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Full length article

## The gestational weight gain and perinatal outcomes among underweight women with twin pregnancies: Propensity score matched analysis from a three-year retrospective cohort



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### ABSTRACT

**Objective:** No recommendations are available for gestational weight gain (GWG) in underweight women with twin pregnancies. We aimed to evaluate whether underweight women with twin pregnancies should gain more weight than normal-weight women in order to optimize perinatal outcomes.

**Study design:** This retrospective cohort study compared the GWG and perinatal outcomes among normal-weight and underweight women who gave birth to viable twins between 2015 and 2018 at the Maternal and Child Health Hospital in Foshan, China. Gestational weight gain (GWG) was categorized as adequate or inadequate GWG, based on the US Institute of Medicine 2009 guidelines for normal-weight women ( $\geq 0.46$  kg/week). The outcomes of interest included spontaneous preterm birth (sPTB)  $<37$  weeks,  $<35$  and  $<32$  weeks, small for gestational age (SGA), gestational hypertensive disorder (GHD), gestational diabetes mellitus (GDM), birth weight discordance (BDW)  $\geq 20\%$ , neonatal intensive unit (NICU) admission and neonatal respiratory distress syndrome (NRDS). Propensity score matching (PSM, in a 1:1 ratio) was utilized to minimize the effects of confounders on the differences in the two cohorts. Multivariable logistic models were also used to verify the results from PSM analysis.

**Results:** There were 475 normal-weight and 111 underweight women included in the analysis. Our results suggested that the incidence of adequate GWG was comparable between underweight and normal-weight women (37.5% vs. 45.1%,  $P=0.141$ ). The prevalence of GDM was significantly lower among underweight women (9.9%) than among normal-weight women (20.4%) ( $P=0.010$ ). There was no evidence of differences in other perinatal outcomes between the two groups. 102 underweight women and 102 normal-weight women were included in PSM analyses. There was a lower incidence of GDM in underweight women than in normal-weight women, but the difference was not significant (9.8% vs. 18.6%,  $P=0.071$ ). No evidence of any differences in the other outcomes, including sPTB, GHD, BWD $\geq 20\%$ , SGA, NICU admission and NRDS, was found between the underweight and normal-weight women. Multivariable logistic regression models yielded similar results.

**Conclusions:** For Chinese twin pregnant women with twin pregnancies, our data does provide evidence to suggest underweight women need to gain more weight than normal-weight women to optimize perinatal outcomes. Future studies with larger number of underweight women with twin gestations are warranted to establish an optimal range of GWG.

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### Introduction

Both maternal body mass index (BMI) and gestational weight gain (GWG) are considered important indicators for evaluating the nutritional status of pregnant women. These indicators have been proven to have implications for perinatal outcomes among twin

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gestations, such as preterm birth, pregnancy-induced hypertension and fetal growth restriction in singletons [1–5].

Theoretically, women who enter pregnancy at a normal BMI and gain weight within the recommended range have a minimum likelihood of experiencing adverse pregnancy outcomes. The GWG recommendations for singleton pregnancies are well established, whereas those for twin pregnancies remain unclear since inconsistent results have been found [2,6,7]. In 2009, the Institute of Medicine (IOM) specified a recommended amount of weight gain, which was initially released in 1990, for normal-weight (17–25 kg), overweight (14–23 kg) and obese women (11–19 kg) with term twin pregnancies [8]. The recommendations for underweight women, however, remain uncertain. The existing recommendations suggest that both lower and upper limits have an inverse relationship with maternal BMI; with a higher pre-pregnancy BMI, a smaller amount of gestational weight gain is required. Thus, we hypothesized that underweight women with twin gestations should gain more weight than normal-weight women during pregnancy to improve perinatal outcomes, based on the 2009 IOM guidelines.

## Methods

### Study design and population

This study was a retrospective cohort study conducted in the Maternal and Child Health Hospital in Foshan, China, between July 2015 and June 2018. Women who had available BMI data at their first antenatal visit in the first trimester and gave birth to viable twins at  $\geq 26$  weeks of gestation were considered eligible participants. Mothers without BMI data in the first trimester or without GWG information were excluded from the dataset. Mothers with monoamniotic twins and pregnancies with major congenital malformations, twin-to-twin transfusion syndrome (TTTS) or intrauterine death were also excluded.

