 0.04 (0.02, 0.07)   | < 0.001 |
| ≥22                              | 39 (11.6)  | -0.01 (-0.03, 0.02) | 0.537   | -0.01 (-0.03, 0.02) | 0.518   | -0.00 (-0.03, 0.03) | 0.979   |
| P for log likelihood ratio test  |            | 0.017               |         | 0.006               |         | 0.042               |         |
|                                  | Event (%)  | OR(95% CI)          | P       | OR(95% CI)          | P       | OR(95% CI)          | P       |
| LBW                              |            |                     |         |                     |         |                     |         |
| Per 1 kg/m <sup>2</sup> increase |            | 0.90 (0.84, 0.98)   | 0.011   | 0.90 (0.83, 0.98)   | 0.011   | 0.88 (0.81, 0.95)   | < 0.001 |
| Inflection point                 |            |                     |         |                     |         |                     |         |
| <22                              | 104 (12.1) | 0.79 (0.70, 0.89)   | < 0.001 | 0.79 (0.70, 0.89)   | < 0.001 | 0.78 (0.69, 0.89)   | < 0.001 |
| ≥22                              | 39 (11.6)  | 1.10 (0.95, 1.26)   | 0.205   | 1.10 (0.95, 1.27)   | 0.196   | 1.02 (0.88, 1.19)   | 0.784   |
| P for log likelihood ratio test  |            | 0.006               |         | 0.006               |         | 0.032               |         |

**Table 3**. Saturation effect analysis of pre-pregnancy BMI on the risk of LBW and birth weight. Model 1: adjusted none. Model 2: adjusted maternal age, education. Model 3: adjusted smoking habit, antenatal visits, sex of the newborn, education, gestational weight gain, maternal age, parity and gestation age at delivery.



**Fig. 3.** Subgroup analyses of the effect of pre-pregnancy BMI on birth weight. Each subgroup analysis adjusted for maternal age, education, parity, gestational age of delivery, sex of the newborn, smoking habit, the number of antenatal visits.

was -0.00 (-0.03, 0.03), and the ORs (95% CI) for the LBW risk were 1.02 (0.88, 1.19). These results suggest that the increased birth weight and decreased LBW risk associated with BMI in pre-pregnancy levels were prominent on the left side (BMI < 22 kg/m²), and the development of birth weight did not significantly increase with the increment of BMI in pre-pregnancy in participants with BMI  $\ge 22$  kg/m². Many previous studies have reported the correlation between pre-pregnancy BMI and birth weight<sup>23,33,34</sup>. What distinguishes our study is the discovery of a saturation effect, along with the identification of a BMI cutoff point of 22 kg/m², which is consistent with Ronnenberg's research<sup>32</sup>. Furthermore, these prior researches never elucidate the reasons for the saturation effects, and the variations in ethnic background, lifestyle behaviors, living conditions, BMI levels, and adjustments of confounding factors were not adequately addressed. Our research population comes from economically underdeveloped regions in southern China, while Vince's research population from Croatia and

Javadi in northwestern Iran. The impact of BMI in pre-pregnancy on populations of different races or regions may be heterogeneous. Due to regional and ethnic differences, there are differences in the normal range of BMI, which may affect the birth weight. In our study, the normal range of BMI is 18.5–23 kg/m², which is far lower than 18.5–24.9 kg/m² in the study of Andraweera et al.<sup>35</sup>. Only 4.2% subjects had the habit of smoking in our study, while 11.8% of pregnant women smoked in Günther's study<sup>36</sup>. The influence of BMI in pre-pregnancy on pregnant women, especially those with diverse lifestyles such as smoking, may exhibit heterogeneity. Additionally, as BMI in pre-pregnancy increases, there is an augmented risk of medical conditions like pregnant women with diabetes complicated by vascular lesions and hypertension<sup>17,18</sup>, exerting a negative impact on birth weight. And this negative impact offsets the positive effect of increased pre-pregnancy BMI on birthweight, resulting in a saturation effect. Given the observed saturation effect of BMI on birth weight and LBW risk, it becomes imperative to explore alternative strategies for preventing the occurrence of LBW.

