The perinatal outcomes by gestational weight gain range at 30 weeks of gestation among pre-pregnancy underweight women

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Abstract

Aims: To evaluate the perinatal outcomes by gestational weight gain (GWG) range at 30 weeks of gestation among underweight pregnant women (pre-pregnancy body mass index ≤ 18.5 kg/m²) in Japan.

Methods: This retrospective study was conducted at a hospital in Japan from 2003 to 2020. The underweight pregnant women (UPW; n = 3643) were divided into quartile groups based on the weight gain at 30 weeks of gestation: group Q1 ≤ 5.7 kg, 5.7 kg < Q2 ≤ 7.2 kg, 7.2 kg < Q3 ≤ 8.8 kg, and 8.8 kg < Q4. Clinical characteristics and outcomes were compared using the t-test, chi-square test, and multivariable logistic regression analysis.

Results: The cumulative incidences of preterm births were 7.5% (n = 70), 5.0% (n = 45), 5.4% (n = 50), and 4.9% (n = 44), and the birth rates of small for gestational age (SGA) infants were 15.7% (n = 147), 9.6% (n = 87), 6.9% (n = 64), and 5.9% (n = 53) in Q1, Q2, Q3, and Q4, respectively. Multivariable analysis revealed that Q1 was significantly associated with preterm births (adjusted odds ratio [aOR] = 1.6; 95% confidence interval [CI] = 1.0–2.3), and Q1 and Q2 were significantly associated with SGA (adj. OR = 3.0; 95% CI = 2.2–4.3; adj. OR = 1.7; 95% CI = 1.2–2.5, respectively). None of the quartile groups were significantly associated with the incidence of primary cesarean sections, gestational diabetes mellitus, and macrosomia.

Conclusions: In UPW, GWG at 30 weeks of ≤5.7 kg and ≤7.2 kg are associated with preterm birth and SGA rates, respectively.

Key words: pregnancy, gestational weight gain, hypertensive disorders in pregnancy, preterm birth, small for gestational age infants.

Introduction

Optimal gestational weight gain (GWG) depends on the pre-pregnancy body mass index (BMI).1,2 Some studies have reported that poor GWG and being underweight pre-pregnancy are associated with preterm birth and delivery of small for gestational age (SGA) neonates.3 However, the optimal GWG for underweight pregnant women (UPW) is still unclear and varies according to guidelines. The Japan Society of Obstetrics and Gynecology guidelines recommend an optimal GWG of 9–12 kg at 40 weeks of gestation for UPW compared with a weight gain of 12.7–18.1 kg at 40 weeks specified by the Institute of Medicine.4,5

A recent study highlights that poor GWG has led to an increase in the number of low birth weight (LBW)
infants in Japan. In fact, the birth rate of LBW neonates is significantly higher in Japan than that worldwide, and the Japanese rate is continuing to increase. The incidence of LBW infants in Japan was 5.2% in 1980, and escalated to 9.4% in 2019; this compares with an average incidence of 6.6% LBW infants for Organization for Economic Co-operation and Development member countries.

There are only a limited number of reports on the increased incidence of SGA infants, preterm deliveries, and cesarean sections (CS) in Japanese UPW with poor GWG. Furthermore, previous studies have represented optimal GWG as the estimated weight gain at 40 weeks of gestation or the weight gain per week. The antenatal weight targets for GWG (earlier than 40 weeks) among UPW have not been reported. Therefore, this retrospective study aimed to evaluate the perinatal outcomes by GWG ranges and determine the appropriate weight gain range at 30 weeks of gestation among UPW.

Methods

We conducted a retrospective study at St. Luke’s International Hospital, an acute-care tertiary-level hospital with 520 beds, from July 22, 2003, to April 30, 2020. This study was approved by the institutional review board of our hospital (approval no. 20-R162) on December 22, 2020. The need for informed consent was waived as the study was retrospective and did not reveal or contain any personal data.

