Is the Gestational Weight Gain Recommended by the National Academy of Medicine Guidelines Suitable for Chinese Twin-Pregnant Women with Gestational Diabetes Mellitus?

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Am J Perinatol 2024; 41(suppl S1):e331–e340.

Abstract

Objectives This study aimed to assess the applicability of the National Academy of Medicine (NAM) interim guidelines for twin pregnancies to the specific population of gestational diabetes mellitus by exploring the relationship between gestational weight gain and adverse pregnancy outcomes in Chinese twin-pregnant women with gestational diabetes mellitus.

Study Design This was a retrospective cohort study of women diagnosed with diabetes in pregnancy between July 2017 and December 2020 at the Maternal and Child Health Hospital in Chongqing, China. The primary variable of interest was maternal total gestational weight gain. The primary outcomes were perinatal outcomes, which included: preeclampsia, small for gestational age, large for gestational age, low birth weight, neonatal pneumonia, neonatal respiratory distress syndrome, and neonatal intensive unit admission, etc. The association between inappropriate gestational weight gain and adverse pregnancy outcomes was estimated using multiple logistic regression analysis.

Results A total of 455 twin-pregnant women who had gestational diabetes mellitus were analyzed. Women with low gestational weight gain had reduced risk of preeclampsia (adjusted odds ratio [aOR], 0.32; 95% CI or confidence interval, 0.17–0.63; $p = 0.001$) and their infants had higher risks of small for gestational age (aOR, 1.93; 95% CI, 1.04–3.58; $p = 0.037$), low birth weight (aOR, 2.27; 95% CI, 1.32–3.90;

Keywords
- twins
- gestational weight gain
- gestational diabetes mellitus
- adverse perinatal outcomes

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received January 5, 2022
accepted after revision June 3, 2022
article published online September 16, 2022

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0042-1754319.
ISSN 0735-1631.

$p = 0.003$), neonatal intensive unit admission (aOR, 3.29; 95% CI, 1.10–5.78; $p = 0.038$), pneumonia (aOR, 2.41; 95% CI, 1.08–5.33; $p = 0.031$), and neonatal respiratory distress syndrome (aOR, 2.29; 95% CI, 1.10–4.78; $p = 0.027$); the infants of women with excessive gestational weight gain had a higher risk of large for gestational age (aOR, 3.76; 95% CI, 1.42–9.96; $p = 0.008$).

Conclusion Gestational weight gain controlled within the range recommended by the NAM could reduce the risk of perinatal adverse outcomes. The 2009 NAM gestational weight gain recommendations can be used for Chinese twin-pregnant women with gestational diabetes mellitus.

Key Points

- Inappropriate gestational weight gain can lead to adverse perinatal outcomes in twin pregnancies.
- Gestational weight gain controlled within recommended range could reduce the risk of poor perinatal outcomes.
- The National Academy of Medicine recommendations are suitable for Chinese twin-pregnant women with GDM.

With the widespread application of assisted reproductive technology in clinical practice in recent years, the incidence of twin pregnancies has been increasing.[1] Compared with women with singleton pregnancies, women pregnant with twins are at greater risk for adverse maternal and neonatal outcomes, including a higher risk of gestational diabetes, hypertensive disorders in pregnancy, premature rupture of membranes (PROMs), postpartum hemorrhage, preterm birth, cesarean delivery, low birth weight (LBW), neonatal respiratory distress syndrome (NRDS), and fetal and neonatal deaths.[2]

Gestational diabetes mellitus (GDM) was strongly associated with the incidence of adverse perinatal disease and mortality in mothers and fetuses, and with long-term adverse health events.[3,4] As reported in a previous study, the incidence of gestational diabetes in twin pregnancies ranges from 3.2 to 21.5%,[5] and the incidence in Beijing of China was as high as 23.7%.[6] Previous studies have shown that women with twin pregnancies have twice the risk of developing GDM compared with women with single pregnancies, as well as excessive gestational weight gain (GWG) was very common in women with GDM.[7]

GDM, prepregnancy body mass index (BMI), and GWG were important factors of pregnancy outcomes. In singleton and twin pregnancies, GWG was widely recognized as a modifiable risk factor for adverse pregnancy outcomes.[8,9] Achieving an adequate GWG was essential for maternal health, fetal development, and lifelong health. As previous studies[10,11] have reported, GWG has an impact on the health of mothers and children. Compared with appropriate GWG, women with excessive GWG were more likely to have gestational hypertension, cesarean delivery, and macrosomia[11]; insufficient GWG increased the risk of LBW and preterm birth.[10] It was theorized that women with twin pregnancies have higher nutritional needs, thus inadequate GWG may have a greater impact on women with twin pregnancies. However, women with twin pregnancies tended to have higher GWG than women with singleton pregnancies, and were more likely to experience hypertensive disorders, cesarean delivery, and gestational diabetes.[12,13]

