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General Section

Associations of pre-pregnancy obesity with adverse pregnancy outcomes and the optimal gestational weight gain in Japanese women

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Summary

Objectives: The authors determined associations of maternal pre-pregnancy obesity with adverse pregnancy outcomes and evaluated how gestational weight gain affects risks for such outcomes in Japanese obese pregnant women. *Materials and Methods:* Among women who delivered at the Perinatal Center for Maternity and Neonatal, Yokohama City University Medical Center, between January 2001 and December 2012, the authors ascertained adverse pregnancy outcome incidences in 207 pre-pregnancy obese (body mass index [BMI] = 30 kg/m^2, obese group), 661 pre-pregnancy overweight (BMI = 25−29.9 kg/m^2, overweight group), and 6,801 pre-pregnancy normal weight (BMI = 18.5−24.9 kg/m^2, normal group) women. Subjects were stratified by weekly weight gain during the second/third trimesters to investigate associations between gestational weight gain and adverse pregnancy outcomes. Optimal weight gain for obese pregnant women was also examined. *Results:* In the obese and overweight groups, incidences of pregnancy induced hypertension (PIH), gestational diabetes mellitus (GDM), large for gestational age (LGA), preterm birth, preterm prelabor rupture of membranes (PPROM), and spontaneous preterm birth were significantly higher than in the normal group. Incidences of adverse pregnancy outcomes were apparently higher in the obese than in the overweight group. In the latter, the incidence of large for gestational age was significantly higher in women with weight gains of 0.5 kg/week, whereas no difference in pregnancy outcomes was observed in the obese group regardless of gestational weight gain. *Conclusion:* In obese women, incidences of adverse pregnancy outcomes were higher, and pregnancy outcomes were difficult to improve with gestational weight control. Thus, it is important to reach an optimal weight before pregnancy.

Key words: Body mass index; Gestational weight gain,; Japanese women; Obesity; Optimal weight.

Introduction

In 2009, the Institute of Medicine (IOM) classified body weight based on body mass index (BMI) as underweight (BMI < 18.5 kg/m^2), normal (BMI = 18.5-24.9 kg/m^2), overweight (BMI = 25.0-29.9 kg/m^2), and obese (BMI = 30 kg/m^2), and then published recommended guidelines for gestational weight gain according to these BMI categories [1]. Because there are many underweight women in Japan, the obesity classification used in Japan partially differs from that developed by the IOM. According to the criteria developed by the Japan Society for the Study of Obesity, women with a BMI of 25 kg/m^2 are classified as obese, and they are not further classified into any subtype [2]. Moreover, regarding gestational weight gain, the recommendation issued by the Japanese Ministry of Health, Labour and Welfare suggests that obese pregnant women with a BMI of 25 kg/m^2 should receive treatments individually tailored to their needs [3].

Regarding associations between pre-pregnancy BMI and pregnancy outcomes, it has been widely reported that the incidences of pregnancy induced hypertension (PIH), gestational diabetes mellitus (GDM), cesarean delivery, preterm birth, macrosomia, and large for gestational age (LGA) increase in pre-pregnancy obese pregnant women [4-8]. Moreover, gestational weight gain has often been reported to be substantially associated with the incidences of preterm birth and PIH [5-9].

The IOM recommendations on gestational weight gain are viewed as controversial because of a claim that the recommended weight gain for pre-pregnancy obese pregnant women is too small, resulting in poor infant outcomes [9-10]. In addition, no recommended rate of weight gain for obese pregnant women is specified in Japan. No consensus has been reached on optimal gestational weight gain for obese pregnant women [10-13].

In this study, including Japanese women with a pre-pregnancy BMI of 25 kg/m^2 who delivered at the present center, the authors examined how pregnancy outcomes vary

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Table 1. — *Comparison of maternal characteristics between pre-pregnancy normal weight, overweight and obese women*

	Normal group (BMI: 18.5–24.9) n = 6801	Overweight group (BMI: 25–29.9) n = 661	Obese group (BMI ≥ 30) n = 207	*p*-value*
Maternal age (years)	32.6 ± 4.9	32.6 ± 5.0	32.30 ± 4.23	0.53
Height (cm)	158.6 ± 5.3	158.0 ± 5.5	158.4± 6.0	0.12
Rates of weight gain in the second and third trimester (kg/week)	0.37 ± 0.15	0.32 ± 0.20	0.23 ± 0.25	<0.001
Total weight gain (kg)	10.2± 3.7	7.1 ± 4.9	3.6 ± 6.7	<0.001
Gestational age (week)	38.7 ± 1.9	38.6 ± 2.2	38.2 ± 2.6	0.21
Nulliparas	3108 (45.7)	282 (42.7)	110 (53.1)	0.03

BMI: body mass index.
Data are mean ± standard deviation or n(%), unless otherwise specified.
* *p*-values represent the overall differences across the three groups that were evaluated using the Kruskal-Wallis test.

