Association of Gestational Weight Gain with Cesarean Section: A Prospective Birth Cohort Study in Southwest China

Lujiao Huang  
Sichuan University

Ju Zhang  
Sichuan Provincial Hospital for Women and Children

Hong Sun  
Sichuan University

Hongli Dong  
Sichuan University

Run Li  
Sichuan Provincial Hospital for Women and Children

Congjie Cai  
Sichuan University

Yan Gao  
Sichuan Provincial Hospital for Women and Children

Cheng Wu  
Sichuan Provincial Hospital for Women and Children

Xi Lan  
Chengdu Fifth People's Hospital

Guo Zeng (✉ zgmu2007@126.com)  
Sichuan University  https://orcid.org/0000-0002-4239-447X

Research article

**Keywords:** gestational gain weight, cesarean section, optimal recommendation, birth cohort study, Chinese population.

**Posted Date:** October 8th, 2020

**DOI:** https://doi.org/10.21203/rs.3.rs-88567/v1

**License:** ☑️  This work is licensed under a Creative Commons Attribution 4.0 International License.  
Read Full License
Abstract

Background: Cesarean section (CS) is a rising public health issue globally, which is even worse in China. Numerous studies have suggested that gestational weight gain (GWG) control may be an effective way to reduce the rate of CS. However, rare study has examined the association between GWG and CS among women in Southwest China. We proposed to examine their association based on a prospective birth cohort, and further to explore the optimal GWG range.

Methods: We retrieved data from a prospective birth cohort conducted in Sichuan Provincial Hospital for Women and Children, Southwest China. Unconditional multivariable logistic regression was used to examine the association between GWG and CS by adjusting for potential confounders. In one analysis, we incorporated the GWG as categorical variable according to the Institute of Medicine (IOM) recommendation, just as the majority of previous studies did. In the other analysis, we directly incorporated the GWG as continuous variable and natural cubic splines was used to characterize the potential nonlinear exposure-response relationship, aiming to identify the optimal GWG. We further stratified the above analysis by pre-pregnancy BMI and GDM, and then a heterogeneity test based on multivariate meta-analysis was conducted to examine whether the stratum specific estimation agreed with each other.

Results: A total of 1363 participants were included. By adopting the IOM recommendation, the adjusted OR of CS was 0.63 (0.47, 0.84) for insufficient GWG and 1.42 (1.06, 1.88) for excessive GWG respectively. When stratified by pre-pregnancy BMI, we further found that BMI may be an effect modifier with a higher risk of excessive GWG seen in the underweight women. By applying a flexible spline regression, the optimal GWG in term of reducing CS based on our data were more stringent than that of IOM recommendation, which were 9-12 kg for underweight women, <20 kg for normal weight women and <10 kg for overweight/obese women.

Conclusion: These results suggested a more stringent recommendation should be applied in Southwest China, and more attention should be given to those underweight women.

1. Background

Over the past decades, the rising rate of cesarean section (CS) has been seen globally [1]. In China, it has increased dramatically from 3.4% in 1988 to 39.3% in 2008 [2]. Although the overall use of CS in China stabled around 40–50% in recent years [3], those rates were still three times higher than the ideal CS rate (i.e. 10 ~ 15%), and greatly exceeded the warning line of 15% recommended by the World Health Organization [4]. Besides, the CS rate without medical indications in China was 11.6%, which was also much higher than that in western developed countries and other Asian countries [5]. In Southwest China, the situation was even worse. Taken the Chengdu city (a supercity in Southwest China with over 16 million population) for example, its CS rate reached an astonishing 57.0% in 2014, which was far higher than the average rate in China [6].
Although CS is often considered as the safest mode of delivery, it is well acknowledged that CS without medical indications may also be associated with multiple adverse maternal and infant outcomes [7]. For pregnant women, CS has been associated with the increased risk of hemorrhage, embolism, Intra-abdominal adhesions, and even death [8]. For the offspring, CS has been associated with the increased risk of developing asthma, allergies, cardiometabolic syndromes, and psychological health in their later life [9–11]. Therefore, preventing the overuse of CS has become an urgent need for maternal health in China. An effective way to address the above issue is to identify the modifiable risk factors and formulate the corresponding intervention to reduce the rate of CS.

Among the numerous risk factors of CS, gestational weight gain (GWG) has aroused considerable attention owing to its potential to be an intervention target. However, most of the previous evidence regarding the association between GWG and CS came from western developed countries [12]. Given that the Body Mass Index (BMI) of pre-pregnancy women in China was substantially lower than that in western developed countries, those findings may not be generalized to the Chinese population. In addition, the majority of previous studies in China and other Asia countries used the guideline from the Institute of Medicine (IOM, currently the US national academy of medicine) to classify the GWG into different groups and to study its association with CS [13–16]. Similar as above, it is also questionable whether the IOM guideline can be the optimal recommendation to reduce the CS rate in China.