Currently, there is little data on the optimal range of GWG for twin pregnancies; the National Academy of Medicine (NAM) presently only provides interim recommendations on GWG for women with twin gestations.[9] The guidelines are based on the GWG interquartile (25th–75th percentiles) range for women with an average birth weight of twins ≥2,500 g at 37 to 42 weeks of gestation. The specific scope was as follows: 16.8 to 24.5 kg for normal weight women (BMI, 18.5–23.9 kg/m^2), 14.1 to 22.7 kg for overweight women (BMI, 24.0–27.9 kg/m^2), and 11.3 to 19.1 kg for obese women (BMI, ≥28.0 kg/m^2). However, the NAM guidelines failed to have sufficient data to provide optimal GWG recommendations to underweight women. Based on the NAM recommendations for twin pregnancies, studies[14–16] in different countries have explored the relationship between GWG and adverse pregnancy outcomes, but due to the small sample size and different exclusion criteria, inconsistent results were obtained. Hyperglycemia during pregnancy and excessive GWG further increased the risk of adverse pregnancy outcomes. The 2009 NAM GWG guidelines for twin pregnancies was not developed specifically for GDM pregnant women, but are widely used by the GDM population. There are limited findings on the association of GDM, BMI, and GWG with pregnancy outcomes in twin pregnancies, few studies have been done specifically on GDM in twins.[17] Therefore, it was important to explore the association of the 2009 NAM GWG guidelines with perinatal outcomes in Chinese twin-pregnant women with GDM and to determine whether a more stringent GWG range for GDM twin pregnancies can improve pregnancy adverse outcomes, which can provide a theoretical basis for the development of specific GWG guidelines in the future.

This study aimed to assess the applicability of the NAM interim guidelines for twin pregnancies to the specific population of GDM by exploring the relationship between

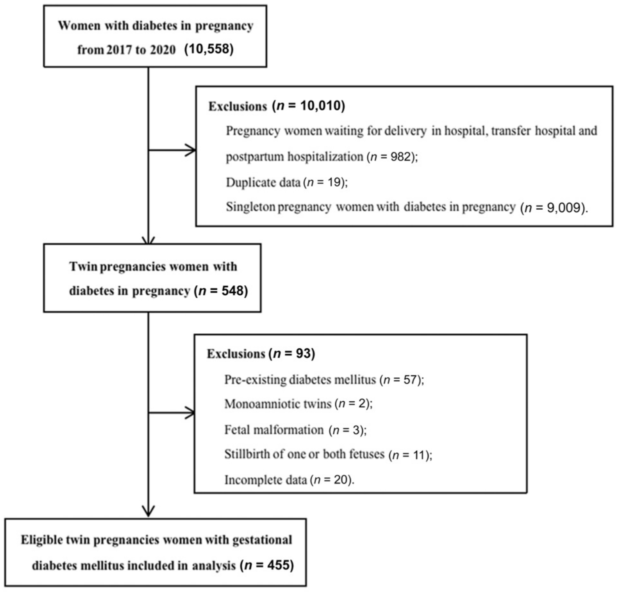

Fig. 1 Flowchart of sample selection.

GWG and adverse pregnancy outcomes in Chinese twin-pregnant women with GDM, and to determine whether adjustments to the current NAM recommendations can improve pregnancy outcomes in women in our study.

Materials and Methods

Study Design and Population

This was a retrospective cohort study of women diagnosed with GDM between July 2017 and December 2020 at a hospital in Chongqing, China. Twin pregnant women aged 18 to 45 years with GDM and gestational age ≥26 weeks were included in the study. Exclusion criteria include: (1) preexisting diabetes mellitus; (2) monoamniotic twins; (3) fetal malformations; (4) stillbirth of one or both fetuses; (5) insufficient or missing data (height or weight of the mother at the first antenatal visit or at the time of delivery).

A total of 455 women with twin pregnancies who had GDM were included (►Fig. 1). GDM was diagnosed by clinicians according to the criteria of the American Diabetes Association, at 24 to 28 weeks of gestation, a 75 g-OGTT (oral glucose tolerance test) was used to diagnose GDM for pregnant women; GDM can be diagnosed when blood glucose measurements met any of the following criteria: fasting (0 h): ≥5.1 mmol/L; 1 hour after taking sugar: ≥10 mmol/L; 2 hours after taking sugar ≥8.5 mmol/L.[18] The study was approved by the Ethics Committee of the hospital.

Information Collection

All data were extracted from maternity ward records and newborn birth records in the delivery room. Maternal characteristics included: maternal age, gestational age, gravidity, nullipara that has never given birth, prepregnancy weight, height, total GWG, use of in vitro fertilization (IVF) in the current pregnancy, insulin therapy, chorionicity, family history of diabetes, and OGTT values. Infant characteristics included: neonatal sex, birth weight, height, and head circumference.

The prepregnancy BMI is calculated as pregestational weight (kg) divided by the square of height (m). Pregestational weight and height were recalled by the pregnant women and recorded. Due to the differences in physical fitness between the Chinese and Western populations, we classified Chinese adults according to the Chinese BMI criteria as underweight (BMI, <18.5 kg/m^2), normal weight (BMI, 18.5–23.9 kg/m^2), overweight (BMI, 24.0–27.9 kg/m^2), and obese (BMI ≥28.0 kg/m^2).[19]

Chorionicity (dichorionic and monochorionic) was determined on the first ultrasound and confirmed by placental pathology after birth. The gestational age at delivery was calculated based on the last menstrual period and was confirmed and corrected by early ultrasound. In the case of pregnancies with IVF, the gestational age was determined from the date of embryo transfer.