Participants

Underweight women (pre-pregnancy BMI ≤ 18.5 kg/m²) who gave birth at St. Luke’s International Hospital during the study period were screened. Multifetal gestations, stillbirths, non-Japanese participants, or pregnant women who delivered before 30 weeks of gestation were excluded. Participants were divided into quartile groups based on GWG at 30 weeks: group Q1 ≤ 5.7 kg, 5.7 kg < Q2 ≤ 7.2 kg, 7.2 kg < Q3 ≤ 8.8 kg, and 8.8 kg < Q4. The association between clinical characteristics in each group and outcomes were investigated.

The primary outcomes were cumulative incidence of preterm births (before 37 weeks of gestation) and SGA infants, and the secondary outcomes were primary CS and maternal and neonatal complications. Maternal complications included gestational diabetes mellitus (GDM), intrapartum hemorrhage (CS >1000 ml, vaginal delivery >500 ml as defined by the American College of Obstetricians and Gynecologists), and post-term delivery (≥42 weeks of gestation). Neonatal complications included neonatal asphyxia (5-min Apgar score < 7), macrosomia (>4000 g), and the need for neonatal intensive care.

Definitions

The variables extracted from each patient’s medical records were age, BMI, nulliparity, advanced maternal age (≥35 years), smoking history (during and/or before pregnancy), use of assisted reproductive therapy (ART), hyperemesis (patients requiring intravenous infusion due to nausea and vomiting), anemia (hemoglobin < 11.0 mg/dl during the first trimester), history of systemic lupus erythematosus, and history of anti-phospholipid antibody syndrome.

We defined an SGA infant as a newborn with a birth weight and height that were below the 10th percentile for all newborns of the same gestational age, according to the Japan Pediatric Society.

In Japan, the diagnostic criteria for GDM were changed in 2010. All patients who were diagnosed before 2010 using the old diagnostic criteria were re-diagnosed using the current criteria. GDM was diagnosed if there is at least one abnormal value ≥92, 180, and 153 mg/dl for fasting, 1-h, and 2-h plasma glucose concentration after a 75 g oral glucose tolerance test.

Statistical analyses

Patient baseline characteristics of each quartile group were described and compared using the chi-square test and analysis of variance. We compared the cumulative incidence of primary pregnancy outcomes (SGA and preterm birth) using the chi-square test. If the results were significant, pairwise comparisons were performed with Bonferroni’s correction. Additionally, we used the Cochran–Armitage test for evaluating trends in the incidences of SGA and preterm birth among the quartile groups. After univariate analysis, multivariable logistic regression analysis was performed to identify risk factors for SGA and preterm births. The GWG was included as an exploratory item among independent variables, and nulliparity, advanced maternal age, smoking history, ART, hyperemesis, anemia during the first trimester, history of systemic lupus erythematosus, and history of anti-phospholipid antibody syndrome were also included using the forced entry method as per previous reports. Associations between other pregnancy outcomes (primary CS, maternal, and neonatal complications) and GWG quartile groups at
30 weeks were also evaluated by multivariable logistic regression analysis.

All statistical hypothesis tests were performed at the 5% significance level. Analyses were performed using SPSS version 19.0J (IBM Japan).

Results

Of the 18 430 women who delivered after 22 weeks of gestation at our hospital during the study period, 4159 were underweight (pre-pregnancy BMI ≤ 18.5 kg/m²). A total of 74 multifetal pregnancies, 60 stillbirths, 152 women of non-Japanese ethnicity, 24 pregnant women who delivered before 30 weeks of pregnancy, and 206 women with missing data were excluded. Therefore, 3643 UPW were included in this study. They were divided into four groups based on GWG quartile ranges at 30 weeks. There were 933 (25.6%) women in Q1, 899 (24.6%) women in Q2, 920 (25.2%) women in Q3, and 891 (24.4%) women in Q4 (Figure 1).