To fill the above research gaps, we proposed to study the association between GWG and CS based on a prospective birth cohort from Southwest China. Unlike most previous studies that adopted the IOM guideline to classify the GWG, we additionally used a flexible spline regression to characterize the potential nonlinear exposure-response curve between GWG and CS, aiming to identify the optimal recommendation of GWG in Southwest China to reduce the CS rate.

2. Methods

2.1. Study population

Data used in this study were retrieved from a prospective birth cohort conducted in Sichuan Provincial Hospital for Women and Children, Southwest China. Data collection was approved by the Institutional Review Board at Sichuan University (approval number: K2017037). More details about this birth cohort and the questionnaire used in this study have been described elsewhere [17]. In summary, pregnant women who had their first prenatal clinic visit were invited to join this birth cohort in 2017. Eventually, 1704 pregnant women were recruited and followed up until two years after delivery. Among all these participants, 26 were excluded for multiple births, 3 were excluded for first prenatal clinic visit < 6 or > 14 weeks, 2 were excluded for pre-pregnancy Diabetes Mellitus, 249 were excluded for having missing data on the main exposure variable (i.e. gestational weight gain), and 9 were excluded for having missing data on the main outcome variable (i.e. delivery modes). Besides, 52 participants were further excluded due to delivery modes other than vaginal delivery or cesarean section. Finally, 1363 participants with the
maternal age ranged from 18 to 45 years old were included in the final sample for the statistical analysis (Fig. 1).

2.2. Data collection and anthropometric measurements
After enrollment and providing written informed consent, all participants were required to completed sequential interviewer-administered questionnaires given by trained staff at different routine prenatal and child health visits. The baseline questionnaire covered a wide range of information about the pregnant mother, including the general demographic and socioeconomic characteristics, lifestyle habits (e.g. pre-pregnancy drinking and smoking habits), physical activity, dietary, mental and sleeping status quality, reproductive history and etc. Specifically, physical activity was assessed by investigating the activity of participants in self-care, housework, leisure activity, transportation and work. Dietary was evaluated through 24-hour dietary recall survey. The status of depression and anxiety were evaluated by the Self-Rating Anxiety Scale (SAS) and the Self-Rating Depression Scale (SDS) respectively. The sleeping quality was evaluated by the Pittsburgh sleep quality index scale (PSQI). Particularly, the physical activity, dietary, mental and sleeping status quality were evaluated three times at the first, second and third trimester respectively. After childbirth, the maternal outcomes were recorded by use of a standardized form including the delivery mode, maternal weight and glucose after delivery, breastfeeding initiation, etc.

Regarding the anthropometric measurements, we only measured height in meters once at enrollment by standardized height-measuring station. However, we measured prenatal weight in kilograms four times from first to third trimester and before delivery respectively by standardized weight scale. For the pre-pregnancy weight, we used the self-reporting data by directly asking the participants at enrollment. We also retrieved the 75-g OGTT results at 24–28 weeks of gestation from the hospital database to further determine whether the participant occurred gestational diabetes mellitus (GDM). GDM was defined as having one or more abnormal values: 5.1 mmol/l or 92 mg/dl for fasting, 10.0 mmol/l or 180 mg/dl for 1-h post-load and 8.5 mmol/l or 153 mg/dl for 2-h post-load glucose.

2.3. Assessment of study variables
The GWG in this study was defined by the difference between the last measured weight (i.e. prenatal weight before delivery) and the pre-pregnancy weight. Then we classified the GWG of each participant into three groups (i.e. below, within and above) according to the IOM recommendations [18], but with the pre-pregnancy BMI stratified by the Chinese recommendation: underweight (BMI < 18.5 kg/m^2), normal weight (18.5 ≤ BMI < 24.0 kg/m^2), overweight (24.0 ≤ BMI < 28.0 kg/m^2) and obese (BMI ≥ 28.0 kg/m^2). In the final analysis, we further combined the overweight and obese group due to only few participants in the obese group. For the outcome variable, we classified the delivery modes into two types in our questionnaire, i.e. vaginal delivery and CS.

A wide range of potential covariates were available for careful consideration of confounding. The definitions of those covariates were displayed as follows. It included maternal age in years (< 25, 25–29, 30–35, ≥ 35), ethnicity (Han, minorities), employment before pregnancy (yes, no), personal income per month in Chinese Yuan(< 3000, 3000–4999, 5000–9999, ≥ 10000), education in schooling years (≤ 12
years, 13–15 years, ≥ 16 years), drinking status before pregnancy (yes or no), smoking status before pregnancy (yes or no), gravidity (1, 2, 3, ≥ 4), parity (primiparous or multiparous), physical activity (MET-h/week), energy intake (kcal/day), anxiety status measured by SAS score, depression status measured by SDS score and sleep quality measured by PSQI score.

