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Critical Threshold of Average Weekly Weight Gain in Overweight Pregnant Women During the Second and Third Trimesters: A Strategy to Prevent Macrosomia

Yaxin Wang[1], Ziyang Wang[2], Yin Sun[1], Lin Yang[2], Liangkun Ma[1], Jiao Li[2], Suhan Zhang[1], Xuanjin Yang[1]

[1]Department of Obstetrics and Gynecology, National Clinical Research Center for Obstetric & Gynecologic Diseases, PUMC Hospital, CAMS and PUMC, Beijing, People's Republic of China; [2]Institute of Medical Information/Medical Library, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, 100020, People's Republic of China

Correspondence: Yin Sun, Peking Union Medical College Hospital, 1 Shuaifuyuan, Dongcheng District, Beijing, People's Republic of China, Email sunyin@pumch.cn

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Objective: The study aimed to obtain more evidence on the association of gestational weight gain and pre-pregnancy body mass index (BMI) with macrosomia.

Methods: The data on 5409 live births delivered at Peking Union Medical College Hospital from July 2020 to June 2022 were collected. Group analyses were performed according to the presence or absence of macrosomia. Multivariable binary logistic regression and incidence heatmaps was used to analyze the related factors of macrosomia.

Results: The following variables were significantly associated with macrosomia: overweight (odds ratio [OR]: 2.24, 95% confidence interval [CI]: 1.62–3.10), obesity (OR: 4.56, 95% CI: 2.93–6.98), excessive gestational weight gain (OR: 2.39, 95% CI: 1.67–3.43), gestational age at delivery at 39–41 weeks (OR: 3.83, 95% CI: 2.56–5.95), gestational age at delivery over 41 weeks (OR: 7.88, 95% CI: 4.37–14.19), education level of junior college or below (OR: 1.95, 95% CI: 1.19–3.09), and multipara (OR: 1.62, 95% CI: 1.09–2.42). "v" represents the mean weekly weight gain during the second and third trimesters. A higher v value increased the risk of macrosomia by 2.6-fold (95% CI: 1.37–4.89, P = 0.003). Compared to normal weight women, after adjustment for different pre-pregnancy BMI subgroups, overweight pregnant women had higher weekly weight gain in the second and third trimesters (OR: 4.57, 95% CI: 2.27–9.10, P < 0.001). Obese pregnant women had higher average weekly weight gain during the second and third trimesters, and the OR value for macrosomia was 11.33 (95% CI: 4.95–25.18, P < 0.001). To reduce the incidence of macrosomia in overweight pregnant women, v = 0.32 could be considered the critical threshold of average weekly weight gain in these women in the second and third trimesters of pregnancy.

Conclusion: Pre-pregnancy BMI and weight gain during pregnancy are closely related to macrosomia. The introduction of average weekly weight gain values in the second and third trimesters of pregnancy probably help pregnant women minimizing adverse pregnancy-related outcomes.

Plain Language Summary:

What is already known about this topic?

Pre-pregnancy BMI and GWG are both risk factors for macrosomia. It is very important to develop effective interventions based on pathogenic factors to promote the health of mothers and children. However, the threshold for maternal weight control in the second and third trimesters of pregnancy is unclear.

What is added by this report?

Our data suggest that the critical threshold of average weekly weight gain in overweight pregnant women during the second and third trimesters 0.32kg per week is beneficial to reduce the incidence of macrosomia.

What are the implications for public health practice?

The results of this study highlight the importance of weight management in women in the second and third trimesters, especially those who are overweight, and reasonable control of weight gain will contribute to maternal and fetal health.

Keywords: pregnancy, pre-pregnancy BMI, gestational weight gain, macrosomia, critical threshold of weight gain

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Introduction

The American College of Obstetricians and Gynecologists (2016) defines fetal macrosomia as a birth weight beyond a specific weight (4000 g).[1] Although many scientists hope to control the incidence of macrosomia by studying the risk factors of macrosomia, the current study shows that the incidence of macrosomia is still high. A retrospective cohort study of US natality data files from 1971 to 2017 reported that the overall incidence of fetal macrosomia was 9.6%.[2] From 1994 to 2005, the prevalence of macrosomia in southeast China showed an increasing trend, from 6.0% in 1994 to 8.5% in 2000, which then stabilized to 7.8% in 2005.[3] A study of 15 hospitals in Beijing, China in 2013 showed that the overall prevalence of macrosomia was 7.7%. The lowest prevalence was 5.4% (89/1659), and the highest prevalence was 8.8%.[4] The incidence of macrosomia in Beijing increased from 6.6% in 1996 to 9.5% in 2000 and decreased to 7.0% in 2010.[5]

Fetal macrosomia is closely associated with maternal and neonatal complications. Maternal complications include emergency cesarean section due to fetal distress or slow or stalled labor, postpartum hemorrhage, and anal sphincter injury. Neonatal complications include shoulder dystocia and related sequelae such as brachial plexus injury, clavicle or humerus fracture, and birth asphyxia.[6] Macrosomia also increases the risk of childhood obesity.[7] Macrosomia is an important global public health concern. It is therefore crucial to elucidate the risk factors of macrosomia and to develop effective intervention approaches to promote maternal health. Macrosomia results from basic conditions such as overweight and presence of diabetes before pregnancy and complications and weight management during pregnancy.[8] Excessive weight gain during pregnancy is a critical factor that affects macrosomia.[9] Previous studies have shown that the increased incidence of macrosomia is related to pregnancy weight gain, maternal age, maternal height, and maternal education level.[10,11] Different studies have, however, yielded inconsistent results, and their findings do not accurately represent the status of Chinese pregnant women. Moreover, most cohort studies lack adequate guidelines regarding weight gain management during pregnancy.