Variables of Interest

The primary variable of interest was maternal total GWG, calculated by subtracting the pregestational weight from the weight at delivery. The NAM recommended range of total GWG correlates with gestational age. Women with twin pregnancies tended to give birth at 37 weeks and earlier, thus we divided total GWG by gestational age (weeks) to calculate the overall GWG rate, expressed in kg/wk. The overall GWG rate was also compared with the NAM recommended GWG rate (total GWG at 37 weeks of NAM recommendations divided by 37 weeks) (►Table 1). The women were finally divided into three groups: the GWG group below the range recommended by the NAM (LGWG), the GWG group within the range recommended by the NAM (AGWG), and the GWG group above the range recommended by the NAM (EGWG) (►Table 1).[9,20] To determine whether adjustments to the current NAM recommendations can improve pregnancy outcomes in women in our study who achieved NAM guidelines, we used different ranges of criteria to classify GWG under the premise of grouping according to BMI, derived by: (1) subtracting 2 kg from the upper NAM value only; (2) subtracting 2 kg from both upper and lower values; (3) using the interquartile range (25th–75th percentile) of maternal GWG of women with appropriate for gestational age (AGA) infants as the GWG recommended range (►Table 1).[21]

Outcomes Variables

The maternal outcomes included: preterm birth (PTB at <37, <35, or <32 weeks' gestational age), cesarean delivery, preeclampsia, gestational hypertension, and PPROMs. Gestational hypertension was defined as a new development of blood pressure of ≥140/90 mm Hg after 20 weeks' gestation without proteinuria. Preeclampsia was diagnosed when there blood pressure of ≥140/90 mm Hg and proteinuria of ≥300 mg/24 h.

The neonatal outcomes included: small for gestational age (SGA), large for gestational age (LGA), LBW, birth weight discordance (BWD) of >20%, neonatal intensive unit

Table 1 National Academy of Medicine guidelines for gestational weight gain

Prepregnancy BMI group	Recommended total weight gain at 37 weeks in kg[a]	Weekly weight gain at 37 weeks in kg/wk[b]	NAM upper limit minus 2 kg[a]	Weekly weight gain at 37 weeks in kg/wk[b]	NAM upper/lower limits minus 2 kg[a]	Weekly weight gain at 37 weeks in kg/wk[b]	Interquartile weight range for AGA infants	Weekly weight gain at 37 weeks in kg/wk[b]
Normal weight or underweight (BMI, <23.9 kg/m^2)	16.8–24.5	0.45–0.66	16.8–22.5	0.45–0.61	14.8–22.5	0.40–0.61	12.5–19.0	0.35–0.54
Overweight (BMI, 24.0–27.9 kg/m^2)	14.1–22.7	0.38–0.61	14.1–20.7	0.38–0.56	12.1–20.7	0.33–0.56	10.0–18.0	0.27–0.49
Obese (BMI, >28.0 kg/m^2)	11.3–19.1	0.31–0.52	11.3–17.1	0.31–0.46	9.3–17.1	0.25–0.46	9.9–15.8	0.26–0.45

Abbreviations: BMI, body mass index; NAM, National Academy of Medicine.
[a]Refers to the 2009 NAM recommendations.
[b]Calculated by dividing recommended total weight gain by 37 weeks.

admission, congenital heart disease (CHD), neonatal hypoglycemia, neonatal pneumonia, and NRDS. SGA and LGA were defined as when birth weight was below the 10th percentile and above the 90th percentile, respectively of the average birth weight for the same gestational age according to the birth weight curve for Chinese twins.[22,23] LBW was defined as neonatal birth weight <2,500 g. BWD was calculated as the absolute value of the birthweight difference divided by the birthweight of the larger twin.

Statistical Analysis

Baseline characteristics and adverse pregnancy outcomes were compared by GWG groups using one-way ANOVA for continuous variables and Chi-square tests (or Fisher's exact test) for categorical variables. The association between inappropriate GWG and adverse pregnancy outcomes was estimated using multiple logistic regression analysis (using the GWG group within the normal range as a reference). Odds ratios (ORs) were calculated for the risk of adverse maternal and infant outcomes, adjusting for the following factors separately: age, gestational age, gravidity, parity, BMI classification, use of IVF, insulin therapy, chorionicity, and family history of diabetes. Hypotheses were tested using a two-tailed test with a significance level of 0.05. All statistical analyses were performed using the statistical software SPSS version 22.0.