2.4. Statistical analysis

Unconditional multivariable logistic regression was used to examine the association between GWG and CS (vaginal delivery as reference) by adjusting for the following confounding variables: maternal age, gravidity, parity, ethnicity, educational level, employment, personal income, smoking, drinking, physical activity, energy intake, anxiety, depression and sleeping status. The determination of potential confounders was informed by a thoroughly review of previous studies. We conducted two separate analysis with different definitions of main exposure (i.e. GWG) for different purposes. In one analysis, we incorporated the GWG as categorical variable according to the IOM recommendation, just as the majority of previous studies did. In the other analysis, we directly incorporated the GWG as continuous variable and natural cubic splines was used to characterize the potential nonlinear exposure-response relationship, aiming to identify the optimal GWG in terms of reducing the CS rate in our study population. We further stratified the above analysis by pre-pregnancy BMI and GDM considering that our conclusions could be profoundly modified by those two factors. And then a heterogeneity test based on multivariate meta-analysis was conducted to examine whether the stratum specific estimation agreed with each other. All statistical analyses in this study were conducted in R software version 4.0.2.

3. Results

A total of 1363 participants were included in this analysis from the Prospective Birth Cohort Study in Southwest China, with the rates of pre-pregnancy overweight/obese, excessive GWG and CS were 12.7%, 27.6% and 43.7% respectively. We compared the sample characteristics between vaginal delivery and cesarean section group in Table 1. Compared to the vaginal delivery group, participants in the CS group generally had a higher rate of excessive GWG (33.0% vs 23.4%, P < 0.001) as well as overweight/obese (17.1% vs 9.3%, P < 0.001). Whereas, the rate of gestational diabetes mellitus between these two groups showed no statistical difference (39.4% vs 36.7%, P < 0.001). Besides, we also found that the maternal age ≥ 35 (13.6% vs 5.6%, P < 0.001), gravidity ≥ 3 (35.1% vs 20.5%, P < 0.001) and multiparous rate (38.5% vs 23.5%, P < 0.001) of CS group higher than that of vaginal delivery group, while ethnicity, education, employment, personal income, physical activity, drinking, smoking, mental and sleeping status showed no statistical difference between two groups.
Table 1
Sample characteristics between vaginal delivery and cesarean section

| Characteristics# | Overall (n = 1363) | vaginal delivery (n = 767, 56.3%) | cesarean section (n = 596, 43.7%) | $\chi^2/T^*$ | P |
|------------------|-------------------|----------------------------------|----------------------------------|-------------|---|
| GWG (continuous, kg) | 13.5 (10.5, 16.2) | 13.1 (10.5, 16.0) | 13.9 (11.0, 16.8) | 8.072 | 0.004 |
| GWG (categorical, kg) | | | | | |
| Below | 382 (28.1) | 245 (32.0) | 137 (23.0) | 21.102 | < 0.001 |
| Within | 604 (44.3) | 342 (44.6) | 262 (44.0) | | |
| Above | 376 (27.6) | 179 (23.4) | 197 (33.0) | | |
| Pre-pregnancy BMI (kg/m$^2$) | | | | | |
| Under weight (< 18.5) | 195 (14.3) | 132 (17.2) | 63 (10.6) | 26.697 | < 0.001 |
| Normal weight (18.5 ~ 24) | 994 (73.0) | 563 (73.5) | 431 (72.3) | | |
| Overweight/obese (≥ 24.0) | 173 (12.7) | 71 (9.3) | 102 (17.1) | | |
| Gestational Diabetes Mellitus | | | | | |
| Yes | 515 (37.8) | 281 (36.7) | 234 (39.4) | 0.932 | 0.334 |
| No | 848 (62.2) | 486 (63.3) | 362 (60.6) | | |
| Maternal age (years) | | | | | |
| ≤ 25 | 232 (17.1) | 151 (19.7) | 81 (13.6) | 47.035 | < 0.001 |
| 25–29 | 716 (52.5) | 436 (56.8) | 280 (47.0) | | |
| 30–35 | 291 (21.3) | 137 (17.9) | 154 (25.8) | | |
| ≥ 35 | 124 (9.1) | 43 (5.6) | 81 (13.6) | | |
| Ethnicity | | | | | |

#The data are presented as median and quartiles for continuous variables (all continuous variables are non-normally distributed) or as n and % for categorical variables.