Medical records were reviewed to obtain baseline information, GWG and perinatal outcomes. Baseline information included maternal BMI in the first trimester, maternal age, educational level, chronic hypertension, pre-existing diabetes mellitus, chorionicity, parity, use of assisted reproductive technology (ART) in current pregnancy, prior cesarean section and prior abortion or miscarriage.

Maternal BMI was calculated by dividing the mother's weight (in kilograms) by her height (in meters squared), and was then categorized as underweight ( $\text{BMI} < 18.5 \text{ kg/m}^2$ ), normal weight ( $18.5\text{--}23.99 \text{ kg/m}^2$ ), overweight ( $24\text{--}27.99 \text{ kg/m}^2$ ) or obese ( $\geq 28 \text{ kg/m}^2$ ), based on the standards of the Working Group on Obesity in China [9]. In this study, only underweight and normal weight women were included for analysis. To assess the adequacy of GWG among the study population, the GWG rate of each participant, which was calculated by dividing the total GWG by gestational age in weeks, was compared with the minimum recommended GWG rate. The minimum GWG was calculated by dividing the lower limit of IOM recommended GWG by 37 weeks, as performed in previously studies [6,7,10]. According to the IOM 2009 guidelines, the minimum recommended GWG rate for normal-weight women was 0.46 kg per week [8]. The GWG of all included participants was categorized as adequate ( $\geq 0.46 \text{ kg/week}$ ) or inadequate ( $< 0.46 \text{ kg/week}$ ). Chorionicity was determined at the first sonographic examination ( $\lambda$ -sign for monochorionicity and T-sign for diamnioticity) and was confirmed by placental pathologic findings after birth.

The primary outcomes of this study were spontaneous preterm birth (PTB)  $< 37$  weeks and small for gestational age (SGA) in either twin fetus. Secondary outcomes included the gestational age at delivery, PTB  $< 35$  weeks and  $< 32$  weeks, gestational hypertensive disorder, gestational diabetes mellitus (GDM) and birth weight

discordance (BWD) greater than 20%, neonatal intensive unit (NICU) admission and neonatal respiratory distress syndrome (NRDS). The gestational age at delivery was based on the last menstrual period and confirmed by early ultrasound, if available. SGA was defined when the birthweight was below the 10th percentile for the gestation age and sex based on twin birth weight curves in Chinese twins [11,12]. Gestational hypertensive disorder was defined when at least one of the following complications occurred: gestational hypertension, preeclampsia and eclampsia, which was diagnosed using standard criteria [13].

### Statistical analysis

All statistical analyses were performed using Stata, version 15.0. The differences in baseline characteristics and outcomes between underweight and normal-weight women were assessed. Continuous variables with a Gaussian distribution were presented as the mean  $\pm$  standard deviation and analyzed by independent sample *t* tests. Categorical variables were presented as the frequency with accompanying percentages and analyzed by the Chi-square test or Fisher's exact test, when appropriate. Propensity score matching (PSM) was utilized to minimize the effects of confounders on the differences in the two cohorts. The propensity score (PS) was used to predict the probability of inclusion into either group (underweight or normal weight) for each participant. This value was calculated using a logistic regression model, in which the maternal BMI category was used as the dependent variable and the following characteristics were used as the independent variables: maternal age, college degree, nulliparity, use of ART, chorionicity, prior cesarean section, prior spontaneous abortion, prior induced abortion and GWG. We then applied a 1:1 nearest-neighbor matching with a caliper of 0.05, a preset value for PSM, to obtain a matched data. After PSM matching, the outcomes were compared between underweight women and normal-weight women. Multivariate logistic regression analysis with adjustments for confounding variables was also adopted to estimate the effect of underweight status on clinical outcomes. Variables with significance of  $P < 0.20$  in baseline analysis were included for adjustment. These results were reported as odds ratios (ORs) and corresponding 95% confidence intervals (CIs). A *P*-value  $< 0.05$  was denoted as statistically significant in all analyses. For subgroup analyses, pregnancy outcomes were compared between underweight and normal-weight women who gained adequate weight ( $\geq 0.46 \text{ kg/week}$ ). Additional analyses were carried out for comparing outcomes by GWG categories (adequate GWG vs. inadequate GWG) among underweight women.