Previously, some scholars have conducted studies on the optimal gestational weight gain under different pre-pregnancy BMI categories. In general, women with higher pre-pregnancy BMI categories should gain less weight during pregnancy.[12] However, although the study included a large sample size of 196,670 women, multiple adverse pregnancy outcomes were selected and many factors affected them. It is less targeted to a certain disease. Hence, in the present study, retrospective birth data collected from Peking Union Medical College Hospital (PUMCH) covering a two-year period (July 2020 to June 2022) were used to determine the relationships among pre-pregnancy body mass index (BMI), gestational weight gain (GWG), and macrosomia. We also attempted to introduce a new index of GWG, which might become a popular concept in future clinical practice. Pre-pregnancy BMI and GWG were classified according to the group standard of "Monitoring and Evaluation of Gestational Weight in Chinese Women" [(T/CNSS-009-2021)],[13] which is more representative of the status of Chinese pregnant women.

Methods

Data Sources

This study received ethical approval from PUMCH (JS-2763). The modular collection of case information was implemented using the medical records of the Obstetrics Center of PUMCH. This study is a retrospective analysis, only involving the clinical information of the patients, and there is no additional sample collection and testing, so the process of signing informed consent is exempted in this study. However, we ensured that the personal information of all our patients was kept confidential, that all data were used only for scientific research, and that the final disclosure did not disclose private information. All procedures were performed in accordance with the Declaration of Helsinki. We recruited all pregnant women who gave birth in the hospital in the corresponding years. The use of an electronic system for all data collection avoided selection bias due to manual collection. A total of 5409 maternal and neonatal cases from July 2020 to June 2022 were enrolled, and the data regarding basic maternal information, pregnancy complications, and neonatal conditions were obtained. Inclusion criteria: (1) singleton pregnancy; (2) maternal age ≥18 years old; (3) the hospital was established and the prenatal examination was performed on time during the whole pregnancy; (4) Complete clinical data (This means that all measures needed for the study should be properly recorded and maintained, and very few women referred for critical conditions will be excluded because of a lack of information about previous prenatal care). Exclusion criteria: (1) abortion;

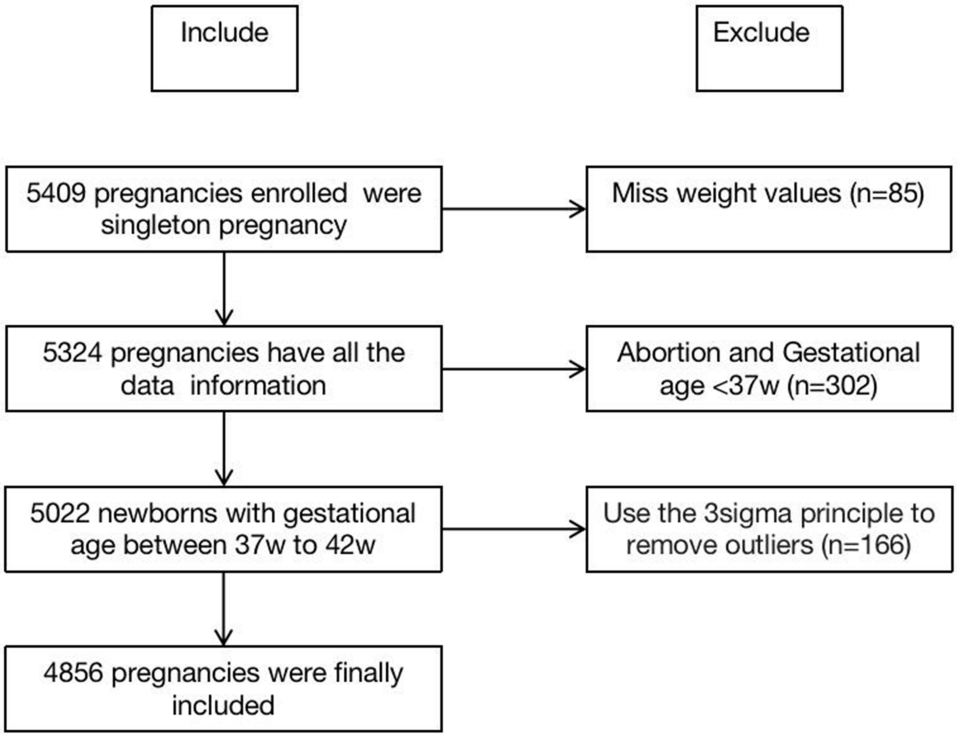


Figure 1 Flowchart of the selection process for the study population. The absence of weight data may be caused by the failure to obtain early electronic data as pregnant women missed early birth examination due to referral from other hospitals. Outliers usually refer to values that are inconsistent with clinical experience (eg, 3520 cm in length and 51 g in weight), which may be related to a recording error and should be excluded.

(2) preterm birth (gestational age <37 weeks); (3) There were obvious abnormalities in electronic data (such as neonatal length 3500 cm, weight 52 g, etc). Finally, according to the inclusion criteria, 4856 pregnant women and their newborns were included in the analysis. The data exclusion rate was 10.22% (553/5409). Figure 1 shows the flowchart of the enrollment and exclusion process for the study population.