* Tests for differences between vaginal delivery and cesarean section were performed using the Wilcoxon two-sample test for non-normally distributed continuous variables or the $\chi^2$ test for categorical variables; P < 0.05 indicates significance.
| Characteristics# | Overall (n = 1363) | vaginal delivery (n = 767, 56.3%) | cesarean section (n = 596, 43.7%) | \( \chi^2 \) or \( T^* \) | P  |
|-----------------|------------------|----------------------------------|----------------------------------|----------------|------|
| Han             | 1334 (97.9)      | 755 (98.6)                       | 579 (97.1)                       | 2.673          | 0.102|
| Minorities      | 29 (2.1)         | 12 (1.4)                         | 17 (2.9)                         |                |      |
| Education (schooling years) |       |                                  |                                  |                |      |
| ≤ 12            | 314 (23.1)       | 165 (21.6)                       | 149 (25.1)                       | 2.909          | 0.233|
| 13–15           | 954 (70.3)       | 545 (71.2)                       | 409 (69.0)                       |                |      |
| ≥ 16            | 90 (6.6)         | 55 (7.2)                         | 35 (5.9)                         |                |      |
| Employment      |                  |                                  |                                  |                |      |
| Yes             | 1141 (83.7)      | 656 (85.5)                       | 485 (81.5)                       | 3.685          | 0.055|
| No              | 222 (16.3)       | 111 (14.5)                       | 111 (18.5)                       |                |      |
| Personal income (Yuan/month) |         |                                  |                                  |                |      |
| < 3000          | 46 (3.4)         | 24 (3.1)                         | 22 (3.7)                         | 1.210          | 0.751|
| 3000–4999       | 397 (29.3)       | 224 (29.4)                       | 173 (29.1)                       |                |      |
| 5000–9999       | 617 (45.5)       | 354 (46.5)                       | 263 (44.3)                       |                |      |
| ≥ 10000         | 296 (21.8)       | 160 (21.0)                       | 136 (22.9)                       |                |      |
| Gravidity       |                  |                                  |                                  |                |      |
| 1               | 594 (43.6)       | 377 (49.2)                       | 217 (36.5)                       | 39.522         | < 0.001|
| 2               | 401 (29.5)       | 232 (30.3)                       | 169 (28.4)                       |                |      |
| ≥ 3             | 366 (26.9)       | 157 (20.5)                       | 209 (35.1)                       |                |      |
| Parity          |                  |                                  |                                  |                |      |
| primiparous     | 942 (70.0)       | 580 (76.5)                       | 362 (61.5)                       | 35.025         | < 0.001|
| multiparous     | 405 (30.0)       | 178 (23.5)                       | 227 (38.5)                       |                |      |

#The data are presented as median and quartiles for continuous variables (all continuous variables are non-normally distributed) or as n and % for categorical variables.

* Tests for differences between vaginal delivery and cesarean section were performed using the Wilcoxon two-sample test for non-normally distributed continuous variables or the \( \chi^2 \) test for categorical variables; P < 0.05 indicates significance.
| Characteristics# | Overall (n = 1363) | vaginal delivery (n = 767, 56.3%) | cesarean section (n = 596, 43.7%) | $\chi^2/T^*$ | $P$ |
|------------------|-------------------|----------------------------------|----------------------------------|-------------|-----|
| **Drinking status** |                   |                                  |                                  |             |     |
| Yes              | 107 (29.5)        | 59 (7.7)                         | 48 (8.1)                         | 0.021       | 0.883 |
| No               | 1256 (70.5)       | 708 (92.3)                       | 548 (91.9)                       |             |     |
| **Smoking status** |                   |                                  |                                  |             |     |
| Yes              | 51 (3.7)          | 26 (3.4)                         | 25 (4.2)                         | 0.402       | 0.526 |
| No               | 1312 (96.3)       | 741 (96.6)                       | 571 (95.8)                       |             |     |
| **Physical activity (MET hours/weeks)** | 102.6 (78.9, 124.1) | 101.9 (78.3, 124.4) | 103.8 (80.4, 123.7) | 0.381 | 0.537 |
| **Energy intake(kcal/day)** | 1724 (1496, 1976) | 1734 (1509, 1994) | 1702 (1455, 1968) | 2.022 | 0.155 |
| **Anxiety (SAS score)** | 36.3 (32.5, 40.4) | 36 (33, 40)                      | 36 (33, 40)                      | 0.217       | 0.642 |
| **Depression (SDS score)** | 38.8 (33.8, 44.2) | 39 (33, 45)                      | 38 (34, 44)                      | 0.071       | 0.791 |
| **Sleeping (PSQI score)** | 4.0 (3.0, 5.0) | 4 (3, 5)                         | 4 (3, 5)                         | 0.014       | 0.907 |

#The data are presented as median and quartiles for continuous variables (all continuous variables are non-normally distributed) or as n and % for categorical variables.

* Tests for differences between vaginal delivery and cesarean section were performed using the Wilcoxon two-sample test for non-normally distributed continuous variables or the $\chi^2$ test for categorical variables; $P < 0.05$ indicates significance.

For the categorical GWG, we found a consistent and steady increase of the risk of CS from below to above IOM recommendation, as seen in Table 2. Overall, compared to those participants within the IOM recommendation, the estimated OR for those below recommendation was 0.63 (95% CI: 0.47–0.84), and for those above recommendation was 1.42 (95% CI: 1.06–1.88). Further stratifying the analysis by BMI, although similar upward trends were found in all strata, the estimated effect size varied substantially depending on the stratum (P for heterogeneity < 0.001). Particularly, we found that the underweight participants were most sensitive to the excessive GWG, given that the greatest OR (2.67, 95% CI: 0.98, 7.26) was seen in the underweight stratum and above the recommendation. Our findings also implied that the overweight/obese participant would gain most benefit by controlling the GWG under a certain level, given that the smallest OR (0.29, 95% CI: 0.09, 0.89) was seen in the overweight/obese stratum and
below the recommendation. In contrast, the estimated effect size was more similar between two strata of GDM than that of BMI (P for heterogeneity = 0.010).