Table 2. — *Comparison of adverse pregnancy outcomes between pre-pregnancy normal, overweight, and obese weight women*

	Normal group (BMI: 18.5–24.9) n = 6801	Overweight group (BMI: 25–29.9) n = 661	Obese group (BMI ≥ 30) n = 207	*p*-value*
PIH				
n (%)	136 (2.0)	33 (5.0)	21 (10.1)	<0.001
OR (95% CI)	1	2.67 (1.55–4.61)	5.80 (3.12–10.78)	
GDM				
n (%)	571 (8.4)	138 (20.9)	103 (49.8)	<0.001
OR (95% CI)	1	3.00 (2.26–4.00)	12.13 (8.52–17.28)	
Macrosomia				
n (%)	27 (0.4)	8 (1.2)	5 (2.4)	0.015
OR (95% CI)	1	2.79 (0.90–8.58)	6.54 (1.84–23.33)	
LGA				
n (%)	381 (5.6)	60 (9.1)	32 (15.5)	<0.001
OR (95% CI)	1	1.72 (1.19–2.48)	2.89 (1.83–4.56)	
Preterm birth				
n (%)	374 (5.5)	49 (7.4)	28 (13.5)	<0.001
OR (95% CI)	1	1.39 (0.94–2.04)	2.75 (1.71–4.42)	
PPROM				
n (%)	122 (1.8)	21 (3.2)	15 (7.2)	<0.001
OR (95% CI)	1	1.78 (0.97–3.29)	4.13 (2.09–8.17)	
Spontaneous preterm birth				
n (%)	238 (3.5)	28 (4.2)	20 (9.7)	<0.001
OR (95% CI)	1	1.23 (0.75–2.01)	3.01 (1.72–5.26)	
Induced preterm birth				
n (%)	136 (2.0)	21 (3.2)	8 (3.9)	0.13
OR (95% CI)	1	1.62 (0.89–2.96)	2.07 (0.91–4.71)	

GDM: by 75-g oral glucose tolerance test, GDM was diagnosed when at least one of the following was found: fasting blood glucose level of ≥ 92 mg/dl, blood glucose level at one hour of ≥180 mg/dl, blood glucose level at two hours ≥ 153 mg/dl. BMI: body mass index; PIH: pregnancy-induced hypertension; GDM: gestational diabetes mellitus; LGA: large for gestational age; PPROM: preterm prelabor rupture of membranes; OR: odds ratio; CI: confidence interval.
* Logistic regression was used to adjust for confounding variables, including maternal age, gestational age at delivery and parity, and the results were expressed as ORs and 95% CIs.

between overweight women with a BMI of 25.0-29.9 kg/m^2 and obese women with a BMI of 30 kg/m^2, as well as whether the IOM-recommended guidelines for gestational weight gain have external validity for Japanese women.

Materials and Methods

Data were retrospectively analyzed using the medical records of women who delivered live singletons at 22 gestational weeks or more between January 2001 and December 2012 at the Perinatal Center for Maternity and Neonate, Yokohama City University Medical Center, Yokohama. Patients with an uncertain gestational weight gain, those with concomitant hypertension or diabetes as the underlying disease, and those who delivered a newborn with congenital anomalies were excluded. Consequently, 7,669 pregnancies of 6,753 women were included in the present study. This study was approved by the ethics committee of the Yokohama City University Medical Center.

Pre-pregnancy BMI (weight [kg] divided by height squared [m^2]) was calculated from pre-pregnancy body weight and height that were reported by the women at the first visit. According to the 2009 IOM guidelines, 207 pregnancies were classified into the pre-pregnancy obese group (BMI = 30 kg/m^2), 661 into the pre-pregnancy overweight group (BMI = 25−29.9 kg/m^2), and 6,801 into the pre-pregnancy normal weight group (BMI = 18.5−25 kg/m^2). The pregnant women were individually instructed during the first trimester by trained maternity nurses to achieve the desired gestational weight gain: 10−12 kg in the pre-pregnancy normal weight group, 5−7 kg in the pre-pregnancy overweight group, and five kg or less in the pre-pregnancy obese group (according to the recommended weight gain set by the Japan Society of Obstetrics and Gynecology from 2000 to 2006) [14], or 7−12 kg, 5−7 kg, and five kg or less in the three aforementioned groups, respectively (according to the recommended weight gain set by the Japanese Ministry of Health, Labour and Welfare from 2007 to 2012) [15].