Method of Grouping

According to the birth weight, the neonates were assigned to two groups: macrosomia group (≥4000 g) and non-macrosomia group (<4000 g). Based on the pre-pregnancy BMI, the parturients were assigned to four groups: low weight group, <18.5 kg/m^2; normal weight group, 18.5 to <24 kg/m^2; overweight group, 24 to <28 kg/m^2; and obese group, ≥28.0 kg/m^2. In accordance with the latest group standard of "Monitoring and Evaluation of Gestational Weight during Pregnancy in China" the total GWG (the difference between before delivery weight and pre-pregnancy weight) was further divided into three groups according to different pre-pregnancy BMI groups as follows: excessive weight gain (>16.0 kg in the underweight group, >14.0 kg in the normal weight group, >11.0 kg in the overweight group, and >9.0 kg in the obese group); appropriate weight gain (11.0–16.0 kg in the underweight group, 8.0–14.0 kg in the normal weight group, 7.0–11.0 kg in the overweight group, and 5.0–9.0 kg in the obese group); and inadequate weight gain (<11.0 kg in the underweight group, <8.0 kg in the normal weight group, <7.0 kg in the overweight group, and <5.0 kg in the obese group).

Indicators of Observation

The following observation indicators were used: (1) general information: age, pre-pregnancy weight, pre-pregnancy BMI, gravidity, parity, physical labor level, and education level and (2) delivery data: weight before delivery, gestational age at delivery, and neonatal birth weight (g). All obstetric examinations and procedures were performed by trained professionals. Age was calculated based on the information provided in the identity documents. Height and weight were measured in the hospital. Pre-pregnancy BMI was calculated using the formula of pre-pregnancy weight (kg) divided by

square of height (m^2). General information, pre-pregnancy weight, and medical history were self-reported by the pregnant women at the first visit. Pregnancy-related complications were obtained from obstetric case information, and all diagnoses met the community criteria. Neonatal weight was measured at birth by using a medical neonatal weight scale. "v" represents the mean weekly weight gain during the second and third trimesters and was calculated by subtracting the weight measured at 24 weeks of gestation from the weight before delivery divided by the corresponding number of weeks (Unit, kg). GWG is the difference between the weight measured at delivery and the weight before pregnancy. The incidence of macrosomia was determined as the number of macrosomia cases divided by the total number of newborns. Logistic regression analysis and heat map were used to analyze the associations of pre-pregnancy BMI and GWG with macrosomia.

Statistical Analysis

Python 3.8 and Statsmodels 0.12.2 were used for statistical analysis of the data. Count data were expressed as examples (%), and Chi-square test or Fisher's exact probability method was used for comparison between the groups. Measurement data showing normal distribution were represented by "$\overline{x} \pm s$". Independent sample *t*-test was used for comparison between the groups. Multi-variable binary logistic regression was used to analyze the related factors of macrosomia. Incidence heatmaps and line plots were used to explain associations between variables. All statistical tests of significance were two-sided. $P < 0.05$ was considered statistically significant.

Results

Characteristics of the Study Population

Table 1 shows the descriptive statistics of this study. The macrosomia and non-macrosomia groups included 189 and 4667 pregnant women, respectively, and the incidence of macrosomia was approximately 3.89%. The macrosomia group showed significantly higher pre-pregnancy BMI, total weight gain during pregnancy, average weekly weight gain during the second and third trimesters of pregnancy, proportion of women with junior college or below education level,

Table 1 Summary of Patient Characteristics of the Macrosomia and Non-Macrosomia Groups

Characteristics		All	Non-Macrosomia	Macrosomia	P[a]
Age (years) mean ± SD		32.85 ± 4.19	32.86 ± 4.17	32.74 ± 4.65	0.722
Pre-pregnancy BMI (kg/m^2) mean ± SD		22.71 ± 3.13	22.64 ± 3.10	24.39 ± 3.29	<0.001
Y (kg) mean ± SD		8.61 ± 5.62	8.57 ± 5.57	9.61 ± 6.66	0.035
v (kg) mean ± SD		0.48 ± 0.23	0.48 ± 0.23	0.53 ± 0.22	0.008
Neonatal weight (kg) mean ± SD		3313.68 ± 379.72	3279.21 ± 344.81	4165.05 ± 120.40	<0.001
Intensity of occupation (N%)[#]	Low degree of manual labor	4752	4568 (96.1%)	184 (3.9%)	0.603
	High degree of manual labor	104	99(95.2%)	5(4.8%)	
Education level (N%)	Junior college and below	328	303 (92.4%)	25 (7.6%)	0.001
	Undergraduate course	2004	1929 (96.3%)	75 (3.7%)	
	Postgraduate or above	2524	2435 (96.5%)	89 (3.5%)	
Multiparity (N%)	no	3708	3575 (96.4%)	133 (3.6%)	0.059
	yes	1148	1092 (95.1%)	56 (4.9%)	
First pregnancy (N%)	no	2381	2279 (95.7%)	102 (4.3%)	0.190
	yes	2475	2388 (96.5%)	87 (3.5%)	

(*Continued*)

Table 1 (Continued).

