Table 4 Percentiles for maternal weight gain (kg) according to gestational length at delivery

	37 weeks N=3561	38 weeks N=8563	39 weeks N=14841	40 weeks N=14259	41 weeks N=5435
25th	6.4	7.0	7.7	8.0	8.1
50th	9.0	9.5	10.0	10.0	10.5
75th	11.0	12.0	12.0	12.5	13.0
90th	13.3	14.0	14.5	15.0	15.5

cantly high in the "high" (1.58, 95% CI: 1.21–2.06) and "very high" (2.26, 95% CI: 1.72–2.97) weight gain groups. A history of prior spontaneous abortions increased the risk of macrosomia (1.49, 95% CI: 1.16–1.92). Pregnancy-induced hypertension was not related to macrosomia. Maternal diabetes was a significant factor increasing macrosomia risk (2.46, 95% CI: 1.49–4.05).

Table 5 Logistic regression analysis for IUGR and macrosomia according to each selected factor

	No. IUGR/total (%)	OR[a]	95% CI[b]	No. macrosomia/ total (%)	OR[a]	95% CI[b]
Total weight gain						
Very low: <25th percentile for gestational length	495/4535 (10.9)	2.87	2.56–3.21	34/4545 (0.7)	0.32	0.21–0.49
Low: 25th–49th	568/7232 (7.9)	1.49	1.35–1.66	39/7243 (0.5)	0.49	0.34–0.70
Moderate: 50th–74th	1312/22315 (5.9)	1		167/22354 (0.7)	1	
High: 75th–89th	281/7507 (3.7)	0.55	0.55–0.72	87/7519 (1.2)	1.58	1.21–2.06
Very high: 90th+	152/4978 (3.1)	0.45	0.45–0.63	83/4989 (1.7)	2.26	1.72–2.97
IVF conception						
Yes	28/455(6.2)	1.09	0.74–1.60	2/457 (0.44)	0.56	0.14–2.27
No	2780/46121 (6.1)	1		408/46202 (0.88)	1	
Past preterm delivery						
Yes	46/585 (7.9)	1.13	0.83–1.54	5/585 (0.9)	0.76	0.30–1.90
No	2762/45991 (6.1)	1		405/46074 (0.9)	1	
Past still birth						
Yes	29/402 (7.3)	1.09	0.74–1.60	5/402 (1.24)	1.11	0.45–2.74
No	2779/46174 (6.1)	1		405/46257 (0.88)	1	
Past spontaneous abortion						
Yes	383/5890 (6.6)	1.10	0.98–1.23	82/5891 (1.39)	1.49	1.16–1.92
No	2425/40686 (6.0)	1		328/40768 (0.8)	1	
Past cesarean delivery						
Yes	68/888 (7.7)	1.20	0.93–1.55	11/888 (1.2)	0.98	0.52–1.82
No	2740/45688 (6.0)	1		399/45771 (0.9)	1	
Pregnancy induced hypertension						
Preeclampsia	42/192 (21.9)	5.25	3.68–7.49	2/192 (1.0)	1.53	0.37–6.35
Gestational hypertension	81/752 (10.8)	2.79	2.19–3.54	11/754 (1.5)	0.85	0.45–1.63
None	2662/45521 (5.8)	1		396/45602 (0.9)	1	
Maternal diabetes						
Yes	36/553 (6.6)	1.55	1.10–2.20	21/554 (3.8)	2.46	1.49–4.05
No	2772/46023 (6.1)	1		389/46105 (0.8)	1	
Maternal Smoking						
Yes	283/2928 (9.7)	1.78	1.56–2.03	20/2930 (0.7)	0.63	0.40–1.01
No	2525/43648 (5.8)	1		390/43729 (0.9)	1	
Maternal Drinking						
Yes	150/2156 (7.0)	1.20	1.02–1.42	18/2158 (0.8)	0.87	0.54–1.42
No	2658/44420 (6.0)	1		392/44501 (0.9)	1	

Adjusted for maternal age, parity, prepregnancy weight, gestational age and infant gender.

[a] OR=odds ratio.

[b] CI=confidence interval.

Table 6 Multivariate logistic regression analysis for IUGR and macrosomia risk

Variables	IUGR			Macrosomia		
	OR[a]	95% CI[b]	*p* value	OR[a]	95% CI[b]	*p* value
Total weight gain						
Very low: <25th percentile for gestational age	2.90	2.59–3.25	<0.01	0.31	0.20–0.47	<0.01
Low: 25th–49th	1.52	1.37–1.69	<0.01	0.49	0.34–0.70	<0.01
Moderate: 50th–74th	1	Referent		1	Referent	
High: 75th–89th	0.68	0.52–0.68	<0.01	1.62	1.24–2.12	<0.01
Very high: 90th+	0.55	0.39–0.55	<0.01	2.41	1.83–3.17	<0.01
Pregnancy-induced hypertension						
Preeclampsia	6.89	4.78–9.92	<0.01	1.01	0.23–4.44	1.00
Gestational hypertension	3.15	2.47–4.03	<0.01	0.69	0.36–1.34	0.28
None	1	Referent		1	Referent	
Maternal diabetes (vs. none)	1.30	0.91–1.84	0.15	3.02	1.80–5.06	<0.01
Maternal smoking (vs. none)	2.08	1.80–2.40	<0.01	0.51	0.31–0.83	<0.01
Maternal drinking (vs. none)	0.94	0.79–1.13	0.54	1.04	0.63–1.72	0.86
Past spontaneous abortion (vs. none)	1.10	0.98–1.23	0.12	1.55	1.20–2.00	<0.01

Adjusted for maternal age, parity, prepregnancy weight, gestational length and infant gender.
Preeclampsia=hypertension with proteinuria ≧2 g/l.
[a] OR=odds ratio.
[b] CI=confidence interval.

Multivariate logistic regression analyses adjusted for maternal age, parity, prepregnancy weight, and infant gender, were performed to estimate the risk of IUGR and macrosomia for the selected significant factors from Table 5, as presented in Table 6. All variables were forced into the model. The ORs for IUGR in mothers with "very low" and "low" weight gains were significantly high, compared to the reference group with "moderate" weight gain, and the ORs in the "high" and "very high" weight gain groups were significantly low. The OR for IUGR was significantly high in mothers with preeclampsia (7.07, 95% CI: 4.91–10.2) and gestational hypertension (3.25, 95% CI: 2.55–4.15). The OR for IUGR was significantly high with maternal smoking (2.08, 95% CI: 1.80–2.40), but not with drinking.