Results

Maternal and Neonatal Baseline Characteristics

Four hundred and fifty-five women with twin pregnancies and GDM met the study criteria. Baseline characteristics were stratified by GWG rate groups (►Table 2). Nearly half of the women had inappropriate GWG: 49.9% ($n = 227$) of the women had GWG below the NAM recommendations and 10.1% ($n = 46$) had GWG above the NAM recommendations. The average age of the overall population was 31.6 ± 3.7 years ($p = 0.032$), and 74.8% ($n = 339$) of the pregnant women used IVF. Among GWG groups, a significant difference was found in neonatal sex ($p = 0.043$). Birth weight, height, and head circumference were significantly different across different GWG groups, highest among infants in the EGWG group (all $p < 0.05$). However, there was no significant difference in the prevalence of maternal BMI classification, use of IVF, insulin therapy, chorionicity, family history of diabetes, 75-g OGTT value or BWD between the three groups.

Maternal and Neonatal Outcomes According to NAM Classification of GWG

Maternal and neonatal outcomes according to the different GWG rate subgroups were shown in ►Table 3. In all pregnant women, the rate of cesarean delivery was 86.4% ($n = 393$), PTB at <37 weeks was 61.5% ($n = 280$), PTB at <35 weeks reached over 20%. There was a high incidence of LBW (71.6%), CHD (32.5%), and neonatal hypoglycemia (22.2%) in all newborns.

The EGWG group had the highest incidence of preeclampsia (30.4%) and LGA (21.7%). The prevalence of preeclampsia

Table 2 Characteristics of twin pregnancies by maternal prepregnancy BMI classification by GWG according to NAM recommendations

Characteristics	All participants ($n=455$)[b]	Weight gain below NAM guideline ($n=227$)[b]	Weight gain within NAM guideline ($n=182$)[b]	Weight gain above NAM guideline ($n=46$)[b]	p-Value[a]
Maternal characteristics					
Maternal age, (y), mean ± SD	31.6 ± 3.7	32.0 ± 3.9	30.4 ± 3.2	31.5 ± 3.5	0.032[a]
≥35 y	64 (14.1)	39 (17.2)	23 (12.6)	2 (4.3)	0.057
GA at birth, (wk), mean ± SD	35.4 ± 2.0	35.3 ± 2.1	35.4 ± 1.9	35.6 ± 1.8	0.451
Gravidity	2.1 ± 1.2	2.1 ± 1.2	2.0 ± 1.3	2.1 ± 1.4	0.844
Nulliparous	373 (82.0)	188 (82.8)	152 (83.5)	33 (71.7)	0.160
Prepregnancy weight, (kg), mean ± SD	56.0 ± 8.0	55.4 ± 7.5	56.3 ± 8.3	57.6 ± 8.7	0.169
Mother's height, (cm), mean ± SD	158.8 ± 4.8	158.5 ± 4.8	158.9 ± 4.8	160.6 ± 4.4	0.019[a]
Maternal BMI classification					
Underweight	40 (8.8)	18 (7.9)	16 (8.8)	6 (13.0)	0.234
Normal	293 (64.4)	158 (69.6)	108 (59.3)	27 (58.7)	
Overweight	106 (23.3)	46 (20.3)	50 (27.5)	10 (21.7)	
Obese	16 (3.5)	5 (2.2)	8 (4.4)	3 (6.5)	
GWG, (kg), mean ± SD	15.6 ± 5.6	11.4 ± 3.1	18.0 ± 2.7	26.0 ± 3.9	< 0.001[a]
Rate of GWG	0.44 ± 0.16	0.32 ± 0.09	0.51 ± 0.07	0.74 ± 0.12	< 0.001[a]
Use of IVF	339 (74.8)	167 (73.9)	141 (77.5)	31 (68.9)	0.444
Insulin therapy	41 (9.1)	21 (9.3)	20 (11.0)	NA	0.065
Chorionicity					
Dichorionic	353 (77.6)	172 (84.7)	150 (87.7)	31 (77.5)	0.248
Monochorionic	61 (13.4)	31 (15.3)	21 (12.3)	9 (22.5)	
Unknown	41 (9.0)	24 (10.6)	11 (6.0)	6 (13.0)	
Family history of diabetes	58 (12.7)	27 (11.9)	26 (14.3)	5 (10.9)	0.711
75-g OGTT (mg/dL)					
Fasting	4.8 ± 0.5	4.8 ± 0.5	4.8 ± 0.5	4.9 ± 0.5	0.140
1 h	9.9 ± 1.4	9.9 ± 1.4	9.9 ± 1.4	10.2 ± 1.6	0.591
2 h	8.4 ± 1.4	8.5 ± 1.3	8.3 ± 1.5	9.9 ± 1.4	0.245
Neonatal characteristics					
Sex					
Male/male	146 (32.7)	84 (37.8)	47 (26.3)	15 (32.6)	0.043[a]
Female/female	146 (32.7)	68 (30.6)	68 (38.0)	10 (21.7)	
Male/female	155 (34.7)	70 (31.5)	64 (35.8)	21 (45.7)	
Birth weight (g)	2,376.1 ± 401.4	2,296.0 ± 390.3	2,432.2 ± 393.1	2,541.1 ± 406.8	< 0.001[a]
Discordance (%), mean ± SD	10.7 ± 8.5	10.8 ± 8.2	10.5 ± 8.9	11.2 ± 11.7	0.788
Birth length (cm)	45.8 ± 2.7	45.5 ± 2.7	46.0 ± 2.8	46.6 ± 2.5	0.014[a]
Birth head circumference	32.8 ± 2.0	32.5 ± 1.9	33.0 ± 2.2	33.3 ± 1.7	0.013[a]