Characteristics		All	Non-Macrosomia	Macrosomia	P[a]
GDM (N%)	no	3834	3682 (96.0%)	152 (4.0%)	0.679
	yes	1022	985 (96.4%)	37 (3.6%)	
HDCP (N%)[#]	no	4773	4585 (96.1%)	188 (3.9%)	0.380
	yes	83	82 (98.8%)	1 (1.2%)	
Gestational age of delivery (N%)	37–39 weeks	1631	1608 (98.6%)	23 (1.4%)	<0.001
	39–41 weeks	2969	2829 (95.3%)	140 (4.7%)	
	>41 weeks	256	230 (89.8%)	26 (10.2%)	
Pre-pregnancy BMI (N%)	Underweight	322	317 (98.4%)	5 (1.6%)	<0.001
	Normal weight	3037	2950 (97.1%)	87 (2.9%)	
	Overweight	1196	1127 (94.2%)	69 (5.8%)	
	Obesity	301	273 (90.7%)	28 (9.3%)	
GWG (N%)	Inadequate	2081	2021 (97.1%)	60 (2.9%)	<0.001
	Excessive	890	818 (91.9%)	72 (8.1%)	
	Appropriate	1885	1828 (97.0%)	57 (3.0%)	
Age (N%)	<25	187	178 (95.2%)	9 (4.8%)	0.729
	25–34	3438	3308 (96.2%)	130 (3.8%)	
	>35	1231	1181 (95.9%)	50 (4.1%)	
PCOS (N%)	no	3366	3234 (96.1%)	132 (3.9%)	0.937
	yes	1490	1433 (96.2%)	57 (3.8%)	
History of smoking (N%)	no	3510	3369 (96.0%)	141 (4.0%)	0.519
	yes	1346	1298 (96.4%)	48 (3.6%)	
History of alcohol consumption (N%)[#]	no	4845	4657 (96.1%)	188 (3.9%)	0.354
	yes	11	10 (90.9%)	1 (9.1%)	
Family history of hypertension (N%)	no	3277	3145 (96.0%)	132 (4.0%)	0.531
	yes	1579	1522 (96.4%)	57 (3.6%)	
Family history of diabetes (N%)	no	3799	3652 (96.1%)	147 (3.9%)	0.948
	yes	1057	1015 (96.0%)	42 (4.0%)	
History of GDM (N%)[#]	no	4759	4574 (96.1%)	185 (3.9%)	0.790
	yes	97	93 (95.9%)	4 (4.1%)	

Notes: Continuous variables are expressed as mean ± standard deviation (SD) and analyzed by ANOVA. Discrete variables are expressed as a percentage (N%) and analyzed by chi-square test.

Abbreviations: BMI, body mass index; GWG, gestational weight gain; OGTT, oral glucose tolerance test; GDM, gestational diabetes mellitus; HDCP, hypertensive disorder complicating pregnancy; PCOS, polycystic ovary syndrome. a, $P < 0.05$ was considered statistically significant. Y, total gestational weight gain; v, mean weekly weight gain in the second and third trimesters, calculated as the difference between body weight before delivery and body weight at 24 weeks of gestation divided by gestational age; #, values in the table are derived from Fisher's exact test.

gestational age at delivery, proportion of overweight/obese women in the pre-pregnancy period, and proportion of pregnant women with excessive weight gain during pregnancy than the non-macrosomia group (all $P < 0.05$). The incidence of macrosomia was higher with lower education level, older gestational age at delivery, higher pre-pregnancy BMI grade, excessive weight gain during pregnancy, and excessive weight gain per week during the second and third trimesters of pregnancy. The two groups showed no significant differences in maternal age, physical labor intensity, multiparity, primiparity, gestational diabetes mellitus (GDM), gestational hypertension, polycystic ovary syndrome, smoking history, drinking history, and family disease history.

Subgroup Analysis with Pre-Pregnancy BMI and GWG

Based on the group standard of "Monitoring and Evaluation of Gestational Weight of Chinese Women during Pregnancy" (T/CNSS-009-2021), the GWG of pregnant women with different pre-pregnancy BMI grades was classified and analyzed (Table 2). It was observed that excessive GWG increased the incidence of macrosomia in pregnant women with different pre-pregnancy BMI grades, and the incidence of macrosomia increased with the increase in pre-pregnancy BMI grade. The incidence of macrosomia was 1.6% and 3.0% in the pre-pregnancy underweight group and the excessive GWG group, respectively. Furthermore, the incidence of macrosomia was 2.9% and 7.0% in the normal pre-pregnancy weight group and the excessive weight gain group, respectively. The pre-pregnancy overweight group and the excessive GWG group showed macrosomia incidence of 5.8% and 11.0%, respectively. Furthermore, macrosomia incidence was 9.3% and 17.0% in the pre-pregnancy obese group and the excessive GWG group, respectively. The average newborn weight also increased with the increase in the maternal pre-pregnancy BMI grade. The average weights of newborns born to women who were underweight, normal weight, overweight, and obese before pregnancy were 3180.05 (375.64) g, 3294.78 (368.67) g, 3372.61 (405.39) g, and 3416.17 (455.91) g, respectively; the mean birth weight of newborns was significantly different among the different groups ($P < 0.001$).