The ORs for macrosomia in mothers with "high" and "very high" weight gains were significantly high, compared to the reference "moderate" weight gain group. The OR for macrosomia was significantly higher in mothers with prior spontaneous abortions (1.55, 95% CI: 1.20–2.00) and diabetes (2.99, 95% CI: 1.79–5.01). Pregnancy-induced hypertension was not related to macrosomia. The OR for macrosomia was significantly low with maternal smoking (0.51, 95% CI: 0.31–0.83), but not with drinking.

4. Discussion

This is the first report on fetal growth and maternal weight gain, prior obstetric history, and pregnancy complications using recent multi-centered data in Japan. Our findings on maternal weight gain and fetal size were in accordance with prior studies in predominantly white populations [12]. The observations on fetal macrosomia risk and maternal diabetes or high maternal weight gain was also consistent with other studies [13–15]. However, the association between prior spontaneous abortions and macrosomia in the subsequent pregnancy was uniquely observed in this study. Spontaneous abortions may be due to underlying glucose intolerance in Asian women, a high-risk population for diabetes [16]. A study on Asian women in Australia showed that women with gestational diabetes had more previous miscarriages/stillbirths compared to non-diabetic women [17]. Further research is needed to examine the relationship between a history of spontaneous abortion and maternal glucose intolerance.

There are several limitations due to the data characteristics of the Perinatal Database. First, it covered only a small proportion of Japanese births in 2001–2002, and was biased to "high-risk" pregnancies. As shown in Table 1, proportions of multiple gestations (7.5%) and preterm births (17.5%) were extremely high compared to national data in 2001–2002 which was 2.1% and 5.5% [4], respectively. Cesarean delivery rate was also quite high (27.2%), compared to hospital-based reports ranging from 7% to 10.3% [18,19].

Second, maternal height was not available in our study, and prepregnancy body size could not be considered in estimating the adequate range of weight gain. The referent weight gain range of 9 kg (50th percentile for 37 weeks) to 13 kg (75th

percentile for 41 weeks) used in this study, is close to values recommended for underweight women (10~12 kg) by JSOG [10]. Mean weight gain in the current study was 1-2 kg less compared to studies in the 1970s when LBW prevalence was lowest [20,21]. Taking into account that more women are underweight before pregnancy, higher target weight gains may be needed. Further studies should be conducted to develop weight gain goals specific to maternal prepregnancy BMI categories, especially for underweight women.

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Increasing trend of spina bifida and decreasing birth weight in relation to declining body-mass index of young women in Japan

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Summary We analyzed the existing data from various surveys on the prevalence of spina bifida, birth weight, and body-mass index (BMI), dietary intake, and smoking habits of Japanese young women. We found that the increasing trend of the prevalence of spina bifida paralleled with the decrease in birth weight, and the decrease in BMI and dietary energy intake and the increase in smoking rate among women of childbearing age. The decreased energy intake is likely due to their distorted self-body image. Based on these findings, we hypothesize that lowering BMI in young women led to increasing prevalence of spina bifida and smaller babies in Japan. This low dietary intake possibly leads to poor folate nutritional status, a risk factor for the development of spina bifida, and increased smoking potentially accelerates these undesirable outcomes. Our hypothesis can be tested using two simultaneous approaches. The first step is an extensive educational campaign for young women to stop smoking, have a realistic body image and eat a sufficient balanced diet. Government officials and health-care workers are encouraged to establish an agenda to educate young women with emphasis on the importance of adequate nutrition during the critical period of reproduction. Together with this campaign, the distribution of folic acid tablets for the prevention of spina bifida can be tried in women of childbearing age through local health centers, which have been well established in Japan.

Introduction

Spina bifida is one of the most common forms of neural-tube defects (NTDs). The cause of the development of NTDs is complex involving genetic and environmental factors, including folate nutritional status [1]. In the early 1990s, the findings of large-scale trials in Europe indicated that periconceptional folic acid (pteroylglutamic acid) supplementation reduces the occurrence or recurrence of pregnancy complicated with NTDs [2,3]. Since then, folic acid fortification to a staple food has been practiced in several countries, which led to a steeper decline in the prevalence of NTDs [4–7]

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than the previously observed steady decline worldwide [8]. In Japan, however, an increasing trend of the prevalence of spina bifida has been observed for the last few decades [8,9], although the mechanism(s) of such a trend is unknown. In addition, birth weight has been declining for the last 30 years in Japan [10]. Limited medical and social attention has been paid to these disturbing phenomena, and no systematic effort to reverse the trend of increasing spina bifida or declining birth weight has been made by either governmental offices or health-related organizations.

We analyzed the existing data of the prevalence of spina bifida, birth weight, and anthropometric measurements, dietary intake and smoking habits of women of childbearing age in the last few decades [9–12]. We present a hypothesis that the increasing prevalence of spina bifida and the decline in birth weight are associated with the low dietary energy intake and high smoking rate, which are reflected by decreasing body-mass index (BMI, kg/m^2) of women of childbearing age. We discuss the possible long-term medical and social consequences of these changes and propose methods to correct such alarming trends as a means to test our hypothesis.

Data analyses

The data used in the present analyses were obtained from reports by various governmental and non-governmental organizations [9–12]. The information on the prevalence of spina bifida was obtained from the report by the International Clearinghouse for Birth Defects Monitoring System [9] and was used to evaluate the trend in the prevalence of spina bifida. This information was based on the data collected by the Japan Association of Obstetricians and Gynecologists, covering about 100,000 births (including stillbirths which occurred at 22 weeks of gestation or later) from 270 hospitals nationwide and representing about 9% of entire births in Japan. Birth weight was obtained from the Vital Statistics Report [10]. Data on dietary intake, anthropometric measurements and smoking habits of women of childbearing age were obtained from the report by the National Nutrition Survey, which was an annual nationwide survey covering about 5000 households in randomly selected 300 census units [11,12]. To evaluate the changes in the last two decades in spina bifida prevalence, birth weight, and BMI, energy intake and smoking habit of young women, a general linear model was used to obtain annual increments of these parameters using the SPSS statistical program.