## Results

The process of participant selection is shown in Fig. 1. A total of 586 women with twin pregnancies were enrolled in this study, including 475 women with a normal BMI and 111 women with an underweight BMI.

The demographic characteristics are presented in Table 1. The average age of the participants was  $30.9 \pm 4.3$  years old. The underweight women were younger than the normal-weight women ( $P = 0.001$ ). Approximately 50% of the participants in both groups had a college education. More than 70% of the underweight women were nulliparous, which was slightly more than the percentage of normal-weight women who were nulliparous (64.0%,  $P = 0.073$ ). Women with a normal weight were more likely to have a previously induced abortion (22.5% vs. 13.5%,  $P = 0.035$ ) and use ART in the current pregnancy (73.7% vs. 55.0%,  $P < 0.001$ ) than were underweight women. The incidence of a previous induced abortion ( $P = 0.013$ ) and the use of ART ( $P < 0.001$ ) were positively associated with the maternal age. No difference was

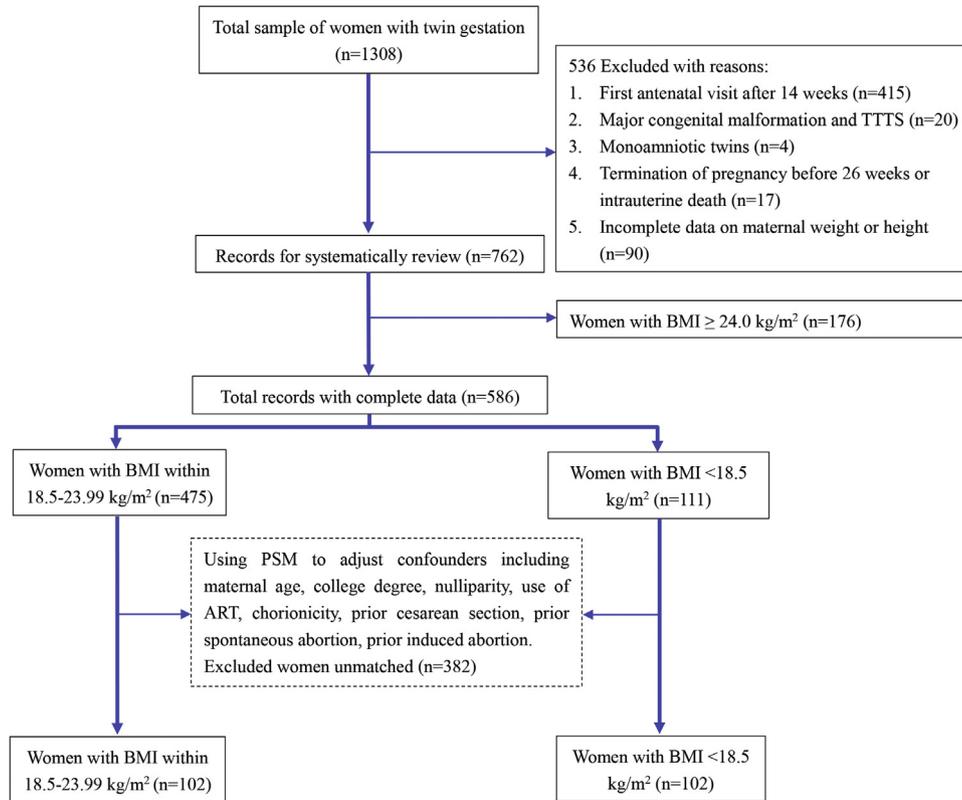


Fig. 1. Flow diagram of selection of patients in this study.

detected in chorionicity between the two groups. More than half of women in both groups had inadequate weight gain throughout the pregnancy, although there was no significant difference between groups ( $P = 0.141$ ).