Abbreviations: BMI, body mass index; GA, Gestational age; GWG, gestational weight gain; IVF, In vitro fertilization; N, number; NA, not available; NAM, National Academy of Medicine; NAM, National Academy of Medicine; OGTT, oral glucose tolerance test; SD, Standard deviation.
[a]$p < 0.05$.
[b]Baseline characteristics are mostly reported as N (%).

and LGA was significantly different among the three GWG subgroups ($p < 0.001$ and $p = 0.002$). The LGWG group had the highest incidence of SGA (18.1%), LBW (78.9%), pneumonia (15.9%), and NRDS (17.2%), and significant differences were found between the three GWG groups ($p = 0.027$, $p = 0.002$, $p = 0.020$, $p = 0.030$). The EGWG group had a higher incidence of PTB at <37 weeks (67.4%), PTB at <32 weeks (13.0%), cesarean delivery (87.0%), gestational hypertension (10.9%), and PPROM (23.9%), and the LGWG group had a higher risk of PTB at <35 weeks (31.3%), neonatal

Table 3 Maternal and neonatal outcomes by maternal prepregnancy BMI classification and by GWG according to NAM recommendations

Outcomes	All participants ($n = 455$)[b]	Weight gain below NAM guideline ($n = 227$)[b]	Weight gain within NAM guideline ($n = 182$)[b]	Weight gain above NAM guideline ($n = 46$)[b]	p-Value[a]
Maternal outcomes					
PTB at <37 wk	280 (61.5)	141 (62.1)	108 (59.3)	31 (67.4)	0.587
PTB at <35 wk	122 (26.8)	71 (31.3)	42 (23.1)	9 (19.6)	0.090
PTB at <32 wk	41 (9.0)	19 (8.4)	16 (8.8)	6 (13.0)	0.596
Cesarean delivery	393 (86.4)	196 (86.3)	157 (86.3)	40 (87.0)	0.992
Preeclampsia	69 (15.2)	19 (8.4)	36 (19.8)	14 (30.4)	< 0.001[a]
Gestational hypertension	32 (7.0)	11 (4.8)	16 (8.8)	5 (10.9)	0.170
PPROM	78 (17.1)	41 (18.1)	26 (14.3)	11 (23.9)	0.265
Neonatal outcomes					
SGA < 10th percentile[c]	63 (13.8)	41 (18.1)	19 (10.4)	3 (6.5)	0.027[a]
LGA > 90th percentile[c]	39 (8.6)	13 (5.7)	16 (8.8)	10 (21.7)	0.002[a]
LBW < 2,500 g[d]	326 (71.6)	179 (78.9)	120 (65.9)	27 (58.7)	0.002[a]
Discordance of >20%	49 (11.3)	23 (10.7)	20 (11.4)	6 (13.3)	0.876
Neonatal intensive unit admission[d]	9 (2.0)	8 (3.5)	1 (0.5)	NA	0.060
Congenital heart disease[d]	148 (32.5)	83 (36.6)	52 (28.6)	13 (28.3)	0.187
Neonatal hypoglycemia[d]	101 (22.2)	51 (22.5)	38 (20.9)	12 (26.1)	0.743
Neonatal pneumonia[d]	53 (11.6)	36 (15.9)	13 (7.1)	4 (8.7)	0.020[a]
Neonatal respiratory distress syndrome[d]	60 (13.2)	39 (17.2)	15 (8.2)	6 (13.0)	0.030[a]

Abbreviations: LBW, low birth weight; LGA, large for gestational age; *N*, number; NA, not available; NAM, National Academy of Medicine; PPROM, preterm premature rupture of membranes; PTB, preterm birth; SGA, small for gestational age.
[a] $p < 0.05$.
[b] Baseline characteristics are mostly reported as *N* (%).
[c] Refers to one or both twins, based on Chinese reference of Zhang Bin et al.
[d] Refers to one or both twins.

Table 4 Neonatal characteristics and outcomes of twin pregnancies by neonatal sex