Results and discussion

It has been well recognized that there is a clear and steady decline in the prevalence of spina bifida in the last few decades worldwide [8]. In contrast, we found that there was a significant trend of steady increase in the prevalence of spina bifida between 1980 and 2000 in Japan. According to our analysis of the data published by the International Clearinghouse [9], the prevalence increased from 2.35 per 10,000 births between 1980 and 1984 to 4.82 per 10,000 births in 2000 ($p < 0.01$), although the international survey data indicated that there was an insignificant increase in spina bifida based on the information collected from 1988 to 1996 in Japan [8]. Simultaneously during the period between 1980 and 2001, the mean birth weights significantly declined from 3.23 to 3.07 kg in males and from 3.14 to 2.98 kg in females ($p < 0.01$) [10].

These two undesirable trends paralleled to steady and significant declines in the mean BMI in the last two decades ($p < 0.01$) [10], in the mean daily dietary energy intake of 1866 kcal in 1995 to 1752 kcal in 2001 ($p < 0.01$), and the increase in the fraction of smoking women, which doubled from 10.5% to 21.3% between 1987 and 1997 ($p < 0.01$) [11]. Furthermore, the mean dietary folate intake in young women (18–29 years old) was lowest among all age groups of women. For example, the mean dietary folate intake in women in this age category (263 μg/day) was significantly lower than that in a group of older women (50–69 years old, 374 μg/day, $p < 0.01$) [11]. In short, the increase in spina bifida prevalence and the decline in the mean birth weight appear to be associated with decreasing mean BMI of young women, which is most likely due to the declining dietary energy intake and the increasing rate of smoking.

Based on the above observation, we hypothesize that by restricting their dietary intake, young Japanese women expose themselves to a "borderline folate nutritional status" during the critical period of neural-tube closure, although it was impossible to establish the causal relationship based on the existing data. We postulate that the following cascade of events has been occurring: Firstly, young women have been extremely conscientious about their body weight and have a distorted body image. According to a survey conducted in 1998, they thought that their bodies looked disproportionately obese [11], although their BMI values were actually within or even below the accepted criteria for healthy individuals [13]. Secondly, this distorted body image leads to self-restricted dietary intake, which is often excessive.

Thirdly, low dietary intake results in a low BMI. In fact, over 20% of the women between age 15 and 29 had BMI below 18.5 kg/m^2 in 1996–2000 [11]. This trend is the opposite of that found in other countries, where the rate of overweight or obesity is increasing regardless of age and gender [14]. In contrast, the BMI values of other age groups have been increasing in Japan.

Fourthly, the low dietary intake possibly leads to the development of the ''borderline status'' of micronutrients including folate. It has also been reported that the intake of green vegetables, one of the best sources of dietary folate, in young women is much lower than those in older age groups [11]. This observation is consistent with the recent findings by Hiraoka *et al.* [15] indicating that serum folate concentrations in younger women were significantly lower than those in older women in Japan, and this may increase the risk of pregnancy complicated with NTDs. This association is not consistent with the finding by Watkins *et al.* [16] who reported that the risk of having infants with spina bifida is higher in obese women than non-obese women, whereas it is consistent with the recent report from California, indicating that maternal dieting behaviors with restricted-food intake in early pregnancy is associated with increased risk of NTDs [17]. Furthermore, in Japan, prenatal multivitamin tablets containing folic acid have not been regularly used. The importance of high folate intake in young women was recently pointed out by Kondo *et al.* [18].

Finally, when they become pregnant, the restricted dietary intake together with the extra burden of nutrient requirement for the rapidly growing fetus and placenta may further advance the ''borderline status'' to the ''inadequate status'' of various nutrients. Such compromised nutritional status may adversely affect fetal growth and development resulting in the decline in birth weight.

Increasing proportion of low-birth weight infants may pose serious medical and social consequences, since low-birth weight infants have a high risk of neonatal morbidity and mortality [19,20]. In addition, inadequate nutritional status *in utero*, caused by excessive dietary restriction, potentially increases the susceptibility to various diseases in later life, known as developmental origins of adult disease [21,22]. Furthermore, the exposure of the fetus to the increased risk of micronutrient deficiency, such as iron, may lead to delayed mental development in later life [23]. Although these untoward effects could be subtle, they may have a medically and economically devastating impact on Japanese society in the near future.

Smoking among young Japanese women has increased in recent decades [11], and it is strongly associated with the risk of having low-birth weight babies [19]. Scientific evidence indicates that smoking adversely affects folate status in pregnant and non-pregnant individuals [24,25]. Although there are only a few reports on smoking prevalence in Japanese pregnant women, a slight, but steady increase (from 5.6% to 10.9%) was observed between 1987 and 2002 [26–28]. Thus, the increasing smoking rate may, to a certain extent, contribute to the increasing prevalence of spina bifida, although the direct causal association is weak between smoking and the risk of developing NTDs [29,30].

Testing the hypothesis

Is it possible to test our hypothesis that the life style (low dietary intake and smoking) of women of childbearing age is the main reason for increasing spina bifida prevalence and declining birth weight? We believe that it is. As a first step, an extensive educational campaign can be initiated. Health-care workers with local or federal government officials should consider educating young women that they should stop smoking, have a realistic image of their bodies, and eat a sufficient balanced diet. It is difficult to predict, however, how long it would take for such an effort to become effective on reversing the trends. Together with this campaign, to prevent spina bifida, the distribution of folic acid tablets can be tried among young women through local health centers, which have been well established in Japan. The cost of such an intervention would be minimal compared to the cost of long-term medical care of infants with spina bifida or low birth weight. In addition, there may also be subtle and long-lasting adverse consequences of fetal malnutrition later in life [21–23]. The actual cost of folic acid tablets can be charged to women as was done in China [31]. The effectiveness of such intervention should be apparent within a few years.

Recommendation

We challenge health-care workers and officials in the area of nutrition and public health to establish an agenda to educate young women on the importance of adequate nutrition during the critical period of reproduction and to implement an intervention of folic-acid supplementation to correct the disturbing trend.