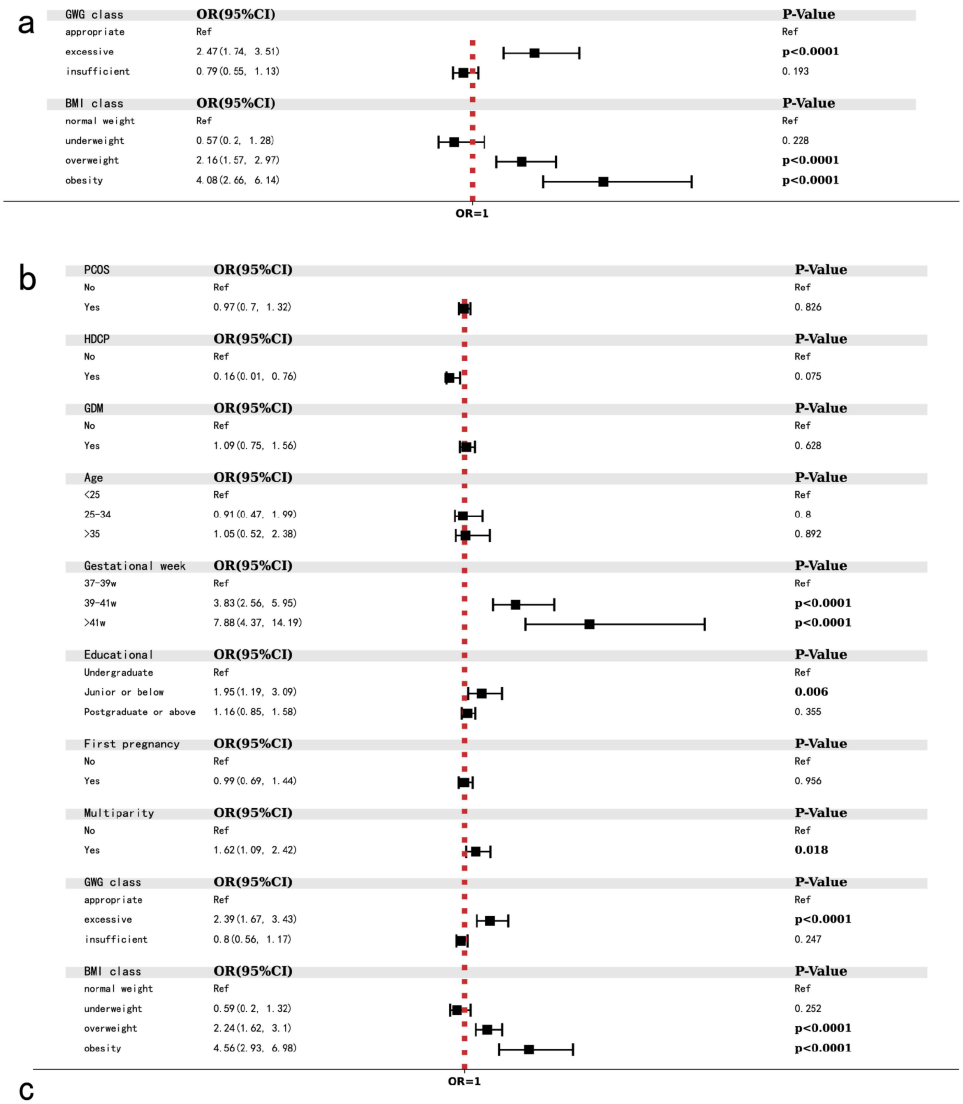
Logistic Regression Analysis

Figure 2a shows the result of the logistic regression model based on pre-pregnancy BMI and weight gain during pregnancy as target variables. Excessive weight gain (OR: 2.47, 95% CI: 1.74–3.51), overweight (OR: 2.16, 95% CI:

Table 2 Weight Gain in Different Pre-Pregnancy Body Mass Index Subgroups

BMI_class	GWG_class	No	Yes	Total	Neonatal Weight [mean(std)]	P
Underweight (BMI < 18.5 kg/m^2)	Inadequate (<11.0 kg)	163 (0.99)	1 (0.01)	164	3180.05 (375.64)	<0.001
	Excessive (>16.0 kg)	33 (0.97)	1 (0.03)	34		
	Appropriate (11.0–16.0 kg)	121 (0.98)	3 (0.02)	124		
Normal weight (18.5 ≤ BMI < 24 kg/m^2)	Inadequate (<8.0 kg)	1051 (0.98)	20 (0.02)	1071	3294.78 (368.67)	1
	Excessive (>14.0 kg)	518 (0.93)	39 (0.07)	557		
	Appropriate (8.0–14.0 kg)	1372 (0.98)	33 (0.02)	1405		
Overweight (24 ≤ BMI < 28 kg/m^2)	Inadequate (<7.0 kg)	637 (0.95)	31 (0.05)	668	3372.61 (405.39)	<0.001
	Excessive (>11.0 kg)	217 (0.89)	28 (0.11)	245		
	Appropriate (7.0–11.0 kg)	275 (0.95)	16 (0.05)	291		
Obese (BMI ≥ 28 kg/m^2)	Inadequate (<5.0 kg)	191 (0.93)	15 (0.07)	206	3416.17 (455.91)	<0.001
	Excessive (>9.0 kg)	50 (0.83)	10 (0.17)	60		
	Appropriate (5.0–9.0 kg)	51 (0.88)	7 (0.12)	58		

Notes: Classification variables are represented by N (%). P represents the *t*-test p value of mean neonatal weight among the different BMI groups; $P < 0.05$ was considered statistically significant. Information given in parentheses after the group indicator is used to classify the groups.



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	OR	P	95% CI
v	2.60	0.003	(1.37, 4.89)
BMI class-normal weight: v	1.28	0.506	(0.62, 2.61)
BMI class-low weight: v	0.44	0.381	(0.06, 2.22)
BMI class-overweight: v	4.57	<0.001	(2.27, 9.10)
BMI class-obesity: v	11.33	<0.001	(4.95, 25.18)

v represents the rate of weight gain in the second and third trimesters; P < 0.05 was considered statistically significant.

Figure 2 Logistic regression analysis based on pre-pregnancy BMI and weight gain during pregnancy as target variables for macrosomia. (**a**) and (**b**). The red line represents the baseline of OR = 1, the black square represents the point estimate of the OR value, and the line segment interval represents the 95% confidence interval. (**c**). Logistic regression analysis of the weight gain rate in the second and third trimesters in the different BMI groups. v represents the average weekly weight gain (v, kg) in the second and third trimesters. BMI class-x: v represents the corresponding risk of macrosomia in different pre-pregnancy BMI groups when the average weekly weight gain was excessive in the second and third trimesters. P values represent differences between groups; P < 0.05 was considered statistically significant.