The maternal characteristics were age, pre-pregnancy body weight, pre-pregnancy BMI, body weight at delivery, BMI at delivery, height, weekly weight gain during the second and third trimesters, total gestational weight gain, gestational age at delivery, and primiparous rate. The main outcomes were PIH, GDM, macrosomia, LGA, preterm birth, spontaneous preterm birth, preterm prelabor rupture of membranes (PPROM), and induced preterm birth, and the incidences of these outcomes were compared among the groups and analyzed. PIH was defined as a case in which hypertension (systolic blood pressure = 140 mmHg and/or diastolic blood pressure = 90 mmHg) on two occasions at least four hours apart first developed after 20 weeks of gestation. Induced preterm birth was defined as preterm delivery by cesarean section and induction of labor due to maternal complications, such as preeclamp-

Table 3. — *Incidence of adverse pregnancy outcomes in pre-pregnancy overweight women by the gestational weight gain.*

		Rates of weight gain in the second and third trimester (kg/week)			
		< 0.23 n = 176 (26.6%)	0.23–0.32** n = 170 (25.7%)	0.32–0.50 n = 233 (35.2%)	> 0.5 n = 82 (12.4%)
PIH	n (%)	12 (6.8)	4 (2.4)	12 (5.2)	5 (6.1)
	OR (95% CI)	2.85 (0.89–9.08)	1.00	2.51 (0.79–7.98)	3.23 (0.83–12.56)
	p-value*	0.08		0.12	0.09
LGA	n (%)	13 (7.4)	12 (7.1)	17 (7.3)	18 (22.0)
	OR (95% CI)	1.01 (0.45–2.30)	1.00	1.04 (0.48–2.26)	3.41 (1.52–7.65)
	p-value*	0.98		0.92	0.003
Preterm birth	n (%)	19 (10.8)	11 (6.5)	11 (4.7)	8 (9.8)
	OR (95% CI)	1.73 (0.80–3.77)	1.00	0.74 (0.31–1.75)	1.65 (0.63–4.33)
	p-value*	0.16		0.49	0.31
PPROM	n (%)	12 (6.8)	4 (2.4)	3 (1.3)	2 (2.4)
	OR (95% CI)	3.05 (0.96–9.68)	1.00	0.51 (0.11–2.31)	0.88 (0.15–5.02)
	p-value*	0.06		0.38	0.89
Spontaneous preterm birth	n (%)	15 (8.5)	6 (3.5)	4 (1.7)	3 (3.7)
	OR (95% CI)	2.57 (0.97–6.81)	1.00	0.44 (0.12–1.56)	0.87 (0.21–3.63)
	p-value*	0.06		0.21	0.84
Induced preterm birth	n (%)	4 (2.3)	5 (2.9)	7 (3.0)	5 (6.1)
	OR (95% CI)	0.71 (0.19–2.72)	1.00	1.13 (0.35–3.66)	2.79 (0.77–10.14)
	p-value*	0.62		0.83	0.12

BMI: body mass index; PIH: pregnancy-induced hypertension; LGA: large for gestational age; PPROM: preterm prelabor rupture of membranes; OR: odds ratio; CI: confidence interval. * Logistic regression was used to adjust for confounding variables, including maternal age, gestational age at delivery and parity, and the results were expressed as ORs and 95% CIs. ** The IOM recommended gestational weight gain during the second and third trimesters for overweight pregnant women as 0.23–0.32 kg/week.

sia, or non-reassuring fetal status. Meanwhile, spontaneous preterm birth was defined as preterm birth other than preterm birth medically indicated by cesarean section and labor induction. LGA was defined as a neonatal birth weight above the 90th percentile of the reference curves of birth weight for gestational week [16].

Gestational age was determined based on the last menstrual period. If gestational age according to the last menstrual period differed by more than seven days from that based on ultrasonography at less than 11 weeks, the latter was used to assign a gestational age.

Next, the cases in the pre-pregnancy overweight (n = 661) and pre-pregnancy obese (n = 207) groups were stratified by weekly weight gain during their second and third trimesters to determine the associations of gestational weight gain with the incidences of PIH, LGA, preterm birth, PPROM, spontaneous preterm birth, and induced preterm birth. The incidences of these events were compared between these subgroups and women with weight gain within the IOM-recommended guidelines to determine optimal weight gain for Japanese women. Weight gain was calculated as weekly weight gain by dividing the difference in weight between during the second and third trimesters and at the time of delivery by the number of gestational weeks between these time points.