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Restricting weight gain during pregnancy in Japan: A controversial factor in reducing perinatal complications

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Abstract

Objective: To evaluate the effectiveness of restricting weight gain during pregnancy to reduce perinatal complications.
Study design: The study was conducted in the Tokyo metropolitan area, and reviewed 3071 mothers and their infants born from singleton pregnancies retrospectively. To examine the influence of increased maternal weight gain on perinatal complications, we performed five-category stratification for weight gain: less than 8.0, 8.0–10.0, 10.1–12.0, 12.1–14.0 and over 14.0 kg.
Results: Total weight gains less than 8.0 kg significantly increased the risk of low birth weight (LBW) and small for gestational age (SGA) infants (OR = 2.19, 95% CI; 1.36–3.52, OR = 1.76, 95% CI; 1.23–2.51) and total weight gain over 14.0 kg significantly increased the risk of large for gestational age (LGA) infants and pregnancy induced hypertension (PIH) (OR = 3.06, 95% CI; 1.88–4.98, OR = 2.87, 95% CI; 1.86–4.42, respectively), compared with women with weight gain of 10.1–12.0 kg. The groups with weight gains of 8.0–10.0 kg and 12.1–14.0 kg did not show adverse perinatal outcomes, including gestational diabetes (GDM), cesarean delivery, postpartum hemorrhage and laceration, significantly different from the 10.1 to 12.0 kg gain group.
Conclusion: Strict restriction of weight gain during pregnancy is not effective in reducing perinatal complications.

Keywords: Maternal weight gain; Prepregnancy body mass index (BMI); Perinatal complications

1. Introduction

Greater maternal weight gains were believed to increase the risks of gestational diabetes (GDM), pregnancy induced hypertension (PIH), eclampsia, cesarean delivery, macrosomia and prolonged difficult labor, postpartum hemorrhage and fetal trauma [1–5]. However, weight gain restriction had adverse birth outcomes. In 1990, the Institute of Medicine (IOM) in the United States revised the guidelines for weight gain during pregnancy, which recommend an optimal weight gain range for women based on their prepregnancy body mass index (BMI) because insufficient weight gain could contribute to premature births and to low birth weight (LBW) term infants [6]. In addition, Thorsdottir et al. [7] suggested that in an American population studied, unnecessary weight gain had no beneficial effect on health and inferred that low weight gain should also be avoided to optimize birth outcome. Restricted weight gain may even have negative consequences for women's well-being in the form of stress and worries optimal weight range, and it may consequently restrict optimal birth weight.

The Japan Society of Obstetrics and Gynecology (JSOG) issued guidelines for optimal weight gain during pregnancy, which are based on prepregnancy BMI, in order to prevent the risk of PIH, in 1997 [8]; recommended weight gains are

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10–12 kg for women of BMI < 18.0, 7–10 kg for women of 18.0 ≦ BMI ≦ 24.0, and 5–7 kg for women of BMI > 24.0, respectively. Although nutritional education or counseling on weight gain restriction has been undertaken in many hospitals or clinics in Japan following this guideline, very few studies were undertaken to assess the adverse effects of excessive maternal weight gain on pregnancy outcome. In addition, it is still controversial whether different cutoff values in various studies might offer results as good as, or better than, those recommended by the JSOG. At present, no upper or lower limit of maternal weight gain is provided to reduce the risk of perinatal complications.

Thus, it is still unclear which weight gain range has the stronger effect in the effort to avoid complications. Studies that report maternal and fetal health outcomes over the entire spectrum of weight change might help to clarify whether there are wider weight gain ranges for women. The purpose of our study was to evaluate the effectiveness of restricting weight gain during pregnancy in reducing perinatal complications.

2. Materials and methods

2.1. Subjects

In this retrospective study, we analyzed data on the 3071 mothers and their infants born at 37–42 weeks of gestation from singleton pregnancies during the years 2002 and 2003 in Nagai Clinic, Saitama, and Sagamihara Kyoudou Hospital, Kanagawa, which are located in Japan's Tokyo metropolitan area. Multiple pregnancies, stillborns and malformed fetuses were excluded from the study. Subjects were classified according to prepregnancy BMI (kg/m^2) into underweight (BMI < 18.5), normal (18.5 < BMI ≦ 25.0), and overweight (BMI > 25.0) groups, following the definitions of the Japan Society for the Study of Obesity [9], because Asian countries have a lower prevalence of obesity, despite their high rates of obesity-related diseases. This criterion differs from that of the National Institute of Health [10].

2.2. Anthropometric measurements and data collection

Other demographic data including age, parity and medical history were obtained from prenatal records. After delivery, the newborn anthropometric characteristics were measured and recorded; birth weight, length, head and chest circumference. Ponderal index was calculated as birth weight (g) divided by length (cm). Low birth weight (LBW: birth weight less than 2500 g), macrosomia (more than 4000 g), small for gestational age (SGA: birth weight below the 10th percentile for gestational age) and large for gestational age (LGA: birth weight above the 90th percentile for gestational age) which were classified by Nishida et al. [11] were also defined as neonatal outcomes. PIH was defined by World Health Organization criteria as a blood pressure over 140/90 mmHg [12]. GDM was defined by the JSOG criteria and diagnosed on the basis of a 75 g oral glucose tolerance test if the following diagnostic criteria are used in two or three categories: a fasting blood glucose of more than 100 mg/dl, a plasma glucose levels 60 min after loading of more than 180 mg/dl, and levels of more than 150 mg/dl 120 min after loading [13]. Postpartum heamorrhage was defined as excessive bleeding (more than 500 ml) due to failure of the myometrium to contract at the placental site.

In this study, total pregnancy weight gain was defined as the difference between measured weight at the last prenatal visit closest to delivery and self-reported prepregnancy weight. In the present study, the 25th, 50th, 75th and 90th percentiles for maternal weight gain are 7.4, 9.6, 11.9 and 14.2 kg, respectively. To examine the influence of increased maternal weight gain on perinatal complications, we stratified the data into five categories for weight gain based on these percentile values, because these values may be useful to clinicians providing optimal weight gain as prenatal care: less than 8.0, 8.0–10.0, 10.1–12.0, 12.1–14.0 and over 14.0 kg.

2.3. Statistical analysis

Differences in continuous variables by prepregnancy BMI category were determined by the Mann–Whitney–Wilcoxon test for non-normally distributed data, or ANOVA with Tukey's adjustment for normally distributed data. Differences in proportion of categorical variables were compared using χ^2-test. Multivariate logistic regression was used to evaluate the association between maternal total weight gain and perinatal complications. Interaction analysis between prepregnancy BMI categories and maternal weight gain during pregnancy was firstly carried out to ascertain the effect on perinatal outcomes before logistic regression was performed. We confirmed that the interaction was not significant. Adjusted odds ratio (OR) and 95% confidence intervals (CI) were estimated. Differences were considered to be significant at $p < 0.05$. Statistical analysis was carried out with SPSS for Windows, version 12.0 (SPSS Inc., Chicago III, USA).