For the continuous GWG, our findings were generally agreed with that of categorical GWG but with more details. Overall, we found a J-shaped exposure-response curve between GWG and CS (Fig. 2A). More specifically, we saw an approximately linear increase of the risk of CS until the GWG reached 20 kg. Since then, the risk of CS began to go up exponentially which implied a threshold effect. Similar to the categorical analysis, the estimated exposure-response curves varied substantially among different BMI strata. Compared to the overall estimation, we found a similar J-shaped exposure-response curve and

### Table 2.

Associations of gestational weight gain categorized by IOM recommendation with cesarean section (vaginal delivery as reference) *

| IOM recommendation | Overall   | Stratified by pre-pregnancy BMI | Stratified by GDM |
|---------------------|-----------|--------------------------------|-------------------|
|                     |           | Under | Normal | Over | χ²/P* | GDM | Non-GDM | χ²/P* |
| Below               | 0.63 (0.47, 0.84) | (0.36, 0.64) | (0.46, 0.29) | (0.09, 0.89) | 0.60 (0.39, 0.65) | (0.43, 0.95) | 0.98 | 128.5, <0.001 |
| Within              | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) | 0.010 |
| Above               | 1.42 (1.06, 2.67) | (0.98, 1.36) | (0.98, 1.69) | (0.66, 1.90) | 1.10 (0.63, 1.58) | (1.12, 1.94) | 2.22 |
|                     | 1.88 | 7.26 | 1.90 | 4.31 | 1.94 |

*The associations of GWG with CS were measured by the adjusted odds ratio (OR) and estimated by the nonconditional multivariate logistic regression by controlling maternal age, gravidity, parity, ethnicity, educational level, employment, personal income, smoking, drinking, physical activity, energy intake, anxiety, depression, sleeping status, pre-pregnancy BMI and GDM. For the stratified analysis, BMI and GMD were then excluded from the confounding set accordingly.

#We ran a heterogeneity test based on multivariate meta-analysis aiming to compare whether the estimates were the same among different strata.

For the continuous GWG, our findings were generally agreed with that of categorical GWG but with more details. Overall, we found a J-shaped exposure-response curve between GWG and CS (Fig. 2A). More specifically, we saw an approximately linear increase of the risk of CS until the GWG reached 20 kg. Since then, the risk of CS began to go up exponentially which implied a threshold effect. Similar to the categorical analysis, the estimated exposure-response curves varied substantially among different BMI strata. Compared to the overall estimation, we found a similar J-shaped exposure-response curve and
threshold value of 20 kg in the normal weight stratum. However, in the under-weight stratum, the estimated exposure-response curve was shown as a U shape. It implied that insufficient GWG would not decrease but increase the risk of CS and the optimal GWG was somewhere around 9–12 kg. In contrast, we saw a steep increase of risk of CS from 0–10 kg GWG for those overweight or obese participants; afterward, the risk of CS began to level off. It implied that the risk of CS was very sensitive to the increase of GWG, but an excessive GWG over 10 kg would not further increase the risk of CS. Once again, we found that the difference of estimations between GDM and non-GDM strata was much smaller than that among BMI strata. For both groups, the estimated exposure-response curves were shown as a J shape, just like the overall estimation.

4. Discussion

In this study, we examined the association between GWG and CS based on a prospective birth cohort from Southwest China. The rates of overweight /obese and excessive GWG (IOM guideline) in our study were 12.7% and 27.6% respectively. Our findings agreed with previously reported large scale national investigation data in China (12.7% and 27.6%) [14, 19]. However, both rates were significantly lower than that in western countries (25.8% and 47.2%) [12, 20]. and also the neighboring Asia countries, such as Japan (20.8% and 37.2) [21] and South Korea (20.5% and 35.6%) [22]. Our findings confirmed that the women in Southwest China were still slimmer than those in developed counties. Not surprisingly, we found a high rate of CS in Southwest China (43.7%). This finding was consistent with the national survey of CS conducted by the National Maternal Near Miss Surveillance System (41.1%) [3]. Although there was an increasing trend in CS globally, the rate of CS in Southwest China was still much higher than that in most other countries, ranging from 7.3% in Africa to 32.3% in North American [23]. The only exception was Latin America and the Caribbean region where the rate of CS reached 40.5% [23].

Although previous studies have shown both pre-pregnancy BMI and GWG were associated with the risk of CS [12, 13, 16]. In this study, we paid particular attention to the GWG rather than pre-pregnancy BMI, mainly because it is more feasible for weight control during the gestation period than before pregnancy [13]. By adjusting for the potential confounding as well as pre-pregnancy BMI, we found a steady increase of the risk of CS with the rise of GWG with the estimated OR for the insufficient and excessive GWG were 0.63 (0.47, 0.84) and 1.42 (1.06, 1.88) respectively. Our results were roughly consistent with most previous studies. Taken the risk of excessive GWG on CS for example, the estimated OR were 1.44 (1.21–1.72) in United States [24], 1.45 (1.40, 1.51) and 1.44 (1.20, 1.73) in mainland China [13, 14], 1.35 (1.16–1.56) in Chinese Taiwan [25], 1.36 (1.25, 1.47) in Japan [21], 1.6 (1.0–2.7) in South Korean [26] and 1.9 (1.4–2.5) in Indian [27]. Several possible mechanisms could explain the association between excessive GWG and CS. Excessive GWG may increase the risk of multiple adverse maternal and infant outcomes [28, 29], such as poor performance in Apgar score, macrosomia and fetal distress for offspring, disfunction in myometrial contractility for pregnancy mother, thereby could increase the risk of cesarean delivery.