Regarding the outcomes, there was no statistically significant evidence of differences in the length of pregnancy, the incidence of spontaneous PTB < 37 weeks, <35 weeks or <32 weeks, gestational hypertensive disorder, BWD  $\geq 20\%$ , SGA in at least one twin, NICU

**Table 1**  
Baseline characteristics and outcomes between normal weight and underweight pregnant women.

Characteristics	Normal maternal BMI 18.5–23.99 kg/m <sup>2</sup> (n = 475)	Maternal BMI < 18.5 kg/m <sup>2</sup> (n = 111)	P-value
Maternal age, year			
<25	178 (37.5)	61 (55.0)	0.001
25–34	177 (37.3)	36 (32.4)	
$\geq 35$	120 (25.3)	14 (12.6)	
College degree <sup>a</sup>	219 (52.0)	53 (52.0)	0.992
Nulliparity	304 (64.0)	81 (73.0)	0.073
Use of ART	350 (73.7)	61 (55.0)	<0.001
MCDA twin gestation	83 (17.5)	24 (21.6)	0.308
Prior caesarean section	72 (15.2)	13 (11.7)	0.353
Prior spontaneous abortion	99 (20.8)	20 (18.0)	0.505
Prior induced abortion	107 (22.5)	15 (13.5)	0.035
Chorionic hypertension	1 (0.2)	0 (0)	1.000
Pre-existing diabetes mellitus	5 (1.1)	0 (0)	0.590
Weight gain during pregnancy			
$\geq 0.46$ kg/week	178 (37.5)	50 (45.1)	0.141
<0.46 kg/week	297 (62.5)	61 (55.0)	
Gestational age at delivery, weeks	36.0 $\pm$ 0.1	36.0 $\pm$ 0.2	0.987
Spontaneous preterm birth <37 weeks	32 (6.7)	11 (9.9)	0.248
Spontaneous preterm birth <35 weeks	22 (4.6)	4 (3.6)	0.636
Spontaneous preterm birth <32 weeks	9 (1.9)	2 (1.8)	1.000
Gestational hypertensive disorder	45 (9.5)	8 (7.2)	0.454
Gestational diabetes mellitus	97 (20.4)	11 (9.9)	0.010
Birth weight discordance $\geq 20\%$	48 (10.1)	11 (9.9)	0.951
SGA in either twin fetus	30 (6.3)	7 (6.3)	0.997
NICU admission	218 (45.9)	55 (49.6)	0.487
NRDS	32 (6.7)	9 (8.1)	0.610

BMI, body mass index; ART, assisted reproductive technology; MCDA, monochorionic diamniotic; SGA, small for gestational age; NICU, neonatal intensive care unit; NRDS, neonatal respiratory distress syndrome.

<sup>a</sup> missing data on 63 subjects.

**Table 2**  
Baseline characteristics and outcomes between normal weight and underweight pregnant women. After 1:1 propensity matching.

Characteristics	Normal maternal BMI 18.5–23.99 kg/m <sup>2</sup> (n = 102)	Maternal BMI < 18.5 kg/m <sup>2</sup> (n = 102)	P-value
Maternal age, year			
<25	61 (59.8)	55 (53.9)	0.461
25–34	25 (24.5)	33 (32.4)	
≥35	16 (15.7)	14 (13.7)	
College degree	57 (55.9)	53 (52.0)	0.574
Nulliparity	79 (77.5)	74 (72.6)	0.419
Use of ART	60 (58.8)	55 (53.9)	0.480
MCDA twin gestation	21 (20.6)	23 (22.6)	0.734
Prior cesarean section	8 (7.8)	12 (11.8)	0.346
Prior spontaneous abortion	12 (11.8)	18 (17.7)	0.236
Prior induced abortion	11 (10.8)	13 (12.8)	0.664
Chorionic hypertension	0 (0)	0 (0)	–
Pre-existing diabetes mellitus	1 (1.0)	0 (0)	1.000
Weight gain during pregnancy (kg/week)			
≥0.46 kg/week	46 (45.1)	48 (47.1)	0.779
<0.46 kg/week	56 (54.9)	54 (52.9)	
Gestational age at delivery, weeks	36.0 ± 0.2	36.0 ± 0.1	0.889
Spontaneous preterm birth <37 weeks	6 (5.9)	9 (8.8)	0.593
Spontaneous preterm birth <35 weeks	4 (3.9)	3 (2.9)	1.000
Spontaneous preterm birth <32 weeks	0 (0)	1 (1)	1.000
Gestational hypertensive disorder	7 (6.9)	7 (6.9)	1.000
Gestational diabetes mellitus	19 (18.6)	10 (9.8)	0.071
Birth weight discordance ≥ 20%	8 (7.8)	11 (10.8)	0.470
SGA in either twin fetus	5 (4.9)	6 (5.9)	1.000
NICU admission	49 (48.0)	49 (48.0)	1.000
NRDS	7 (6.9)	8 (7.8)	1.000