Our study comes with notable strengths that enrich the interpretation of our findings. Set in Jiangxi Province, a region with economic underdevelopment in southern China, our research zone features generally low BMI in pre-pregnancy values. This distinctive context provides a rare opportunity to scrutinize the interplay between BMI and birth weight within a lower BMI range. Additionally, we took a nuanced approach by delving into and explaining the nonlinear correlation between BMI in pre-pregnancy and both birth weight and LBW risk. This exploration adds a layer of understanding to the intricate dynamics of how BMI in pre-pregnancy influences birth outcomes. Recognizing the inherent limitations of observational studies and their susceptibility to potential confounding, we applied rigorous statistical adjustments to mitigate the impact of residual confounders. This meticulous approach enhances the credibility and applicability of our results, contributing to the overall strength of our study. Therefore, to optimize pregnancy management, we recommend (1) developing individualized nutrition and exercise guidance based on pre-pregnancy BMI, (2) integrating pre-pregnancy BMI into electronic health record automated alert systems, and (3) establishing coordinated tiered management through community physician-nutritionist teams, aiming to improve pregnancy outcomes.

Our study has several limitations that warrant consideration. Firstly, owing to the retrospective design, causal inferences cannot be drawn from the data, and the observed associations do not imply causation. Secondly, participants in our study were recruited exclusively from Jiangxi Province in southern China, where BMI values tend to be generally low. As a result, the generalizability of our conclusions to other regions should be approached with caution and requires further validation. Thirdly, the lack of information on hypertensive disorders of pregnancy, gestational diabetes mellitus, and past medical history in our study may have limited our comprehensive understanding of the relationship between pre-pregnancy BMI and birth weight. Lastly, despite our efforts to account for numerous influencing factors, possibility still exists that some potential confounding factors were not included in our analysis.

# **Conclusions**

In summary, our study suggested BMI in pre-pregnancy value saturation effect on the birth weight and LBW risk among Jiangxi Province populations. Maternal BMI in pre-pregnancy values<22 kg/m² were associated with decreased LBW risk and increased birth weight. Additional research is essential for the true impact of BMI in pre-pregnancy on birth weight, and LBW risk, along with potential underlying mechanisms at play.

# Data availability

The authors confirm that the data supporting the findings of this study are available within the article.

Received: 31 January 2024; Accepted: 15 May 2025 Published online: 22 May 2025

#### References

- 1. World Health Organization. UNICEF-WHO Low Birthweight Estimates: Levels and Trends 2000–2015 (United Nations Children's Fund (UNICEF), 2019).
- Kale, P. L. & Fonseca, S. C. Intrauterine growth restriction, prematurity, and low birth weight: risk phenotypes of neonatal death, Rio de Janeiro State, Brazil. Cad. Saude Publica. 39 (6), e00231022. https://doi.org/10.1590/0102-311XPT231022 (2023). PMID: 37377302; PMCID: PMC10547104.
- 3. Dalfra', M. G., Burlina, S. & Lapolla, A. Weight gain during pregnancy: A narrative review on the recent evidences. *Diabetes Res Clin Pract.*;188:109913. (2022). https://doi.org/10.1016/j.diabres.2022.109913. (2022).
- 4. Nedelec, R., Miettunen, J., Männikkö, M., Järvelin, M. R. & Sebert, S. Maternal and infant prediction of the child BMI trajectories; studies across two generations of Northern Finland birth cohorts. *Int. J. Obes. (Lond)*;45(2):404–414. (2021). https://doi.org/10.1038/s41366-020-00695-0. (2020).
- Hamadneh, S. & Hamadneh, J. Active and passive maternal smoking during pregnancy and birth outcomes: A study from a developing country. Ann. Glob. Health. 87 (1), 122. https://doi.org/10.5334/aogh.3384 (2021). PMID: 34900622; PMCID: PMC8641528.
- Erasun, D. et al. Low birth weight trends in organisation for economic Co-operation and development countries, 2000–2015: economic, health system and demographic conditionings. BMC Pregnancy Childbirth. 21 (1), 13. https://doi.org/10.1186/s12884-020-03484-9 (2021).
- Trombe, K. S. D. et al. Is birth weight associated with pregestational maternal BMI? BRISA cohort, Ribeirão Preto, Brazil. Braz J. Med. Biol. Res. 54 (1), e10037. https://doi.org/10.1590/1414-431X202010037 (2020).
- 8. Xiong, J. et al. Maternal anaemia and birth weight: a cross-sectional study from Jiangxi Province, China. Fam Pract. https://doi.org/10.1093/fampra/cmac148. (2023).
- Diabelková, J. et al. Risk factors associated with low birth weight. Cent. Eur. J. Public Health.; 30(Supplement):S43-S49. (2022). https://doi.org/10.21101/cejph.a6883. PMID: 35841225.
- Le, K. & Nguyen, M. Armed conflict and birth weight. Econ. Hum. Biol. 39, 100921. https://doi.org/10.1016/j.ehb.2020.100921 (2020).