1.57–2.97), and obesity (OR: 4.08, 95% CI: 2.66–6.14) were associated with macrosomia, and the risk of delivery of the fetus with macrosomia was also significantly increased under the corresponding conditions. To further validate the findings, adjustment was made for the risk values of GWG and pre-pregnancy BMI by incorporating basic maternal

information and other relevant confounding factors (Figure 2b). Compared to the initial model, the risk direction of the corrected model showed no significant change. In the combined corrected model, excessive weight gain (OR: 2.39, 95% CI: 1.67–3.43), overweight (OR: 2.24, 95% CI: 1.62–3.10), and obesity (OR: 4.56, 95% CI: 2.93–6.98) remained the risk factors for macrosomia, with a little change in the risk degree. This indicates that the basic characteristics of pregnant women and the occurrence of pregnancy-related complications do not act as confounding factors. The results of the present study showed that gestational age of 39–41 weeks at childbirth (OR: 3.83, 95% CI: 2.56–5.95), gestational age of more than 41 weeks at childbirth (OR: 7.88, 95% CI: 4.37–14.19), and the education level of junior college or below (OR: 1.95, 95% CI: 1.19–3.09; OR: 1.62, 95% CI: 1.09–2.42) were also the risk factors for macrosomia. To provide more timely and detailed information on GWG, we introduced the concept of average weekly weight gain (v, kg) in the second and third trimesters. By keeping the adjustment variables unchanged, the OR value of the rate of weight gain in the second and third trimesters of pregnancy was again calculated by logistic regression, and the results are shown in Figure 2c. The risk of macrosomia increased 2.6-fold (95% CI: 1.37–4.89, P = 0.003) when the average weekly weight gain was relatively high in the second and third trimesters. In the same situation, based on stratification by pre-pregnancy BMI grade, the overweight pregnant women OR for macrosomia was 4.57 (95% CI: 2.27–9.10, P < 0.001); obese pregnant women OR for macrosomia was 11.33 (95% CI: 4.95–25.18, P < 0.001).

Critical Threshold of Weight Gain in the Overweight Population

Because of the unbalanced number of subgroups, we did not discuss the comparison results of v separately under the pre-pregnancy BMI groups. To show the relationship between pre-pregnancy BMI, v, and macrosomia more intuitively, we used the incidence of macrosomia to construct a heatmap (Figure 3a). The color depth in the heatmap indicates the incidence of macrosomia in the corresponding population. Squares with a darker color indicated that a higher pre-pregnancy BMI or a larger v was associated with a higher incidence of macrosomia. The incidence of macrosomia in Figure 3b refers to the cumulative incidence of macrosomia, that is, the incidence of macrosomia in all pregnant women included in the upper limit of a certain v value. The overall incidence of macrosomia in the normal weight pre-pregnancy BMI group was 3.00%, which is the desired threshold for controlling the incidence of macrosomia. We observed that the incidence of macrosomia in the entire study population crossed the standard line at the levels of v<0.01 kg and v=0.32 kg, respectively, and showed a steady increasing trend after v = 0.32 kg.

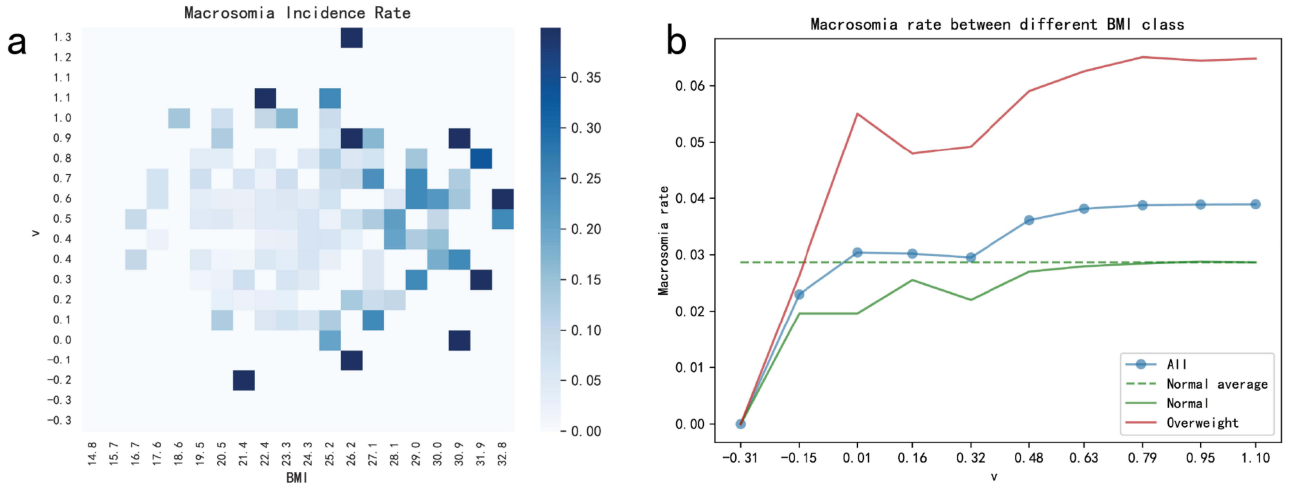

Figure 3 Heatmap of macrosomia incidence, pre-pregnancy BMI, and v. (**a**). The abscissa represents the pre-pregnancy BMI value, the ordinate represents v, and the scale on the right represents the incidence of macrosomia in the population under the corresponding conditions. The darker the blue color, the higher is the incidence of macrosomia in the corresponding population. (**b**). Line plots of macrosomia incidence in different pre-pregnancy BMI populations. The horizontal axis v represents the mean weekly weight gain during the second and third trimesters (kg), and the vertical axis represents the incidence of macrosomia in all women with a v value as the upper limit. The lower right corner is the distinguishing mark; blue represents the entire study population, green represents the normal weight pre-pregnancy BMI group, and red represents the overweight pre-pregnancy BMI overweight group. The green dotted line represents the average incidence in the normal population.