In addition, our results implied that the pre-pregnancy BMI may modify the association between GWG and CS. After stratifying our analysis by BMI, the most increased risk of CS due to excessive GWG was seen in
those underweight women, meanwhile, the most reduced risk of CS due to insufficient GWG was seen in those overweight women. The findings were consistent with those previous studies conducted in both China [13] and the USA [30]. Both studies implied that excessive GWG may do more harm for those underweight women than their obese counterparts regarding reducing CS. In most clinical practices, weight control was mainly recommended for overweight women. However, our result also suggested that we should pay more attention to the issue of excessive GWG for underweight women. In contrast, the modification effect of GDM on GWG-CS association was negligible.

In recent years, more and more studies began to question the IOM guideline of GWG mainly for two reasons. One is that the IOM guideline is developed mainly based on the Caucasian standard, thus it may not be applicable to other racial and ethnic groups [31]. Another one is that the IOM guideline has limitations in insufficient information on adverse outcomes (only 5 maternal and offspring outcomes were considered in developing the IOM guideline), thus it may not be applicable to other adverse outcomes [12]. To explore the optimal GWG in terms of reducing CS in Chinese population, we additionally incorporated the GWG as a continuous variable into a flexible spline regression model. For those normal weight women, we found that the risk of CS would go up exponentially once GWG exceeded 20 kg, which implied a threshold effect and the optimal GWG should be controlled under 20 kg. While for those underweight and overweight/obese women, the recommendations based on our findings were 9–12 kg and < 10 kg respectively. Compared to the IOM guideline [18], our recommendation was more stringent and lower than that of IOM, especially for those underweight women. This finding was generally consistent with that reported in Japan [32] and Singapore [33]. However, results from South Korea [31] suggested a considerably higher and wider optimal GWG range than the IOM guideline.

To the best of our knowledge, this is the first study in southwest China aiming to examine the association between GWG and CS. Compared with other studies, we have taken a large number of covariates into accounts to allow stringent control of potential confounding. Besides, the sophisticated natural spline regression adopted in this study can also allow us to have a fine characterization of the association between GWG and CS, thereby exploring the optimal GWG ranges. However, this study also has several limitations that warrant mentioning. The first one is that the sample size of this analysis is relatively small, which may hinder the representativeness and generality of this study. Just for this reason, we did not distinguish the elective and non-elective cesarean section in our analysis to avoid insufficient statistical power. The second is that we did not take the change of GWG over different trimesters into accounts in our analysis. The main reason we did not use the trimester-specific GWG is that the rate of missing data would be much higher than that by using the overall GWG. Therefore, we chose the overall GWG as our main exposure to obtain a larger effective sample size.

5. Conclusions

Overall, we investigated the association between GWG and CS in a population from Southwest China based on a prospective birth cohort. We confirmed that the elevated risk of CS was associated with the rise of GWG. Our findings also suggested that the risks may be varied by the pre-pregnancy BMI, and we
should pay more attention to the issue of excessive GWG for those underweight women. Besides, our results also suggested that a more stringent recommendation of GWG should be applied in Southwest China.

**Abbreviations**

GWG: gestational gain weight; CS: cesarean section; IOM: Institute of Medicine; OR: odds ratio; BMI: body mass index; GDM: gestational diabetes mellitus; SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale; PSQI: Pittsburgh sleep quality index scale.

**Declarations**

**Ethics approval and consent to participate**

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. Written informed consent was obtained from all the participants before they took part in the study. Data collection was approved by the Institutional Review Board at Sichuan University (approval number: K2017037).

**Consent for publication**

Not applicable.

**Availability of data and materials**

The datasets analyzed in this study are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare no conflict of interest.

**Funding**

This research was funded by Danone Nutrition Center for Dietary Nutrition Research and Education (grant number DIC2016-06). The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

**Authors’ Contributions**

Conceptualization, L.H. and G.Z.; methodology, L.H., C.C. and X.L.; software, L.H., J.Z. and H.S.; formal analysis, L.H., J.Z., H.D., R.L., Y.G. and C.W.; investigation, J.Z., H.S., H.D., R.L., C.C., Y.G., C.W. and X.L; data curation, C.C. and X.L.; writing—original draft preparation, L.H.; writing—review and editing, L.H. and G.Z.; visualization, L.H.; supervision, G.Z.; funding acquisition, G.Z. All authors have read and agreed to the published version of the manuscript.
Acknowledgments: All participants are gratefully acknowledged.

References

1. Boerma, T.; Ronsmans, C.; Melesse, D. Y.; Barros, A. J.; Barros, F. C.; Juan, L.; Moller, A.-B.; Say, L.; Hosseinpoor, A. R.; Yi, M., Global epidemiology of use of and disparities in caesarean sections. The Lancet 2018, 392, (10155), 1341-1348.