Characteristics and outcomes	Male/male ($n = 146$)[b]	Female/female ($n = 146$)[b]	Male/female ($n = 155$)[b]	p-Value[a]
Birth weight (g)	2,456.72 ± 353.57	2,336.23 ± 396.75	2,338.32 ± 441.61	0.017[a]
Birth length (cm)	46.22 ± 2.83	45.53 ± 2.47	45.57 ± 2.77	0.062
Birth head circumference (cm)	33.25 ± 2.28	32.64 ± 1.70	32.55 ± 1.96	0.012[a]
SGA < 10th percentile[c]	18 (12.3)	22 (15.1)	21 (13.5)	0.792
LGA > 90th percentile[c]	17 (11.6)	7 (4.8)	14 (9.0)	0.107
LBW < 2,500 g[d]	101 (69.2)	103 (70.5)	116 (74.8)	0.523
Discordance of >20%	15 (10.9)	16 (11.7)	16 (10.5)	0.946
Neonatal intensive unit admission[d]	2 (1.4)	3 (2.1)	2 (1.3)	0.844
Congenital heart disease[d]	39 (26.7)	48 (32.9)	59 (38.1)	0.110
Neonatal hypoglycemia[d]	23 (15.8)	41 (28.1)	35 (22.6)	0.040[a]
Neonatal pneumonia[d]	11 (7.5)	20 (13.7)	22 (14.2)	0.143
Neonatal respiratory distress syndrome[d]	15 (10.3)	16 (11.0)	29 (18.7)	0.057

Abbreviations: LBW, low birth weight; LGA, large for gestational age; SGA, small for gestational age.
[a] $p < 0.05$.
[b] Baseline characteristics are mostly reported as *N* (%).
[c] Refers to one or both twins, based on Chinese reference of Zhang Bin et al.
[d] Refers to one or both twins.

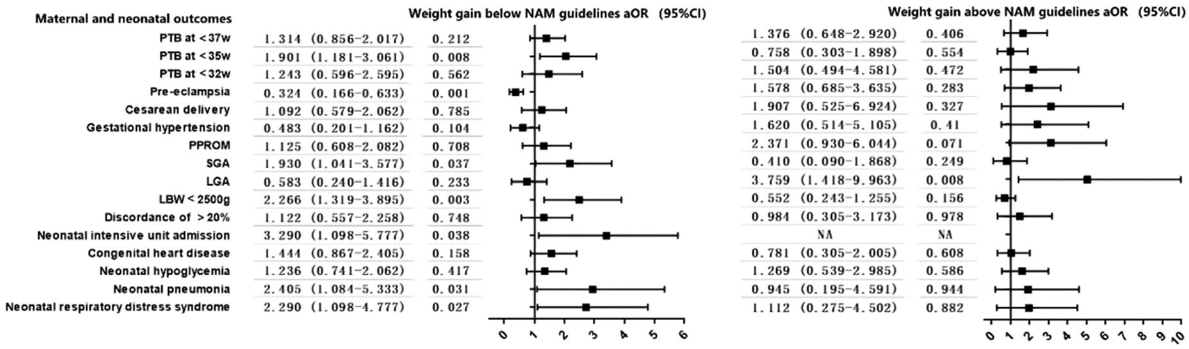

Fig. 2 Association of GWG below and above NAM recommendation with adverse pregnancy outcomes. Adjusted for age, gestational age, gravidity, parity, BMI classification, use of IVF, insulin therapy, chorionicity, family history of diabetes. CI, confidence interval; GWG, gestational weight gain; IVF, In vitro fertilization; LBW, low birth weight; LGA, large for gestational age; NAM, National Academy of Medicine; OR, odds ratio; PPROM, Preterm premature rupture of membranes; PTB, preterm birth; SGA, Small for gestational age.

intensive unit admission (3.5%) and CHD (36.6%). However, no intergroup statistical differences were observed in PTB, cesarean delivery, gestational hypertension, or PPROM among these GWG groups.

Neonatal Characteristics and Outcomes in Different Neonatal Sex Groups

In ►Table 4, we further analyzed neonatal characteristics and outcomes according to neonatal sex. The three groups included male/male ($n = 146$), female/female ($n = 146$), and male/female ($n = 155$). Both birth weight and birth head circumference were significantly different among these sex groups ($p = 0.017$ and $p = 0.012$). On the contrary, we did not find differences in the average birth length and adverse outcomes such as SGA, LGA, and LBW< 2,500 g in the three sex groups ($p = 0.792$, 0.107, and 0.523). Interestingly, there was a significant difference in the prevalence of neonatal hypoglycemia among sex groups ($p = 0.040$) and the female/female group had the highest rate of neonatal hypoglycemia (28.1%). We also divided the birth order of the twins into two groups, shown in ►Supplementary Table S1 (available in the online version). On paired-samples *t*-test analysis, birth weight was associated with birth order ($p < 0.001$), with the first born being larger than the second.

Association of GWG Below and Above NAM Recommendation with Adverse Pregnancy Outcomes