3. Results

The investigation was undertaken using data from 3071 mothers who gave birth in selected hospitals in the metropolitan area of Tokyo between January 2002 and December 2003. Table 1 presents the maternal and neonatal demographic characteristics. Out of 3071 deliveries, 16.1% were underweight (BMI < 18.5 kg/m^2; $n = 493$, minimum 14.8), 74.9% were normal (18.5 ≦ BMI ≦ 25.0 kg/m^2; $n = 2301$) and 9.0% were obesity (BMI > 25.0 kg/m^2;

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Table 1
Demographic characteristics

	All category, $n = 3071$	BMI category (kg/m^2)			p-Value
		Underweight, $n = 493$ (16.1%)	Normal, $n = 2301$ (74.9%)	Obesity, $n = 277$ (9.0%)	
Mother					
Age (year)	29.4 ± 4.3	28.6 ± 4.3 bc	29.4 ± 4.3 ac	30.7 ± 4.2 ab	<0.001
Over 35 years old (%)	11.3	8.1	11.4	16.2	<0.01
Under 20 years old (%)	1.3	1.0	1.5	0.4	NS
Height (cm)	158.2 ± 5.1	158.7 ± 5.1	158.2 ± 5.1	157.8 ± 5.5	NS
Weight gain (kg)	9.6 ± 3.7	10.5 ± 3.3 bc	9.8 ± 3.4 ac	6.6 ± 4.8 ab	<0.001
Prepregnancy BMI (kg/m^2)	21.0 ± 3.0	17.6 ± 0.7	20.9 ± 1.6	28.1 ± 2.9	<0.001
Primiparous (%)	51.6	58	51.5	41.2	<0.001
Smoking (%)	15.8	16.8	16.8	15.8	NS
Infant					
Gestational week (w)	39.5 ± 1.0	39.4 ± 1.0	39.5 ± 1.0	39.5 ± 1.0	NS
Birth weight (g)	3061.8 ± 353.3	2993.0 ± 343.1 bc	3065.8 ± 348.7 ac	3150.5 ± 385.7 ab	<0.001
Birth length (cm)	49.0 ± 1.7	48.7 ± 1.7 bc	49.0 ± 1.7 ac	49.3 ± 1.9 ab	<0.001
Head circumstance (cm)	33.0 ± 1.2	33.0 ± 1.2	33.0 ± 1.2	33.2 ± 1.3	NS
Chest circumstance (cm)	31.6 ± 1.5	31.4 ± 1.4 bc	31.7 ± 1.5 a	31.8 ± 1.6 a	<0.05
Ponderal index (kg/m^3)	26.0 ± 2.4	25.8 ± 2.0 c	26.0 ± 2.5	26.2 ± 2.0 a	<0.05
Placenta weight (g)	579.3 ± 102.4	553.6 ± 92.3 bc	580.1 ± 101.6 ac	618.5 ± 101.6 ab	<0.001

BMI: body mass index, NS: nonsignificant; BMI categories (underweight < 18.5, normal 18.5–25.0, obesity > 25.0). Values are presented as mean ± S.D. or %; letters show the values that are significantly different ($p < 0.05$, Tukey's test or Mann–Whitney test).

$n = 277$, maximum 43.1). The average maternal age was 29.4 ± 4.3.

The mean weight gains during pregnancy for the underweight and normal women were 10.5 kg (range −0.8 to +21.5), 9.8 kg (range −1.7 to +24.0), respectively. For obese women, the median weight gain was 6.9 kg (range −9.6 to +24.0). There were significant differences among the three groups ($p < 0.001$). Smoking prevalence was 15.8% in all categories with no significant difference among the three groups. Although the numbers of gestational weeks when classified by prepregnancy BMI were not significantly different, the mean birth weight in underweight women was lower than those of the normal and obese women (2993.0 ± 343.1 g, 3065.8 ± 348.7 g, 3150.5 ± 385.7 g, respectively, $p < 0.001$). In addition, the mean length and chest circumference were significantly lower ($p < 0.001$, $p < 0.05$, respectively) than those of the normal and obese women.

Table 2 shows the results of pregnancy outcome classified by prepregnancy BMI. The proportion of LBW infants was higher in underweight women than in normal and obese women (7.5%, 4.6%, 4.7%, respectively, $p = 0.03$). The proportion of SGA infants was higher in underweight women than in normal and obese women, but the differences were not significant (11.0%, 8.0%, 8.7%, respectively, $p = 0.1$). PIH prevalence was 8.5%, where the prevalence of underweight, normal and obese women was 4.1%, 7.1% and 27.4%, respectively ($p < 0.001$). The PIH prevalence in obese women was 6 times that in the underweight women. The proportion of cesarean sections was also higher in the obese women than in underweight and normal women (9.7%, 3.4%, 3.8%, respectively, $p < 0.001$).

Table 3 shows the perinatal outcomes by prepregnancy BMI category. In underweight women, the odds ratio of LBW and SGA were significantly increased by 1.7 (95% CI; 1.15–2.51), 1.45 (95% CI; 1.13–2.00), respectively,

Table 2
Frequencies of perinatal outcomes

	All category, $n = 3071$	BMI category (kg/m^2)			p-Value
		Underweight, $n = 493$ (16.1%)	Normal, $n = 2301$ (74.9%)	Obesity, $n = 277$ (9.0%)	
LBW	155 (5.0)	37 (7.5)	105 (4.6)	13 (4.7)	0.03
SGA	262 (8.5)	54 (11.0)	184 (8.0)	24 (8.7)	0.10
LGA	170 (5.5)	16 (3.2)	127 (5.5)	27 (9.7)	<0.001
Macrosomia	20 (0.7)	1 (0.2)	15 (0.7)	4 (1.4)	0.12
PIH	260 (8.5)	20 (4.1)	164 (7.1)	76 (27.4)	<0.001
GDM	138 (4.5)	28 (5.7)	97 (4.2)	13 (4.7)	0.36
C/S	132 (4.3)	17 (3.4)	88 (3.8)	27 (9.7)	<0.001
Postpartum hemorrhage	90 (2.9)	13 (2.6)	66 (2.9)	11 (4.0)	0.54
Laceration	588 (19.1)	105 (21.3)	422 (18.3)	61 (22.0)	0.14

Values are presented as n (%); BMI categories (underweight < 18.5, normal, 18.5–25.0, and obesity > 25.0). p-Value based on χ^2-test for percent. LBW: low birth weight, SGA: small for gestational age, LGA: large for gestational age. PIH: pregnancy induced hypertension, GDM: gestational diabetes, C/S: cesarean section.