2. Feng, X. L.; Xu, L.; Guo, Y.; Ronsmans, C., Factors influencing rising caesarean section rates in China between 1988 and 2008. Bulletin of the World Health Organisation 2012, 90, (1), 30-9, 39A.

3. Liang, J.; Mu, Y.; Li, X.; Tang, W.; Wang, Y.; Liu, Z.; Huang, X.; Scherpbie, R. W.; Guo, S.; Li, M., Relaxation of the one child policy and trends in caesarean section rates and birth outcomes in China between 2012 and 2016: observational study of nearly seven million health facility births. BMJ 2018, 360, k817.

4. Betrán, A. P.; Torloni, M. R.; Zhang, J.-J.; Gülmezoglu, A.; Section, W. W. G. o. C.; Aleem, H.; Althabe, F.; Bergholt, T.; de Bernis, L.; Carroli, G., WHO statement on caesarean section rates. International Journal of Obstetrics Gynaecology 2016, 123, (5), 667-670.

5. Pisake Lumbiganon, M. L., A Metin Gülmezoglu, João Paulo Souza, Surasak Taneepanichskul, Pang Ruyan, Deepika Eranjanie Attygalle, Naveen Shrestha, Rintaro Mori, Duc Hinh Nguyen, Thi Bang Hoang, Tung Rathavy, Kang Chuyun, Kannitha Cheang, Mario Festin, Venus Udomprasertgul, Maria Julieta V Germar, Gao Yanqiu, Malabika Roy, Guillermo Carroli, Katherine Ba-Thike, Ekaterina Filatova, José Villar, World Health Organization Global Survey on Maternal and Perinatal Health Research Group, Method of delivery and pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal health 2007-08. The Lancet 2010, 375, (9713), 490–499.

6. Li, H.-T.; Luo, S.; Trasande, L.; Hellerstein, S.; Kang, C.; Li, J.-X.; Zhang, Y.; Liu, J.-M.; Blustein, J., Geographic variations and temporal trends in cesarean delivery rates in China, 2008-2014. Jama 2017, 317, (1), 69-76.

7. Sandall, J.; Tribe, R. M.; Avery, L.; Mola, G.; Visser, G. H.; Homer, C. S.; Gibbons, D.; Kelly, N. M.; Kennedy, H. P.; Kidanto, H., Short-term and long-term effects of caesarean section on the health of women and children. The Lancet 2018, 392, (10155), 1349-1357.

8. Nicola Jackson, S. P.-B., Physical sequelae of caesarean section. Best Practice & Research Clinical Obstetrics & Gynaecology 2001, 15, (1), 49-61.

9. Chen, H.; Tan, D., Cesarean section or natural childbirth? cesarean birth may damage your health. Frontiers in psychology 2019, 10, 351.

10. Hansen, S.; Halldorsson, T.; Olsen, S.; Rytter, D.; Bech, B.; Granström, C.; Henriksen, T.; Chavarrro, J., Birth by cesarean section in relation to adult offspring overweight and biomarkers of cardiometabolic risk. International journal of obesity 2018, 42, (1), 15-19.

11. Bager P, W. J., Westergaard T., Caesarean delivery and risk of atopy and allergic disease: meta-analyses. Clin Exp Allergy. 2008, 38, (4), 634-642.
12. Voerman, E.; Santos, S.; Inskip, H.; Amiano, P.; Barros, H.; Charles, M.-A.; Chatzi, L.; Chrousos, G. P.; Corpeleijn, E.; Crozier, S., Association of gestational weight gain with adverse maternal and infant outcomes. Jama 2019, 321, (17), 1702-1715.

13. Xiong, C.; Zhou, A.; Cao, Z.; Zhang, Y.; Qiu, L.; Yao, C.; Wang, Y.; Zhang, B., Association of prepregnancy body mass index, gestational weight gain with cesarean section in term deliveries of China. Scientific Reports 2016, 6, (1), 1-6.

14. Wang, X.; Zhang, X.; Zhou, M.; Juan, J.; Wang, X., Association of prepregnancy body mass index, rate of gestational weight gain with pregnancy outcomes in Chinese urban women. Nutrition & metabolism 2019, 16, (1), 54.

15. Mefkure Eraslan Sahin, I. C. M., Effect of Gestational Weight Gain on Perinatal Outcomes in Low Risk Pregnancies with Normal Prepregnancy Body Mass Index. BioMed Research International 2019, 2019, 3768601.

16. Tomohito Tanaka, K. A., Michihiko Nakamura, Takayoshi Kanda, Daisuke Fujita, Yoshiki Yamashita, Yoshito Terai, Hideki Kamegai, Masahide Ohmichi, Associations between the pre-pregnancy body mass index and gestational weight gain with pregnancy outcomes in Japanese women. J. Obstet. Gynaecol. Res. 2014, 40, (5), 1296–1303.