### Participant characteristics

The patient characteristics of the quartile groups are shown in Table 1. In the univariate analysis, age ($p = 0.013$), advanced maternal age ($p = 0.021$), smoking history ($p < 0.001$), ART ($p < 0.001$), and anemia during the first trimester ($p = 0.048$) were significant in the quartile groups. There was a strong correlation between maternal weight at gestational week 30 and at delivery (weighted kappa = 0.66, Spearman’s rho = 0.81, $p < 0.001$).

### Primary outcomes

The cumulative incidence of preterm births was higher in Q1 (7.5%) than in Q2 (5.0%), Q3 (5.4%), and Q4 (4.9%); however, the differences were not significant ($p = 0.058$). Regarding the incidence of SGA infants, 147 (15.7%) women in Q1, 87 (9.6%) in Q2, 64 (6.9%) in Q3, and 53 (5.9%) in Q4 delivered SGA infants.

Univariate analysis revealed that the delivery of SGA infants was significantly different between the four groups ($p < 0.001$). The proportions of underweight women who delivered preterm and SGA

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**Figure 1 Study population.** Among the underweight women who delivered at our hospital, women who had multifetal gestations, stillbirths, were non-Japanese, or who delivered before 30 weeks of gestation were excluded. A total of 3643 women were included and were divided into quartile groups based on weight gain at 30 weeks of gestation: Group Q1 ≤ 5.7 kg, 5.7 kg < Q2 ≤ 7.2 kg, 7.2 kg < Q3 ≤ 8.8 kg, and 8.8 kg < Q4.

**TABLE 1** Patient characteristics of the four quartile groups based on gestational weight gain at 30 weeks of gestation

| Variable                        | Q1, n = 933 | Q2, n = 899 | Q3, n = 920 | Q4, n = 891 | p Value |
|---------------------------------|-------------|-------------|-------------|-------------|---------|
| Age, mean (SD)                  | 34.0 (4.5)  | 34.1 (4.3)  | 33.8 (4.3)  | 33.5 (4.5)  | 0.013   |
| BMI, mean (SD)                  | 17.6 (0.6)  | 17.6 (0.7)  | 17.6 (0.7)  | 17.6 (0.7)  | 0.509   |
| Nulliparous, n (%)              | 644 (69.0)  | 619 (68.8)  | 621 (67.5)  | 603 (67.6)  | 0.853   |
| Advanced maternal age, n (%)    | 426 (45.6)  | 429 (47.7)  | 407 (44.2)  | 362 (40.6)  | 0.021   |
| Smoking history, n (%)          | 39 (4.1)    | 30 (3.3)    | 50 (5.4)    | 75 (8.4)    | <0.001  |
| ART, n (%)                      | 107 (11.4)  | 106 (11.7)  | 70 (7.6)    | 61 (6.8)    | <0.001  |
| Hyperemesis, n (%)              | 36 (3.8)    | 39 (4.3)    | 28 (3.0)    | 24 (2.6)    | 0.210   |
| Anemia, n (%)                   | 146 (15.6)  | 112 (12.4)  | 108 (11.7)  | 108 (12.1)  | 0.048   |
| History of SLE, n (%)           | 5 (0.5)     | 3 (0.3)     | 4 (0.4)     | 4 (0.4)     | 0.93    |
| History of APS, n (%)           | 5 (0.5)     | 8 (0.8)     | 5 (0.5)     | 9 (1.0)     | 0.53    |
| GWG at delivery* (kg ± SD)      | 6.9 ± 1.9   | 9.2 ± 1.4   | 10.9 ± 1.5  | 13.3 ± 2.2  | <0.001  |
| GWG per week* (kg ± SD)         | 0.17 ± 0.049| 0.23 ± 0.037| 0.28 ± 0.040| 0.34 ± 0.057| <0.001  |