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Table 3
Adjusted odds ratios (OR) of perinatal outcomes by prepregnancy BMI

	BMI category (kg/m^2)		
	Underweight, OR (95% CI)	Normal, OR	Obesity, OR (95% CI)
LBW	1.7 (1.15–2.51)	1.0	1.03 (0.57–1.86)
SGA	1.45 (1.13–2.00)	1.0	1.04 (0.67–1.64)
LGA	0.56 (0.33–0.96)	1.0	1.91 (1.23–2.96)
Macrosomia	0.3 (0.04–2.31)	1.0	2.31 (0.75–7.11)
PIH	0.55 (0.34–0.89)	1.0	4.89 (3.58–6.68)
GDM	1.37 (0.89–2.11)	1.0	1.11 (0.61–2.02)
C/S	0.89 (0.52–1.51)	1.0	2.72 (1.72–4.31)
Postpartum hemorrhage	0.91 (0.50–1.67)	1.0	1.41 (0.73–2.72)
Laceration	1.24 (0.98–1.58)	1.0	1.19 (0.88–1.62)

CI: confidence interval; BMI categories (underweight < 18.5, normal, 18.5–25.0, obesity > 25.0). LBW: low birth weight, SGA: small for gestational age, and LGA: large for gestational age. PIH: pregnancy induced hypertension, GDM: gestational diabetes, C/S: cesarean section. Adjusted for maternal age, parity and maternal weight gain.

compared with the normal. On the other hand, in the obese women, the odds ratios of LGA, PIH and cesarean section were increased significantly, by 1.91 (95% CI; 1.23–2.96), 4.89 (95% CI; 3.58–6.68), 2.72 (95% CI; 1.72–4.31), respectively, compared with the normal. No increase in odds ratio was observed for macrosomia, GDM, postpartum hemorrhage and laceration in prepregnancy BMI categories.

Table 4 shows the distribution of perinatal complications within maternal weight gain categories. Women with total weight gain less than 8 kg had significantly increased risk of LBW and SGA infants (OR = 2.19, 95% CI; 1.36–3.52, OR = 1.76, 95% CI; 1.23–2.51, respectively). On the other hand, women with total weight gains over 14 kg showed a significantly increased the risk of LGA infants and PIH (OR = 3.06, 95% CI; 1.88–4.98, OR = 2.87, 95% CI; 1.86–4.42, respectively). There was no statistically significant difference in the incidence of GDM, cesarean delivery, macrosomia, postpartum hemorrhage and laceration between the weight gain categories. Total weight gain with 8–10 and 12.1–14 kg groups did not show any significant influence on the other perinatal outcomes.

4. Comment

This is the first epidemiological study in which we have examined the ranges of maternal weight gain in 2 kg intervals ranging from less than 8 kg to more than 14 kg, and whether they affect or protect against the perinatal complications as classified by prepregnancy BMI among Japanese women. In order to define where in the range of maternal weight gain the risk increases, the women were divided into five categories as follows: under 8.0, 8.0–10.0, 10.1–12.0, 12.1–14.0, over 14.0 kg. This study may contribute to analysis of the factors causing recent trends of increases in the proportion of LBW infants and of decreases in the average birth weight in Japan, because the birth weights have gradually declined from 3.16 to 3.07 kg for boys and 3.08 to 2.99 kg for girls from 1990 to 2000, and the prevalence rates of LBW infants have also increased 5.7–7.8 for boys and 7.0–9.5 for girls, during the same periods [14]. In our results, the total incidence of LGA infant was only 5.5%, which was well below 10%. An analysis of the major factors causing recent trends is important in order to reduce the risk of perinatal complications and contribute to

Table 4
Adjusted odds ratio (OR) of perinatal outcomes by weight gain

	Maternal weight gain (kg)									
	<8.0, n = 925 (30.1%)		8.0–10.0, n = 747 (24.3%)		10.1–12.0, n = 635 (20.7%)		12.1–14.0, n = 414 (13.5%)		>14.0, n = 350 (11.4%)	
	n (%)	95% CI	n (%)	OR (95% CI)	n (%)	OR	n (%)	OR (95% CI)	n (%)	OR (95% CI)
LBW	68 (7.4)	2.19 (1.36–3.52)	38 (5.1)	1.32 (0.79–2.21)	25 (3.9)	1.0	14 (3.4)	0.84 (0.43–1.63)	10 (2.9)	0.71(0.37–1.50)
SGA	110 (11.9)	1.76 (1.23–2.51)	64 (8.6)	1.08 (0.73–1.59)	51 (8.0)	1.0	21 (5.1)	0.59 (0.35–0.99)	16 (4.6)	0.54 (0.30–0.99)
LGA	41 (4.4)	0.65 (0.39–1.06)	19 (2.5)	0.51 (0.28–0.91)	31 (4.9)	1.0	34 (8.2)	1.88 (1.00–2.95)	45 (12.9)	3.06 (1.88–4.98)
Macrosomia	4 (0.4)	0.27 (0.07–1.05)	3 (0.4)	0.44 (0.11–1.76)	6 (0.9)	1.0	3 (0.7)	0.84 (0.21–3.41)	4 (1.1)	1.27 (0.35–4.59)
PIH	68 (7.4)	0.57 (0.38–0.88)	47 (6.3)	0.84 (0.55–1.30)	46 (7.2)	1.0	43 (10.4)	1.72 (1.00–2.69)	56 (16.0)	2.87 (1.86–4.42)
GDM	40 (4.3)	0.95 (0.58–1.57)	34 (4.6)	1.02 (0.61–1.70)	28 (4.4)	1.0	17 (4.1)	0.94 (0.51–1.75)	19 (5.4)	1.28 (0.70–2.32)
C/S	40 (4.3)	0.76 (0.45–1.26)	29 (3.9)	0.84 (0.49–1.44)	28 (4.4)	1.0	23 (5.6)	1.39 (0.78–2.46)	12 (3.4)	0.82 (0.41–1.65)
Postpartum hemorrhage	23 (2.5)	0.65 (0.35–1.19)	20 (2.7)	0.76 (0.41–1.41)	22 (3.5)	1.0	4 (1.0)	0.28 (0.09–0.81)	21 (6.0)	1.82 (0.91–3.22)
Laceration	171 (18.5)	0.88 (0.68–1.14)	144 (19.3)	0.96 (0.73–1.26)	123 (19.4)	1.0	72 (17.4)	0.9 (0.65–1.24)	79 (22.3)	1.26 (0.91–1.74)

CI: confidence interval; LBW: low birth weight, SGA: small for gestational age, LGA: large for gestational age; PIH: pregnancy induced hypertension, GDM: gestational diabetes, C/S: cesarean section; adjusted for maternal age, parity and prepregnancy BMI.