17. Xi Lan, Y.-q. Z., Hong-li Dong, Ju Zhang, Feng-ming Zhou, Yan-hong Bao, Rong-ping Zhao, Cong-jie Cai, Dan Bai, Xin-xin Pang, Guo Zeng, Excessive gestational weight gain in the first trimester is associated with risk of GDM: a prospective study from Southwest China. Public Health Nutr 2019, 23, (3), 394-401.

18. Council, N. R., Weight gain during pregnancy: reexamining the guidelines. National Academies Press: 2010.

19. Liu, Y.; Dai, W.; Dai, X.; Li, Z., Prepregnancy body mass index and gestational weight gain with the outcome of pregnancy: a 13-year study of 292,568 cases in China. Archives of gynecology and obstetrics 2012, 286, (4), 905-911.

20. Goldstein, R. F.; Abell, S. K.; Ranasinha, S.; Misso, M.; Boyle, J. A.; Black, M. H.; Li, N.; Hu, G.; Corrado, F.; Rode, L., Association of gestational weight gain with maternal and infant outcomes: a systematic review and meta-analysis. Jama 2017, 317, (21), 2207-2225.

21. Enomoto, K.; Aoki, S.; Toma, R.; Fujiwara, K.; Sakamaki, K.; Hirahara, F., Pregnancy Outcomes Based on Pre-Pregnancy Body Mass Index in Japanese Women. PloS one 2016, 11, (6), e0157081.

22. Wie, J. H.; Park, I. Y.; Namkung, J.; Seo, H. W.; Jeong, M. J.; Kwon, J. Y., Is it appropriate for Korean women to adopt the 2009 Institute of Medicine recommendations for gestational weight gain? PloS one 2017, 12, (7), e0181164.

23. Betrán, A. P.; Ye, J.; Moller, A.-B.; Zhang, J.; Gülmezoglu, A. M.; Torloni, M. R., The increasing trend in caesarean section rates: global, regional and national estimates: 1990-2014. PloS one 2016, 11, (2), e0148343.

24. Durst, J. K.; Sutton, A. L.; Cliver, S. P.; Tita, A. T.; Biggio, J. R., Impact of gestational weight gain on perinatal outcomes in obese women. American journal of perinatology 2016, 33, (09), 849-855.
25. Hung, T.-H., Pregestational body mass index, gestational weight gain, and risks for adverse pregnancy outcomes among Taiwanese women: a retrospective cohort study. Taiwanese Journal of Obstetrics Gynecology 2016, 55, (4), 575-581.

26. Jung H. Park, B. E. L., Hye S. Park, Eun H. Ha, Seung W. Lee and Young J. Kim, Association between pre-pregnancy body mass index and socioeconomic status and impact on pregnancy outcomes in Korea. J. Obstet. Gynaecol. Res. 2011, 37, (2), 138–145.

27. Bhavadharini, B.; Anjana, R. M.; Deepa, M.; Jayashree, G.; Nrutya, S.; Shobana, M.; Malanda, B.; Kayal, A.; Belton, A.; Joseph, K., Gestational weight gain and pregnancy outcomes in relation to body mass index in Asian Indian women. Indian journal of endocrinology metabolism 2017, 21, (4), 588.

28. Chin, J. R.; Henry, E.; Holmgren, C. M.; Varner, M. W.; Branch, D. W., Maternal obesity and contraction strength in the first stage of labor. American Journal of Obstetrics Gynecology 2012, 207, (2), 129.e1-129.e6.

29. Catalano, P. M.; Shankar, K., Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. BMJ 2017, 356, j1.

30. Morgan L. Swank, A. B. C., Christine K. Farinelli, Elliott K. Main, Kathryn A. Melsop, William M. Gilbert, and Judith H. Chung, The impact of change in pregnancy body mass index on cesarean delivery. J Matern Fetal Neonatal Med 2014, 27, (8), 795–800.

31. Choi, S. K.; Lee, G.; Kim, Y. H.; Park, I. Y.; Ko, H. S.; Shin, J. C., Determining optimal gestational weight gain in the Korean population: a retrospective cohort study. Reproductive Biology Endocrinology 2017, 15, (1), 1-7.

32. Morisaki, N.; Nagata, C.; Jwa, S. C.; Sago, H.; Saito, S.; Oken, E.; Fujiwara, T., Pre-pregnancy BMI-specific optimal gestational weight gain for women in Japan. Journal of epidemiology 2017, 27, (10), 492-498.

33. Ee, T. X.; Allen Jr, J. C.; Malhotra, R.; Koh, H.; Østbye, T.; Tan, T. C., Determining optimal gestational weight gain in a multiethnic Asian population. Journal of Obstetrics Gynaecology Research 2014, 40, (4), 1002-1008.

Figures
Figure 1

The flowchart of analysis sample selection.
Figure 2

The estimated nonlinear exposure-response curve between gestational weight gain and cesarean section. A: the overall estimation (95% CI as the shaded area). B: Estimations stratified by BMI. C: Estimations stratified by GDM. We did not display the 95% CI in the sub-figure B and C to avoid the overlapped shaded area hinder a clear comparison among different strata.