After controlling for potential confounders for maternal and neonatal outcomes, we found that compared with women with AGWG, women with LGWG had a reduced risk of pre-eclampsia (aOR, 0.32; 95% CI, 0.17–0.63; $p = 0.001$) and their infants had higher risks of PTB at <35 weeks (aOR, 1.90; 95% CI, 1.81–3.06; $p = 0.008$), SGA (aOR, 1.93; 95% CI, 1.04–3.58; $p = 0.037$), LBW (aOR, 2.27; 95% CI, 1.32–3.90; $p = 0.003$), neonatal intensive unit admission (aOR, 3.29; 95% CI, 1.10–5.78; $p = 0.038$), pneumonia (aOR, 2.41; 95% CI, 1.08–5.33; $p = 0.031$), and NRDS (aOR, 2.29; 95% CI, 1.10–4.78; $p = 0.027$); the infants of women with EGWG had a higher risk of LGA (aOR, 3.76; 95% CI, 1.42–9.96; $p = 0.008$) (►Fig. 2). Compared with women with AGWG, women with EGWG were at increased risk of PTB at <37 weeks (aOR, 1.38; 95% CI, 0.65–2.92), cesarean delivery (aOR, 1.91; 95% CI, 0.53–6.92), gestational hypertension (aOR, 1.62; 95% CI, 0.54–5.11), and PPROM (aOR, 2.37; 95% CI, 0.93–6.04), though no statistically significant differences were found in PTB at 37 weeks, cesarean delivery, and gestational hypertension.

Effect of Adjusting Weight Gain Targets on Pregnancy Outcomes in Women Who Reached Appropriate GWG

After adjusting the weight gain targets, we found subtracting 2 kg from the upper NAM limit resulted in a lower percentage of women reaching appropriate GWG, and subtracting 2 kg from both upper and lower values and using interquartile weight range for AGA infants resulted in a higher percentage of women reaching appropriate GWG in most BMI categories when compared with NAM (►Table 5). Compared with the NAM criteria, we also found the proportion of women reaching appropriate GWG with these modified targets (NAM

Table 5 Proportion of pregnancy women reaching appropriate GWG with GDM based on NAM and modified criteria

	NAM recommendation	NAM upper limit minus 2 kg	NAM upper/lower limits minus 2 kg	Interquartile weight range for AGA infants
All population	40.0%	35.4%	48.8%	54.5%
Prepregnancy BMI group				
Normal weight or underweight (BMI <23.9 kg/m^2)	37.2%	32.7%	46.2%	53.5%
Overweight (BMI, 24.0–27.9 kg/m^2)	47.2%	42.5%	53.8%	55.7%
Obese (BMI, >28.0 kg/m^2)	50.0%	43.8%	68.8%	68.8%

Abbreviations: BMI, body mass index; GDM, gestational diabetes mellitus; GWG, gestational weight gain;

upper/lower limits minus 2 kg and using interquartile weight range for AGA infants) were 46.2% or 53.5 versus 37.2% (p <0.001) in normal weight or underweight group (►Table 5).

However, after implementing these modified GWG targets, we did not find statistical differences in the adverse outcomes for pregnant women who reached appropriate GWG when compared with NAM goals (►Supplementary Table S2, available in the online version).

Discussion

In a previous study, more than 67.06% of twin-pregnant women had excessive GWG during pregnancy.[24] However, in our study, nearly 50% of women had GWG below the NAM recommendations. We found birth weight, height, and head circumference increased with increasing GWG, consistent with previous studies.[13,25] In addition, our study also demonstrated that birth weight and head circumference were linked to sex. First, like-sexed male twins had higher average birth weight and head circumference than like-sexed female twins or unlike-sexed twins. A Japanese study[26] found that the median birth weight of males was approximately 0.05 kg to 0.1 kg heavier than that of females. Probably due to the small sample size, we found no significant difference in birth length in the neonatal sex groups, but the descriptive values showed that the average birth length tends to be higher in like-sexed male twins. Second, the weight of the first-born twins in the same maternal environment was higher than the second-born twins, consistent with previous report.[26] We speculated that birth order was not a determinant of LBW, but since the fetal position may affect intrauterine development and nutrition, a well-grown fetus is more likely to show greater vitality at birth and thus be born before another fetus.

The prevalence of LBW in our study was 71.6%, significantly higher than the prevalence of LBW seen in the 2007 Chinese national sample survey (4.6%),[27] which indicated that twin pregnancies are more likely to have LBW. Our study found that women with GWG below the NAM recommendation were more likely to produce SGA and LBW newborns, and the LGWG group had the highest rate of neonatal CHD, consistent with the Pecheux's study.[14] In our study, newborns in the LGWG group were also more likely to get pneumonia, NRDS and neonatal intensive unit admission. On the contrary, we also found a 276% increase in the risk of LGA in the EGWG group. In a previous Chinese study, twin-pregnant women who gained weight above guidelines were more likely to have LGA >90th percentile and less likely to have LBW <2,500 g,[10] whereas preeclampsia was more frequent among excessive GWG twin-pregnant women, which was similar to our results.[10,14,28–30] It may be that EGWG leads to an increased maternal systemic inflammation response, and the resulting damage to vascular endothelial cells may cause preeclampsia.[31] Therefore, GWG would potentially be a preventable risk factor for preeclampsia. However, LGWG increased the probability of adverse neonatal outcomes such as LBW in twins and low weight was detrimental to the development of newborn, which leads to an increased probability of neonatal intensive unit admission. Because the costs of neonatal intensive care unit are very high, we thought LGWG may have a large negative impact on the family economy in twin pregnancies. Therefore, we must increase weight management in LGWG twin-pregnant women. We suggested that the twin-pregnant women should pay more attention to their intake of nutrients and weight retention, especially women combined with GDM.