BMI, body mass index; ART, assisted reproductive technology; NICU, neonatal intensive care unit; SGA, small for gestational age; NRDS, neonatal respiratory distress syndrome; MCDA, monochorionic diamniotic.

admission or NRDS between normal-weight and underweight women, shown in Table 1. The incidence of GDM among normal-weight women (20.4%), however, was nearly twice that among underweight women (9.9%,  $P = 0.010$ ).

In the propensity analysis, a total of 204 matched participants (102 for each group) were involved. There was no evidence of differences in the baseline characteristics between the two groups ( $P > 0.05$ ) (Table 2). As for the unmatched analysis, all outcomes were similar between the underweight women and normal-weight women, except for the incidence of GDM, which remained higher in normal-weight women (18.6%) than in underweight women (9.8%), although the difference was not statistically significant here ( $P = 0.071$ ).

The multivariate logistic regression analyses yielded similar results as for those from PSM, after we adjusted for confounding variables including maternal age, nulliparity, use of ART, prior induced abortion and inadequate GWG (Table 3). Underweight women were not associated with any adverse outcomes of interest. We did observe a decreased risk of GDM among underweight women (OR = 0.51; 95% CI: 0.26–1.01).

**Table 3**  
The associations between maternal underweight status (BMI < 18.5 kg/m<sup>2</sup>) and maternal and neonatal outcomes in multivariate logistic regression models.

Outcomes	aOR <sup>a</sup>	95% CI
Spontaneous preterm birth <37 weeks	1.58	0.75–3.35
Spontaneous preterm birth <35 weeks	0.73	0.24–2.24
Spontaneous preterm birth <32 weeks	0.99	0.20–4.91
Gestational hypertensive disorder	0.72	0.32–1.62
Gestational diabetes mellitus	0.51	0.26–1.01
Birth weight discordance ≥ 20%	0.90	0.44–1.84
SGA in either twin fetus	1.06	0.44–2.58
NICU admission	1.18	0.77–1.82
NRDS	1.31	0.58–2.95

aOR: adjusted odds ratio; CI, confidence interval; SGA, small for gestational age; NICU, neonatal intensive care unit; NRDS, neonatal respiratory distress syndrome.

<sup>a</sup> adjusted for maternal age, nulliparity, use of ART, prior induced abortion and gestational weight gain.

A subgroup analysis was conducted between the normal-weight and underweight women who gained adequate weight (≥ 0.47 kg/week). Among the 178 normal-weight and 50 underweight women, no statistically significant differences were found between the two cohorts in any adverse outcomes (Supplementary material, Table S1). We further compared outcomes by GWG categories among the 111 underweight women. A slightly shorter duration of pregnancy was found among women with inadequate GWG, than in those with adequate GWG (35.6 ± 0.2 vs. 36.4 ± 0.1 weeks) (Table S2). No difference was found in the other outcomes (Table S2 and Table S3).

## Discussion

In the present study, based on the recommended weight gain in IOM 2009 guidelines, we found that among twin pregnancies, underweight women and normal-weight women had a comparable amount of weight gain and experienced similar perinatal outcomes. As the recommendations for gestation weight gain among underweight women with twin pregnancies have yet to be established, our findings have clinical implications for patient counselling in prenatal care.