Discussion

A previous study conducted in 2013 revealed that the overall prevalence of macrosomia in Beijing was 7.7%.[4] In the present study, we retrospectively analyzed birth records of PUMCH from July 2020 to June 2022 for maternity and childbirth-related information to determine the incidence and risk factors for macrosomia. The results showed that the incidence of macrosomia was 3. 9% among the 4856 single-term newborns included in the analysis. The incidence of macrosomia in this study was lower than that reported in previous studies. On the one hand, the pregnant women in PUMCH have higher education level and pay more attention to weight change. Reasonable control of weight gain during pregnancy is beneficial to reduce the incidence of macrosomia. On the other hand, the Obstetrics Center of PUMCH provided systematic diet and exercise knowledge for pregnant women through the pregnant women's school. Another study by our team also confirmed that prenatal health education for pregnant women can improve the incidence of adverse pregnancy outcomes to a certain extent.[14] Both BMI and GWG showed significant differences in the descriptive statistics presented in Table 2. The results suggest that women who are overweight or obese before pregnancy have a higher propensity to gain more weight during pregnancy. Furthermore, an increasing trend was observed in the proportion of women with excessive GWG in the pre-pregnancy underweight group (10. 6%), pre-pregnancy normal weight group (184%), pre-pregnancy overweight group (20.4%) and pre-pregnancy obese group (18.5%). This implies that although pre-pregnancy BMI and GWG are independent risk factors for macrosomia, a certain correlation exists between them. This might be related to the long-term unhealthy lifestyle and dietary habits of pregnant women. Hence, lifestyle intervention should be included in the comprehensive management of pregnant women.

The regression model showed that the inclusion of maternal characteristics and comorbidities during pregnancy did not significantly alter the direction and risk values of pre-pregnancy BMI and GWG. The gestational age of delivery can also be interpreted as the intrauterine growth time of the fetus. In our study group, the delivery at 39–41 weeks had already increased the risk of macrosomia in the fetus; this finding suggests that in addition to the ultrasound-based determination of fetal weight exceeding 4000 g, the gestational age of delivery should also considered a risk factor of macrosomia. Particularly, if the pregnant woman also has other large infant risk factors, the appropriate adjustment of childbirth intervention time after comprehensive assessment could be beneficial to the pregnancy outcome. Low education level leads to an increased risk of macrosomia delivery, which may be associated with the living and dietary habits of pregnant women.[15] The pregnancy outcome can be improved by educating pregnant women about pregnancy health, enhancing their health literacy, and adjusting their lifestyle. A retrospective cohort study analyzed women who delivered three consecutive births at the same medical center (1994–2013) and included only nondiabetic women who delivered at full term (≥37 weeks) in all three births. The results showed that the mean birth weight percentages of the first, second, and third births were 47.2% ± 26.3%, 58.3% ± 25.8%, and 61.5% ± 24.7% ($P < 0.001$). A total of 45.9% of the women had the highest fetal birth weight at the third delivery ($P < 0.001$). That is, women who have repeated full-term births show an increase in fetal birth weight at the third birth as compared to that in the first two births.[16] Previous studies have also shown that women who underwent an emergency cesarean section to induce labor and delivery, particularly those having abnormal delivery, are more likely to give birth to infants with macrosomia.[17] In recent years, few studies have investigated the influence of multipara on pregnancy outcomes, and most of these investigations were cohort studies that lacked mechanistic exploration. In addition, in the present study, although the results of the chi-square test suggested differences in the incidence of macrosomia for the three occupational intensity groups, it was difficult to conduct accurate assessment due to the large differences in the number of subgroups, differences between physical activity and standardized exercise during pregnancy, high heterogeneity, and certain deviations in self-reporting; hence, a specific analysis could not be performed. However, in future studies, it is essential to specifically investigate the role of occupational intensity on pregnancy outcomes, which requires to clearly delineate the degree of physical labor and correlate it with physical activity (sports) outside of daily work.

Presently, the recommended ranges of GWG for pregnant women have been clearly defined. However, many pregnant women show excessive GWG or insufficient GWG at different stages of pregnancy and finally meet the overall requirements. Considering that large fluctuations in body weight within a short period of time could harm the growth and development of the fetus and affect the stable hormone levels of pregnant women, and because the majority of pregnant women do not have a stable body weight in the first trimester due to nausea and vomiting, we introduced the

concept of average weekly weight gain (v) in the second and third trimesters in this study. This will help pregnant women to assess for themselves whether their daily weight gain is stable and appropriate. In the present study, the average weekly weight gain in the second and third trimesters of pregnancy in the macrosomia and non-macrosomia groups was 0.53 ± 0.22 and 0.48 ± 0.23 kg, respectively, with a significant difference between the two groups (P = 0.008). As shown in Figure 3a, the overall trend in the incidence of macrosomia revealed that if the pre-pregnancy BMI reaches a high value, the incidence of macrosomia will remain high even if the weight gain during pregnancy is controlled at zero or negative levels. Similarly, if the weight gain during pregnancy is not properly controlled, even if the pre-pregnancy BMI is good, the incidence of macrosomia will still be significantly increased. The heatmap (Figure 3a) of macrosomia incidence represents the incidence of macrosomia in the study population under the corresponding conditions. As shown in the figure, pre-pregnancy BMI = 21.4 and v = −0.2 are taken as examples. Although few cases met this condition, the occurrence of macrosomia will be regarded as special cases; this is, however, not within the scope of the discussion of the overall trend. Hence, we conclude that pre-pregnancy BMI and v are independent influencing factors for macrosomia. Pre-pregnancy BMI and v should be considered important evaluation factors for appropriate weight management during pregnancy. Strengthening targeted management could reduce the incidence of macrosomia and improve delivery outcomes to a certain extent.