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assessment of the current JSOG guidelines for optimal weight gain.

Underweight women had a higher incidence of LBW infants than the normal group. Consistent with previous reports, in our study, low maternal prepregnancy BMI had a significant impact on perinatal outcomes, such as LBW and SGA [15–17]. In our study, 7.5% of the LBW infants and 11% of the SGA infants were attributed to women who were underweight at conception. Low maternal BMI could result from chronically poor energy intake, which would reduce fat stores and compromise visceral and somatic protein status. Poor maternal nutritional status during pregnancy has also been associated with reduced placental weight and surface area, which could limit nutrient transfer from the maternal circulation to the fetus, even if dietary intake increased later in pregnancy [18]. These findings indicate that an adequate BMI range before conception may help to prevent adverse perinatal complications.

On the other hand, in our study, obese women had a higher incidence of LGA infants, PIH and cesarean section deliveries. Vahratian et al. reported that overweight women (BMI > 26.1–29.0) and obese women (BMI > 29.0) were 1.2 and 1.5 times more likely, respectively, to have cesarean deliveries than women of normal weight (19.8 < BMI < 26.0) [19]. Many researchers reported that maternal obesity is associated with increased complications of pregnancy, labor, and delivery, infant macrosomia and birth defect, such as LGA infant, PIH and cesarean section deliveries [20–22]. Therefore, appropriate maternal BMI at conception may help to reduce the risk for pregnancy complications and adverse pregnancy outcomes.

However, the relation between prepregnancy BMI and the incidence of complications varied according to the maternal weight gain during pregnancy. Several investigators have suggested that the LBW risk among women with poor weight gain is increased if they also reported a low prepregnant BMI [23–24]. Our study found that the risk of LBW infants decreases when a woman's weight gain exceeds 8 kg, and the risk of PIH and cesarean section delivery decreases when women gain less than 14 kg. These results seem to support the importance of adequate maternal weight gain to avoid the incidence of perinatal complications even though the prepregnant BMI can be considered a potential predictor of adverse outcomes.

Birth weight is an important correlate of neonatal and infant health and has been recently associated with adult onset disease, including cardiovascular diseases, non-insulin dependent diabetes mellitus [25–27]. In addition, reduced ponderal index, which indicates asymmetric growth restriction is associated with reduced cognitive development and lower intelligence quotient in children [28–30]. A recent study showed that women delivering small infants may have a higher risk of heart disease than women having larger infants [31], and that women with PIH have a higher risk of hypertension and heart disease later in life [32]. These results seem to support the importance of appropriate birthweight and optimal weight gain of women in pregnancy to reduce adverse prenatal outcomes.

In regard to reduced birth size, the risk of LBW and SGA infant was high among the women with weight gain of less than 8 kg. They were nearly twice as likely to deliver LBW and SGA infants as those with weight gains of 10.1–12 kg. On the other hand, a low risk was found in women with weight gain more than 8 kg. This means an appropriate maternal weight gain may be a strong predictor of reduction of the risk of LBW and SGA infants. Thus, our findings highlight the importance of poor maternal weight gain as a potentially correctable cause of adverse perinatal outcomes.

LGA were associated with excessive weight gain during pregnancy [33]. Although normal women with more than 14 kg weight gain during pregnancy showed a three times greater risk for LGA infants, than the women with weight gains 10–12 kg, there was no significant association between maternal weight gain and the incidence of LGA among underweight and obese groups. Regarding the neonatal birth size, these results indicate that the upper limit of weight gain of up to 14 kg for women regardless of the prepregnant BMI is optimal and may result in absence of complications.

A few studies reported that excessive weight gain would induce a higher risk of adverse perinatal outcomes, PIH, GDM and cesarean delivery [1–5]. Optimal weight gain for Japanese pregnant women was set by JSOG in order to prevent the risk of PIH, in 1997 [8]. According to Murakami et al. [34], weight gain during pregnancy seems to have no significant influence on perinatal outcomes, such as GDM and PIH. They found that the incidence of PIH was not significantly increased in Japanese women who gained more than 12.5 kg compared to those gained 8.5–12.5 kg. They had different classification of maternal weight gain as follows: less 8.5 kg, 8.5–12.5 kg and over 12.5 kg, and analyzed the data using 8.5–12.5 kg as the reference group. Their finding was of great interest to clinicians, in assessing the effects of restricting weight gain on perinatal outcome. Consistent with their findings, our study found that GDM was not associated with weight gain. On the other hand, the incidence of PIH was higher among women gaining up to 14 kg. The reason for this inconsistency may be redefining classification for maternal weight gain and setting the references.

There are some limitations in our study. First, we did not find any significant relation between perinatal complications and maternal weight gain, possibly due to limited classification for obesity and weight gain range. NIH defined overweight as a BMI 25.0–29.9 kg/m^2 and obesity is a BMI > 30 kg/m^2 [10]. In our study, 9% were overweight and only 1.8% had obesity by NIH criteria (data not shown). The rate of obesity (BMI > 30 kg/m^2) among reproductive–aged women is around 33% in US [35], in 2000. On the other hand, although the prevalence of obesity is increasing and becoming a major risk factor for common disease for most Japanese people, BMI has been decreasing only in reproductive–aged women, presumably due to excessive

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dieting. The rate of obesity (BMI > 25 kg/m^2) among Japanese women aged 20–29 and 30–39 years old significantly had decreased over the last two decades, 1980–2000 (11.1 to 6.9%, 14.7 to 12.9%, respectively) [36].