Abbreviations: APS, anti-phospholipid antibody syndrome; ART, assisted reproductive therapy; BMI, body mass index; GWG, gestational weight gain; SLE, systemic lupus erythematosus. and *Cases of preterm birth before 37 weeks were excluded while calculating gestational weight gain.
infants in the quartile groups are shown in Figures 2 and 3, respectively. In the univariate analysis using Bonferroni correction as a multiple comparison procedure, a significant association for the delivery of SGA infants was identified between Q1 and Q2 ($p < 0.001$), Q1 and Q3 ($p < 0.001$), Q1 and Q4 ($p < 0.001$), and Q2 and Q4 ($p = 0.003$).

Nulliparity, advanced maternal age, smoking history, ART, hyperemesis, and anemia were included in the multivariable model for preterm births. Nulliparity, advanced maternal age, smoking history, ART, hyperemesis, anemia, history of systemic lupus erythematosus, and history of anti-phospholipid antibody syndrome were included in the multivariable model for SGA. Multivariable analysis revealed that Q1 was significantly associated with preterm births (adjusted odds ratio [adj. OR] = 1.6; 95% confidence interval [CI] = 1.0–2.3; $p = 0.017$) (Table 2). Additionally, Q1 (adj. OR = 3.0; 95% CI = 2.2–4.3; $p < 0.001$) and Q2 (adj. OR = 1.7; 95% CI = 1.2–2.5; $p = 0.002$) were significantly associated with the delivery of SGA infants (Table 2).

Secondary outcomes

Multivariable analysis of the secondary outcomes revealed that Q1 and Q2 were significantly associated with increased incidence of GDM and decreased incidence of post-term delivery. In addition, Q1, Q2, and Q3 were significantly associated with intrapartum hemorrhage. Q1 was an independent risk factor for requiring neonatal intensive care. No significant difference was noted in the incidence of primary CS, macrosomia, and neonatal asphyxia between quartile groups (Table 3).

Discussion

In this study, a GWG of $\leq 5.7$ kg at 30 weeks of gestation was significantly associated with an increased risk of preterm birth. Additionally, a GWG of $\leq 7.2$ kg significantly contributed to the delivery of an SGA infant. A GWG $\leq 5.7$ kg at 30 weeks of gestation significantly increased the risk of newborns requiring neonatal intensive care. In UPW, small weight gains could not reduce the adverse outcomes that are known to increase with excessive GWG, such as CS and macrosomia.

This study demonstrated that adequate weight gain in UPW may be associated with a lower risk of preterm birth. A low pre-pregnancy BMI is, in itself, a risk factor for preterm birth. However, in this study, the preterm birth rate was the highest in Q1, while the rates in groups Q2, Q3, and Q4 were similar to the Japanese average preterm birth rate (approximately 5.7% since 2000). This suggests that, even if pre-pregnancy BMI is low, appropriate GWG can prevent preterm births. In the present study, the higher the maternal weight gain, the lower the proportion of SGA. According to the Developmental Origins of Health and Disease theory, LBW infants have higher
TABLE 2 Results of multivariate logistic regression analysis for the association of gestational weight gain at 30 weeks of gestation with primary outcomes: Preterm births and small for gestational age infants

|                      | Preterm births | Small for gestational age infants |
|----------------------|---------------|----------------------------------|
|                      | Adjusted OR   | 95% CI p Value                   | Adjusted OR   | 95% CI p Value |
| Q1 (≤5.7 kg)         | 1.6a          | 1.0–2.3a                         | 3.0b          | 2.2–4.3b ≤0.001 |
| Q2 (≤7.2 kg)         | 1.0a          | 0.6–1.5a                         | 1.7b          | 1.2–2.5b 0.002  |
| Q3 (≤8.8 kg)         | 1.1a          | 0.7–1.6a                         | 1.2b          | 0.8–1.7b 0.340  |
| Q4 (>8.8 kg)         | Ref           | Ref                              | Ref           | Ref           |

Abbreviations: CI, confidence interval; OR, odds ratio.; aAdjusted for nulliparity, advanced maternal age, smoking history, assisted reproductive therapy, hyperemesis, and anemia during the first trimester. and bAdjusted for nulliparity, advanced maternal age, smoking history, assisted reproductive therapy, hyperemesis, anemia during the first trimester, history of systemic lupus erythematosus, history of anti-phospholipid antibody syndrome.