- 11. Aizawa, M. et al. Association between frequency of breakfast intake before and during pregnancy and infant birth weight: the Tohoku medical megabank project birth and Three-Generation cohort study. *BMC Pregnancy Childbirth.* **23** (1), 268. https://doi.org/10.1186/s12884-023-05603-8 (2023).
- 12. Parrettini, S., Caroli, A. & Torlone, E. Nutrition and metabolic adaptations in physiological and complicated pregnancy: focus on obesity and gestational diabetes. Front. Endocrinol. (Lausanne). 11, 611929. https://doi.org/10.3389/fendo.2020.611929 (2020).
- 13. Voerman, E. et al. Maternal body mass index, gestational weight gain, and the risk of overweight and obesity across childhood: an individual participant data meta-analysis. *PLoS Med.* 16 (2), e1002744. https://doi.org/10.1371/journal.pmed.1002744 (2019).
- 14. Thakali, K. M., Zhong, Y., Cleves, M., Andres, A. & Shankar, K. Associations between maternal body mass index and diet composition with placental DNA methylation at term. *Placenta* 93, 74–82. https://doi.org/10.1016/j.placenta.2020.02.018 (2020).
- 15. Rogozińska, E. et al. Effects of antenatal diet and physical activity on maternal and fetal outcomes: individual patient data meta-analysis and health economic evaluation. *Health Technol. Assess.* 21 (41), 1–158. https://doi.org/10.3310/hta21410 (2017).
- Mohamed, H. J. J. et al. Maternal diet, nutritional status and infant birth weight in Malaysia: a scoping review. BMC Pregnancy Childbirth. 22 (1), 294. https://doi.org/10.1186/s12884-022-04616-z (2022).
- 17. Vats, H., Saxena, R., Sachdeva, M. P., Walia, G. K. & Gupta, V. Impact of maternal pre-pregnancy body mass index on maternal, fetal and neonatal adverse outcomes in the worldwide populations: A systematic review and meta-analysis. *Obes. Res. Clin. Pract.* 15 (6), 536–545 (2021).
- 18. Sun, Y. et al. Effects of pre-pregnancy body mass index and gestational weight gain on maternal and infant complications. *BMC Pregnancy Childbirth.* **20** (1), 390. https://doi.org/10.1186/s12884-020-03071-y (2020).
- 19. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* **363** (9403), 157–163 (2004).
- 20. Chen, Y. H. et al. Influent factors of gestational vitamin D deficiency and its relation to an increased risk of preterm delivery in Chinese population. Sci. Rep. 8 (1), 3608. https://doi.org/10.1038/s41598-018-21944-3 (2018).
- Vince, K., Brkić, M., Poljičanin, T. & Matijević, R. Prevalence and impact of pre-pregnancy body mass index on pregnancy outcome: a cross-sectional study in Croatia. J. Obstet. Gynaecol. 41 (1), 55-59 (2021).
- Javadi, M., Rafiei, S., Zahedifar, F. & Barikani, A. Relationships between maternal characteristics and infant birth weight. *Int. J. Health Care Qual. Assur.*;32(4):688–697. (2019). https://doi.org/10.1108/IJHCQA-05-2017-0081. PMID: 31111782.
- 23. Bhowmik, B. et al. Maternal BMI and nutritional status in early pregnancy and its impact on neonatal outcomes at birth in Bangladesh. BMC Pregnancy Childbirth. 19 (1), 413. https://doi.org/10.1186/s12884-019-2571-5 (2019). PMID: 31711436; PMCID: PMC6849244.
- Tucker, A. R., Brown, H. L. & Dotters-Katz, S. K. Maternal weight gain and infant birth weight in women with class III obesity. Am. J. Perinatol. 38 (8), 816–820. https://doi.org/10.1055/s-0039-3402721 (2021). Epub 2019 Dec 31. PMID: 31891955.
- 25. Comas Rovira, M. et al. The influence of obesity and diet quality on fetal growth and perinatal outcome. *Nutr Hosp.*;39(6):1205–1211. English.https://doi.org/10.20960/nh.04076. (2022).
- Wei, J. et al. Parental pre-pregnancy body mass index and risk of low birth weight in offspring: A prospective cohort study in central China. Front. Public. Health. 10, 1036689. https://doi.org/10.3389/fpubh.2022.1036689 (2022).
- Gul, R. et al. Pre-pregnancy maternal BMI as predictor of neonatal birth weight. PLoS One. 15 (10), e0240748. https://doi.org/10.1371/journal.pone.0240748 (2020).
- 28. Nakanishi, K. et al. Severity of low pre-pregnancy body mass index and perinatal outcomes: the Japan environment and children's study. BMC Pregnancy Childbirth. 22, 121 (2022).
- 29. Hambidge, K. M. et al. Anthropometric indices for non-pregnant women of childbearing age differ widely among four low-middle income populations. *BMC* 18, 45 (2018).
- 30. Marciniak, A. et al. Fetal programming of the metabolic syndrome. Taiwan. J. Obstet. Gynecol. 56(2), 133-138 (2017).
- 31. Noor, N., Kural, M., Joshi, T., Pandit, D. & Patil, A. Study of maternal determinants influencing birth weight of newborn. *Arch. Med. Health Sci.* 3, 239–243 (2015).
- 32. Ronnenberg, A. G. et al. Low preconception body mass index is associated with birth outcome in a prospective cohort of Chinese women. J Nutr.;133(11):3449-55. (2003). https://doi.org/10.1093/jn/133.11.3449.
- 33. Zhu, S. M. et al. Maternal lipid profile during early pregnancy and birth weight: A retrospective study. Front. Endocrinol. (Lausanne). 13, 951871. https://doi.org/10.3389/fendo.2022.951871 (2022).
- 34. Uchinuma, H. et al. Gestational body weight gain and risk of low birth weight or macrosomia in women of Japan: a nationwide cohort study. Int J Obes (Lond). ;45(12):2666–2674. (2021). https://doi.org/10.1038/s41366-021-00947-7. Epub 2021 Sep 1. Erratum in: Int. J. Obes. (Lond). 2022;46(6):1251.
- 35. Andraweera, P. H. et al. Effect of birth weight and early pregnancy BMI on risk for pregnancy complications. *Obes. (Silver Spring)*. 27 (2), 237–244 (2019).
- 36. Günther, V. et al. Impact of nicotine and maternal BMI on fetal birth weight. BMC Pregnancy Childbirth. 21 (1), 127. https://doi.org/10.1186/s12884-021-03593-z (2021).