This study also analyzed the average weekly weight gain in the second and third trimesters of pregnancy that was more likely to be beneficial for reducing the incidence of macrosomia in overweight women (BMI ≥ 24 kg/m^2). As shown in Figure 3b, the increase in macrosomia incidence in the entire study population after v = 0.32 can be considered to be contributed by overweight women, after controlling for other confounding variables. The figure illustrates that the incidence of macrosomia in the overweight group converges with the standard line at v = −0.15, reaches the first peak at v = 0.01, and then begins to decline; thus, the incidence of macrosomia is controlled below 0.05, within the range of v = 0.16–0.32. Limiting the incidence of macrosomia to that in women with normal pre-pregnancy weight would require an average weekly weight gain of 0.15 kg in overweight women during the second and third trimesters; this is, however, not consistent with clinical practice. Hence, we consider v = 0.32 as the recommended upper limit of average weekly weight gain for overweight pregnant women in the second and third trimesters to allow these women to gain the maximum allowable weight during pregnancy while reducing the incidence of macrosomia. These results are applicable to overweight pregnant women who wish to reduce the risk of macrosomia and to assist them to monitor and evaluate their weight gain during the second and third trimesters. There is a synergistic effect between pre-pregnancy overweight or obesity and gestational weight gain, and their co-existence will increase the risk of many diseases in pregnant women.[18] Therefore, weight management for this population is particularly important.

Currently, the proportion of adults who are overweight or obese is increasing worldwide.[19] Overweight and obesity in women have a remarkable effect on reproductive health, particularly pregnancy.[20,21] Obese women have a higher risk of GDM, preeclampsia, complicated surgical delivery, fetal macrosomia, and neonatal morbidity.[22] Although we analyzed and studied only macrosomia in the present study, several studies have confirmed that excessive weight gain during pregnancy is associated with various pregnancy-related complications. Platner et al studied 515,148 birth records in New York and found that weight gain of more than 9 kg during pregnancy was associated with a 20% increase in severe maternal morbidity as compared to women who gained the recommended weight during pregnancy (the upper limit was 25 kg).[23]

Macrosomia also increases the risk of childhood obesity. An association between macrosomia and an increased risk of obesity was noted in children under 3 years of age in western China. For example, in one study, 714 of 1767 infants had macrosomia. The risk of childhood obesity in macrosomia defined according to the height-weight ratio was 1.9-fold (95% CI: 1.04–3.49) that of the normal birth weight.[7] Studies on the pathogenetic factors of macrosomia have shown that the expression levels of five miRNAs in the miR-17-92 cluster are significantly increased in the placenta of macrosomia births; these miRNAs can promote macrosomia development by targeting regulators in the cell cycle pathway.[24] Brian T Joyce et al also confirmed that the *MEST* and *IGF2* genes play a potential regulatory role in fetal growth and development.[25] There is even a 60-year follow-up study investigating the association of overweight before pregnancy, weight gain during pregnancy, and colorectal cancer in adulthood, proving that in utero events are important colorectal cancer risk factors.[26] This implies that obesity could become a vicious cycle of genetic, epigenetic, and metabolic factors that are transmitted from the mother to the child.

Effective weight management during pregnancy will critically affect maternal and infant health outcomes. However, many pregnant women have very limited understanding of excessive weight gain during pregnancy.[27] Pregnant women have a lower level of health knowledge, show passive involvement in interactions with doctors, and rely on family advice and cultural practices to adopt health behaviors suitable for pregnancy. A small number of pregnant women with high health literacy actively seek health information but have difficulty in finding reliable resources. Therefore, the effectiveness of lifestyle interventions during pregnancy should be emphasized in clinical practice,[28] and patient attention and education level of the related practitioners should be improved to consider overweight and obesity as important risk factors of macrosomia. Strict control of GWG is simultaneously required to improve pregnancy outcomes.

The present study has certain strengths and limitations. In terms of strengths, first, we used the electronic medical records from the hospital to collect all the prenatal examination data; this reduced the manual work time and the possible errors during manual data entry, thus facilitating error correction and review of the accuracy of medical records. Second, this study provides new evidence for the importance of weight management during pregnancy; the study further indicates that it is even more critical for women with poor pre-pregnancy health conditions to maintain a healthy lifestyle during pregnancy. Finally, this study introduced a new index of GWG, ie, the average weekly weight gain in the second and third trimesters; this index could guide healthcare providers and pregnant women and their families to evaluate the appropriate weight gain in each trimester. Regarding limitations, the present study was a single-center study, the pregnant women had higher education levels than those in other regions, and the population representation was poor. The results from the study may not be entirely generalizable and this was an observational study and thus causality cannot be inferred. The relevance of our research results and the significance of the new indicator of weight gain should be verified in larger samples and multicenter populations. Moreover, our sample size did not allow us to determine the appropriate average weekly weight gain in the second and third trimesters in more specific subgroups; this aspect should be the focus of future research studies.

Conclusion

This study found that pre-pregnancy BMI and gestational weight gain had a certain effect on the macrosomia, and there was an interaction between them. Pregnant women who are overweight before pregnancy should keep their body weight gain to less than 0.32kg/week during the second and third trimesters to reduce the incidence of macrosomia. This finding highlights the importance of healthy pre-pregnancy preparation and weight management during pregnancy to reduce adverse pregnancy outcomes. Although the results of our study have some limitations, they also provide some evidence for research in this field. Further discussion on the differentiation of weight management under different BMI category refinement is needed in the future, which is essential for improving maternal and child health.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

This study was reviewed by the Ethics Committee of Peking Union Medical College Hospital (JS-2763). All experimental protocols were approved by a named institutional and licensing committee. All the steps/ methods were performed in accordance with the relevant guidelines and regulations.

Consent for Publication

All the authors approved the publication of the manuscript.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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