Previous studies[12,20,32] on the effect of GWG on preterm birth in twin pregnancies had inconsistent results, but most of the findings tend to suggest that EGWG reduces the risk of PTB in twin pregnancies. In our study, we did not find any association between GWG and PTB <37 weeks or <32 weeks, consistent with a study of twins in China.[10] The study[10] showed that neither insufficient nor excessive GWG was associated with preterm birth <37, <35, and <32 weeks. This may be due to fact that China had a more comprehensive primary health care system. When a pregnant woman was diagnosed with twin pregnancy, the doctor took targeted strategies to extend the gestational week. Our study found that pregnant women with LGWG had a high incidence of PTB at <35 weeks. Pregnant women with AGWG had the lowest incidence of PTB in the three GWG groups, which indicated that very low or high GWG was likely to cause poor outcomes, consistent with previous studies.[33–37] Based on our findings, we emphasized the need for adequate GWG in women with twin pregnancies, as this can potentially reduce the burden of LBW and preterm birth. However, for pregnant women with GDM, while enhancing nutrition during pregnancy, strict weight management was needed to prevent excessive GWG. Prevention of excessive GWG also has a positive impact on improving maternal and neonatal outcomes.

There were no internationally and specifically recommended guidelines for GWG for pregnant women with GDM, therefore NAM has proposed that in singleton and twin pregnancies guidelines should be widely applied to this specific population of pregnant women with GDM. But there has been controversy over whether the guidelines for weight gain during pregnancy proposed by the NAM were applicable to different nations and twin-pregnant women with GDM. Some researchers believed that the 2009 NAM recommendations did not apply to the Asian population. Jiang et al[37] pointed out the 2009 NAM GWG guidelines may be too lenient for Chinese pregnant women, so we made appropriate adjustments based on the 2009 NAM GWG: (1) subtracting 2 kg from the upper NAM value only; (2) subtracting 2 kg from both upper and lower values and used the interquartile range (25th–75th percentile) of maternal GWG of women with AGA infants as the GWG recommended range. Compared with the 2009 NAM GWG guideline, our study did not find a significant difference in the incidence of adverse maternal and infant outcomes among our adjusted GWG recommendations, consistent with a prior study.[21] But the incidence of adverse outcomes was relatively lower for those who reached an appropriate weight based on NAM classification. Therefore, we considered that the 2009 NAM GWG recommendations can be used for Chinese twin-pregnant women with GDM. This needs to be explored in future Chinese studies with a larger sample.

Strengths and Limitations

This study had several strengths. It was the first study in China to assess the applicability of NAM guidelines for twin pregnancies to the specific population of GDM. Second, women were treated with consistent diagnostic criteria and treatment goals, and endocrinologists were included, thus ensuring consistency of baseline information. There are some limitations in our study. The main limitations of this study were that the sample size was not large enough, especially the number of overweight women, this may affect the outcome of the group. It was a retrospective, single-center study, pregnant women's recall bias when recalling prepregnancy weight may affect GWG values. Also, the GWG ratio we calculated was based on the assumption that the total weight growth rate of the whole pregnancy was constant, but the weight gain of pregnant women showed a curve change throughout the pregnancy. Prospective studies are needed in the future to follow GWG at different trimesters. The effects of the COVID-19 pandemic, travel restrictions, lockdowns, etc. could have contributed to eating patterns for women and, thus, may have affected weight gain during the first half of 2020. In addition, a limitation of the study should also be that the population was specifically with Chinese pregnant women, so the findings may not be generalizable to other populations.

Conclusion

Based on the 2009 NAM guidelines, our study confirmed that GWG controlled within the range recommended by the NAM could reduce the risk of perinatal adverse outcomes, such as preeclampsia, SGA, LGA, LBW, neonatal pneumonia, NRDS, and neonatal intensive unit admission. We considered that the 2009 NAM GWG recommendations can be applied for Chinese twin-pregnant women with GDM. This finding has important implications for the development of the health care system for pregnant women with diabetes in China. Further research should be undertaken to investigate the recommendations for GWG in Chinese twin pregnancies, especially in pregnant women with GDM, and to determine whether interventions aimed at optimizing GWG can improve outcomes in these high-risk pregnancies.

Ethical Statement

The study was approved by the Ethics Committee of Chongqing Women's and Children's Health Centre. ([2020] Trial [Division] No. 022)

Authors' Contributions

Y.L. and X.C. contributed toward the concept and design. J. D. and X.F. drafted the manuscript. J.D., X.F., R.T., J.X., L.P., and Y.C. did the statistical analysis. Y.L., X.C., and Z.Z. provided the administrative, technical, or material support. J.H. and J.B. did the supervision. All authors did the critical revision of the manuscript for important intellectual content. They had full access to all the data in the study and took responsibility for the integrity, accuracy, acquisition, analysis, and interpretation of the data.

Note

The funder had no role in the design and conduct of the study, collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Funding

Yanqun Liu was supported by the National Natural Science Foundation of China (grant no.: 81903334).

Conflict of Interest

None declared.

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