Data were expressed as means ± standard deviation or frequencies (percentage). The IBM SPSS Statistics version 19 program was used for statistical analyses. The authors applied the Kruskal-Wallis test and the Mann-Whitney U-test for determining the significance of differences in continuous variables. Fisher's exact tests were used to detect differences in categorical data by group. Statistical tests were considered significant at a p-value of < 0.05. Moreover, logistic regression was used to adjust for confounding variables, including maternal age, gestational age at delivery, and parity. The results obtained were expressed as odds ratios (OR) and 95% confidence intervals (CI).

Results

Of 7,669 pregnancies, the pre-pregnancy normal weight group accounted for 78.3% (n = 6801), the pre-pregnancy overweight group for 7.4% (n = 661), and the pre-pregnancy obese group for 2.3% (n = 207).

Table 1 shows maternal characteristics according to the BMI categories. No difference was observed in either maternal age or gestational age at delivery; however, weekly gestational weight gain (pre-pregnancy normal weight group: 0.37 ± 0.15 kg, pre-pregnancy overweight group: 0.32 ± 0.20 kg, and pre-pregnancy obese group: 0.23 ± 0.25 kg; $p < 0.001$) and total gestational weight gain (pre-pregnancy normal weight group: 10.18 ± 3.67 kg, pre-pregnancy overweight group: 7.07 ± 4.94 kg, and pre-pregnancy obese group: 3.61 ± 6.71 kg; $p < 0.001$) were significantly lower in the higher BMI categories.

Table 2 shows the incidences of PIH, GDM, macrosomia, LGA, preterm birth, spontaneous preterm birth, PPROM, and induced preterm birth according to the BMI categories. There were significant differences in the incidences of PIH, GDM, macrosomia, LGA, preterm birth, spontaneous preterm birth, and PPROM among the three groups, and the incidences were significantly higher in those with a high pre-pregnancy BMI. Although the incidences of induced preterm birth tended to be higher with a high pre-pregnancy BMI, the difference did not reach statistical significance.

Table 3 shows the incidences of PIH, LGA, preterm birth, PPROM, spontaneous preterm birth, and induced preterm

Table 4. — *Incidence of adverse pregnancy outcomes in pre-pregnancy obese women by the gestational weight gain.*

		Rates of weight gain in the second and third trimesters (kg/week)			
		<0.18 n = 76 (36.7%)	0.18–0.27** n = 37 (17.9%)	0.25–0.5 n = 71 (34.3%)	> 0.5 n = 23 (11.1%)
PIH	n (%)	5 (6.6)	5 (13.5)	6 (8.5)	5 (21.7)
	OR (95% CI)	0.46 (0.12–1.75)	1.00	0.69 (0.19–2.51)	1.90 (0.46–7.81)
	p-value*	0.25		0.57	0.37
LGA	n (%)	9 (11.8)	6 (16.2)	11 (15.5)	6 (26.1)
	OR (95% CI)	0.62 (0.19–1.98)	1.00	1.01 (0.33–3.15)	1.67 (0.44–6.30)
	p-value*	0.42		0.98	0.45
Preterm birth	n (%)	16 (21.1)	4 (10.8)	3 (4.2)	5 (21.7)
	OR (95% CI)	2.39 (0.73–7.87)	1.00	0.39 (0.08–1.87)	2.60 (0.60–11.17)
	p-value*	0.15		0.24	0.20
PPROM	n (%)	10 (13.2)	2 (5.4)	2 (2.8)	1 (4.3)
	OR (95% CI)	2.56 (0.52–12.58)	1.00	0.45 (0.06–3.40)	0.71 (0.06–8.56)
	p-value*	0.25		0.44	0.78
Spontaneous preterm birth	n (%)	12 (15.8)	3 (8.1)	3 (4.2)	2 (8.7)
	OR (95% CI)	2.22 (0.58–8.56)	1.00	0.50 (0.09–2.63)	1.13 (0.17–7.52)
	p-value*	0.25		0.41	0.90
Induced preterm birth	n (%)	4 (5.3)	1 (2.7)	0 (0)	3 (13.0)
	OR (95% CI)	2.32 (0.25–22.03)	1.00		6.79 (0.63–72.85)
	p-value*	0.46		1.00	0.11