# **Author contributions**

Xiao-Ju He and Wen-Yan Fu designed this study. Jun Xiong drafted the manuscript. Xiao-Ju He and Jun Xiong revised the manuscript. All authors read and approved the final manuscript. Huan Li and Xiao-Qing Tan took part in the whole investigation. Jun Xiong, Wen-Yan Fu, Huan Li, Xiao-Ju He and Xiao-Qing Tan analyzed the data. Huan Li and Xiao-Qing Tan supervised the investigation process.

#### Funding

This work was supported by the Science and Technology Plan Fund of Jiangxi Provincial Health and Family Planning Commission (No. 202210036), Science and technology plan project of Jiangxi Administration of Traditional Chinese Medicine (2021B672), Science and Technology Research Project of Education Department of Jiangxi Province(190141), National Natural Science Foundation of China (#81760504).

### **Declarations**

# Competing interests

The authors declare no competing interests.

#### Ethics approval and consent to participate

Ethical approval was obtained from the ethics review boards of the Second Affiliated Hospital of Nanchang University. Written informed consent was obtained from each participant before enrolment in this study before samples collection.

### Additional information

Correspondence and requests for materials should be addressed to X.-J.H. or W.-Y.F.

Reprints and permissions information is available at www.nature.com/reprints.

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

**Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <a href="https://creativecommons.org/licenses/by-nc-nd/4.0/">https://creativecommons.org/licenses/by-nc-nd/4.0/</a>.

© The Author(s) 2025