The majority of prior studies excluded underweight women with twin gestations from analysis due to the lack of recommendations for this population [10,14–16]. In fact, the optimal weight gain range for underweight women with twin gestations should be as important as that for overweight or obese women. No consensus had been reached regarding whether underweight women should gain more weight than normal-weight women should. A large cohort study by Chen et al. [17], which included 854 underweight women with twin pregnancies and applied Chinese-recommended GWG, demonstrated that a GWG below the recommended (< 18 kg) was associated with an increased risk for SGA newborns. The Chinese-recommended GWG for underweight women was slightly higher than the IOM recommendations (< 17 kg) applied in the current study, and it was valid for SGA newborns. However, there is a lack of

validation regarding other pregnancy outcomes. Another study conducted in America assessed the adequacy of GWG among underweight women with twin pregnancies using the IOM-recommended GWG for normal-weight women [18], and whose conclusions are consistent with this current study. The rationale for this group underweight and normal weight women together in this study was not explained, but reflects the lack of guidance for the underweight woman [18].

A 2018 study conducted in the USA that included 55 underweight and 609 normal-weight women with twin pregnancies, demonstrated that when underweight women and normal-weight women gained a similar amount of weight, they experienced similar pregnancy outcomes [19]. These findings were confirmed by our study, in which we included twice the number of underweight women from a different population origin in a middle income country. In subgroup analyses, we also found comparable outcomes between underweight and normal-weight women with adequate GWG. The similarity in GWG and pregnancy outcomes between underweight and normal-weight women may imply that underweight women with twin gestations do not necessarily need to gain more weight than normal-weight women do to optimize their pregnancy outcomes. When we compared the outcomes by GWG categories among underweight women, we observed a shorter length of pregnancy in inadequate GWG women. Similar results were also reported for other BMI categories in other studies [18,20,21]. However, we did not find evidence of any difference in the other outcomes, which may be due to the limited number of patients in each GWG category.

We observed a lower risk of GDM among underweight women than among normal-weight women, although the risk was nonsignificant after adjustments for confounders. In contrast, Liu et al. [19] found a similar incidence of GDM between underweight (5.5%) and normal-weight women (6.7%) with twin gestations, although this could be a chance observation due to the limited number of underweight women. A lower risk of GDM in underweight women was previously reported in studies on women with singletons in China [22–25] as well as other countries [26–29]. According to the meta-analysis by Najafi et al. [30], the presence of a dose-response relationship between maternal BMI and GDM supports these findings. Thus, we speculated that the lower risk of GDM among underweight women with twin pregnancies may be concealed by the small size of the study population in the current study. Larger-scale studies may help to determine the difference in the prevalence of GDM between normal-weight and underweight women with twin pregnancies in the future.

One merit of our study is that we obtained robust results using PSM, which allows for more confounders and is better at eliminating collinearities than is multivariate logistic analysis [31]. It cannot be denied that this study has some limitations. First, an inherent potential for bias cannot be avoided in retrospective data. Longitudinal data on gestational weight were unable to be accessed and compared between underweight and normal-weight women. Second, we used the measured weight at the first prenatal visit before 14 weeks, instead of the self-reported pre-pregnancy weight. This value has some limitations, despite its correlation of satisfactory strength with pre-pregnancy weight [32]. Third, although the number of underweight women was twice that in a prior study [19], it still limited our ability to explore the role of excessive weight gain in perinatal outcomes, since there were only two underweight women with excessive weight gain. Thus, a large-scale population research is warranted.

In conclusion, we found similar GWG and perinatal outcomes between underweight and normal-weight women with twin pregnancies, and we suggest adherence to the recommended amount of weight gain (17–25 kg) for underweight women.

## Author contributions

D.L and S.W conceived and designed the study. J.R and S.Y checked for the data accuracy and completeness. G.C provided methodology suggestion. D.F and P.L and performed the statistical analysis. Z.Z interpret the results. D.L drafted the manuscript. Y.L and H.M revised the manuscript. X.G and Z.L is the guarantor of the manuscript. All authors approved the final manuscript as summited.

## Declaration of Competing Interest

The authors declare no conflict of interest.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ejogrb.2019.10.009>.

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