BMI: body mass index; PIH: pregnancy-induced hypertension; LGA: large for gestational age; PPROM: preterm prelabor rupture of membranes; OR: odds ratio; CI: confidence interval. * Logistic regression was used to adjust for confounding variables, including maternal age, gestational age at delivery and parity, and the results were expressed as ORs and 95% CIs.** The IOM recommended gestational weight gain during the second and third trimesters for obese pregnant women as 0.18–0.27 kg/week.

birth in the 661 pregnancies in the pre-pregnancy overweight group according to gestational weight gain in relation to the IOM gestational weight gain recommendations. The IOM-recommended gestational weight gain during the second and third trimesters for overweight pregnant women is 0.23−0.32 kg/week. As weekly weight gain was lower than this recommended rate, the incidences of PIH, PPROM, and spontaneous preterm birth tended to be higher. However, the differences were not significant. On the other hand, the incidence of LGA was significantly higher in women with a weight gain of 0.5 kg/week.

Table 4 shows the incidences of PIH, LGA, preterm birth, PPROM, spontaneous preterm birth, and induced preterm birth in the 207 pregnancies in the pre-pregnancy obese group according to gestational weight gain in relation to the IOM gestational weight gain recommendations. The IOM-recommended weekly gestational weight gain during the second and third trimesters for obese pregnant women is 0.18−0.27 kg/week. There were no significant differences in any event among any of the weight gain categories.

Discussion

In the pre-pregnancy obese and overweight group, the incidences of PIH, GDM, macrosomia, LGA, preterm birth, PPROM, and spontaneous preterm birth were significantly higher than those in the pre-pregnancy normal weight group. Moreover, incidences of adverse pre-pregnancy outcomes were apparently higher in the pre-pregnancy obese group than in the pre-pregnancy overweight group. The pregnancy outcomes in the pre-pregnancy overweight group differed according to the amount of gestational weight gain, whereas no differences were observed within the pre-pregnancy obese group.

As pre-pregnancy BMI became higher, pregnancy outcomes became poorer. Baeten *et al.* [17] conducted a retrospective cohort study on the associations between obesity and pregnancy outcomes in 159,072 primiparous women with a live singleton delivery and reported that the incidences of PIH, GDM, and preterm birth were higher with a higher pre-pregnancy BMI [15]. Moreover, Khatibi *et al.* [18] conducted a retrospective cohort study on the association between pre-pregnancy BMI and preterm birth in 83,554 women with a live singleton delivery and reported that, although the incidences of preterm birth and spontaneous preterm birth were higher with a higher pre-pregnancy BMI, there was no difference in the incidence of induced preterm birth. There are many other similar reports and the results of the present study support their views [19-21].

In the pre-pregnancy overweight group, the incidence of LGA was significantly higher in women with a gestational weight gain of 0.5 kg/week, and there were differences in pregnancy outcomes. However, the pre-pregnancy obese group showed no difference in any pregnancy outcome according to gestational weight gain. It has also previously

been reported that the impact of gestational weight gain on infant birth weight is lower with a higher pre-pregnancy BMI, and the results of the present study are also consistent with those reports [22-23].

There were differences in the incidences of adverse pregnancy outcomes according to BMI categories. In the pre-pregnancy overweight group, unlike in the pre-pregnancy obese group, pregnancy outcomes varied depending on gestational weight gain. Thus, the IOM obesity classification, which divides obesity into overweight (BMI = 25.0−29.9 kg/m^2) and obese (BMI = 30 kg/m^2) subtypes, seems to be an appropriate classification for Japanese women. In the pre-pregnancy overweight group, although it was difficult to determine optimal weight gain due to the lack of any consistent tendency in the incidence of each event in relation to the IOM-recommended gestational weight gain of 0.23−0.32 kg/week, it was suggested that optimal weight gain might be somewhere between 0.23 −0.5 kg/week. On the other hand, in the pre-pregnancy obese group, the present results suggested that adverse pregnancy outcomes could not be reduced by weight control during pregnancy.

The present study has some limitations. First, it was a single-center retrospective study with an insufficient sample size and a low incidence of events. Second, the authors did not examine other factors that may have confounded the present investigation.

In summary, obese pregnant Japanese women should also be classified as overweight with a BMI of 25.0−29.9 kg/m^2 or obese with a BMI of ³30 kg/m^2, instead of classifying those with a BMI of 25 kg/m^2 together as obese; and achieving an optimal pre-pregnancy weight is important because of the high incidences of adverse pregnancy outcomes and difficulty in improving pregnancy outcomes by weight control during pregnancy in obese pregnant women with a BMI of 30 kg/m^2.

The authors consider the present investigation to serve as a pilot study. In the future, larger cohort studies need to be conducted to investigate optimal weight gain for obese pregnant Japanese women.

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