TABLE 3 Results of multivariate logistic regression analysis for the association of gestational weight gain at 30 weeks of gestation with secondary outcomes: Primary cesarean section, maternal complications, and neonatal complications

|                      | Q1 (n = 933) | Q2 (n = 899) | Q3 (n = 920) | Q4 (n = 891) |
|----------------------|-------------|-------------|-------------|-------------|
|                      | Adjusted OR (95% CI) p Value | Adjusted OR (95% CI) p Value | Adjusted OR (95% CI) p Value | Adjusted OR (95% CI) p Value |
| Primary cesarean sectiona | 0.8 (0.6–1.1) 0.20 | 1.0 (0.7–1.4) 0.67 | 0.9 (0.7–1.3) 0.85 | Ref Ref |
| Maternal complications |             |             |             |             |
| GDMb                 | 2.7 (1.7–4.4) <0.01 | 1.8 (1.1–3.1) 0.01 | 1.5 (0.9–2.6) 0.07 | Ref Ref |
| Intrapartum hemorrhageb | 0.6 (0.5–0.8) <0.01 | 0.7 (0.5–0.9) <0.01 | 0.7 (0.5–0.9) <0.01 | Ref Ref |
| Post-term deliveryc  | 0.1 (0.0–0.8) 0.03 | 0.1 (0.0–0.9) 0.04 | 0.8 (0.2–2.3) 0.71 | Ref Ref |
| Neonatal complicationsc |             |             |             |             |
| Neonatal intensive careb | 1.6 (1.1–2.3) <0.01 | 1.0 (0.7–1.5) 0.74 | 0.8 (0.5–1.2) 0.39 | Ref Ref |
| Neonatal asphyxiac | 1.5 (0.4–4.6) 0.46 | 1.1 (0.3–3.9) 0.77 | 1.3 (0.4–4.3) 0.59 | Ref Ref |
| Macrosumiaa           | 0.3 (0.0–1.8) 0.22 | 0.0 | 0.99 | 0.5 (0.1–2.3) 0.43 |

Abbreviations: CI, confidence interval; GDM, gestational diabetes mellitus; OR, odds ratio.; aAdjusted for nulliparity, advanced maternal age, and assisted reproductive therapy.; bAdjusted for nulliparity, advanced maternal age, assisted reproductive therapy, and anemia during the first trimester.; cAdjusted for nulliparity, advanced maternal age, smoking history, and assisted reproductive therapy. and dAdjusted for gestational diabetes mellitus.

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Therefore, it remains unclear if the mode of gaining weight (e.g., through diet) reduces perinatal adverse outcomes, such as preterm births and delivery of SGA neonates. Regardless of their weight control, underweight women may be less likely to gain weight during pregnancy. Furthermore, the proportion of underweight women in the Japanese younger population has increased. In 2017, 21.7% of Japanese women of reproductive age were underweight compared with 13.4% in 1981. Thus, preconception counseling is required, including education and awareness of a healthy weight before pregnancy, as this could help women planning pregnancy achieve an appropriate BMI.

In conclusion, GWG of ≤5.7 kg at 30 weeks and ≤7.2 kg are associated with preterm birth and SGA rates, respectively. This indicator may be useful for health care providers and pregnant women themselves in weight management to prevent perinatal adverse outcomes.

Author Contributions

All authors meet the ICMJE authorship criteria.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. Upon reasonable request, we will share the original data, but at this time we are unable to do so due to hospital regulations.

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