Secondly, our sample size was small and too few women in this study had a diagnosis of GDM, PIH, macrosomia and postpartum hemorrhage during pregnancy. The rate of perinatal complications was examined in five stratified categories for weight gain based on prepregnancy BMI, making statistical differences. Thus, we believe large-scale randomized trials are needed to assess more precisely the acceptable range of weight gain for incidence of perinatal complications.

This study shows that the perinatal outcomes for women with a gestational weight gain of 8–10 kg and 12.1–14.0 kg were not significantly different from those for women with gestational weight gain 10.0–12.0 kg. Restricted weight gain is not strongly protective against maternal complications. This indicates that optimal weight gain should not be too low and current JSOG guidelines should be re-assessed. Our findings will be useful to clinicians providing antenatal care. Appropriate gestational weight gain is important for achieving healthy pregnancies, deliveries and birth outcomes for women. In addition, women who were underweight and obese before pregnancy should be aware of the potential hazards of low or high preconception BMI. We need to further research and validate clinically effective and practical interventions in optimizing better health outcomes for infants and mothers.

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Manuscript categories: Original Article

Title: Risk factors for small for gestational age

Running title: Risk factors for SGA infants

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Abstract

Background: The purpose of the paper was to determine the risk factors for small for gestational age (SGA) infants at full term, in Japan.

Methods: The study was conducted at four hospitals and clinics in the Tokyo metropolitan area. A retrospective review of 2972 mothers and their infants born from singleton pregnancies at any time during the years 2002 and 2003 was conducted.

Results: Of these women, 8.4% gave birth to SGA infants. The proportion of SGA infant was significantly higher among heavy smokers (>10 cigarettes/day; 13.7%, $p<0.01$). The odds ratio for SGA decreased significantly in proportion to the pregnancy body mass index (OR 0.89, 95%CI. 0.84-0.94, $p<0.001$). The odds ratio of SGA for stratified maternal weight gain was 1.79 (95%CI. 1.24-2.58, p=<0.01) for weight gain less than 8.0 kg, 1.16 (95%CI. 0.79-1.71, $p=0.45$) for weight gain 8.0-10.0 kg, and 0.49 (95%CI.0.3-0.78, $p<0.01$) for weight gain over 12 kg.

Conclusion: Our study clearly confirms the detrimental effect of a low prepregnancy body mass index, low maternal weight gain and maternal smoking during pregnancy on the incidence of SGA infants.

Key Words small for gestational age (SGA), maternal weight gain, prepregnancy body mass index (BMI)

Introduction

Birth weight in infants is an important predictor not only of perinatal health, but also of growth, development and well-being in adult life.[1] Reduced size at birth, which includes low birth weight (LBW: birth weight less than 2500 g) and small for gestational age (SGA: the lowest 10th percentile for gestational age) infants are at greater risk than infants of normal birth weight, of having reduced educational capacity, school performance and intellectual development.[2]

Some adult health risks show a clear negative correlation with infant birth weight. The fetal origins hypothesis that low birth weight may be associated with an increased risk of subsequent development of a variety of complications in adulthood including cardiovascular disease, non-insulin dependent diabetes mellitus, hypertension and dyslipidemia.[1,3-4] In addition, a recent study reported that SGA was associated with adult psychological disorders as well. Wiles et al. reported that children born full term but weighing less than 5.5 lb had increased psychological distress in later life, and that 1 SD decrease in birth weight for gestational age was associated with increased psychological distress in adulthood.[5]

The Maternal and Child Health Statistics of Japan survey revealed that the average birth weight has gradually declined since 1985. Mean birth weights were 3.2 for boys and 3.12 kg for girls in 1985, and these declined to 3.07 and 2.99 kg, respectively in 2004, although there was no difference of average gestational age between those years.[6] It is important to identify the SGA risk factors that may reduce the incidence of infant mortality and morbidity, and

finally reduce the risk of diseases in later adulthood. The purpose of this study was to determine the risk factors for SGA infants at full term in Japan.

Materials and Methods

Subjects

The study was conducted at the obstetrics and gynecology divisions of four hospitals and clinics located in different administrative wards of the Tokyo metropolitan area. However the number of delivery per year of each hospitals and clinics was different, the average maternal age, parity, incidence of cesarean section for subjects, was similar. Therefore, we combined the data to analyze the risk factors for SGA. It is a retrospective study; undertake using data from 2972 Japanese mothers and their infants born at 37 to 41 weeks of gestation from singleton pregnancies at any time during the years 2002 and 2003. Exclusion criteria were as follows: stillbirth, fetal malformations, gestational or pregestational diabetes and pregnancy induced hypertension.

Anthropometric Measurements and Data Collection

Gestational age was estimated from the last menstrual period (LMP) and confirmed by ultrasound examination mainly at 8-11 gestational weeks. SGA was defined as the lowest 10th percentile for gestational age at birth in the population standard for gestational age, sex and parity according to the reference developed by Nishida et al,[7] which had commonly been used

as birth size standards for Japanese neonates.

Maternal prepregnancy weight was self reported. BMI was calculated as prepregnancy body weight divided by the square of height (kg/m^2). Subjects were classified according to the prepregnancy BMI into underweight (BMI<18.0), normal (18.0<BMI ≦ 24.0), and obese (BMI>24.0) groups, according to the standards set by the Japan Society of Obstetrics and Gynecology (JSOG). The WHO expert group has proposed that the range of normal BMI for Asian populations should be narrowed, because the WHO guidelines for BMI criteria (underweight<18.5, normal 18.5-25.0, and obese>25.0) are based on data from Western countries, and many Asian countries have a lower prevalence of obesity, yet have high rates of obesity-related diseases.[8] We used the BMI criteria formulated by the JSOG because the normal range specified by the JSOG is narrower than that of the WHO.

Other demographic data including age, parity and medical history were obtained from prenatal records. After delivery, the newborn anthoropometric characteristics and recorded; birth weight, length, head and chest circumference were measured. Total maternal weight gain was defined as the difference between measured weight at the last prenatal visit closest to delivery and self-reported prepregnancy weight. In the present study, the 25^{th}, 50^{th}, 75^{th} and 90^{th} percentiles for maternal weight gain are 7.4, 9.5, 11.7 and 14.0 kg, respectively. To examine the influence of increased maternal weight gain on birth weight or incidence of SGA, we stratified weight gain into four categories based on these percentile values; less than 8.0, 8.0-10.0, 10.1-12.0 and over 12.0 kg. Smokers were defined as women who had smoked

cigarettes during pregnancy, regardless of smoking status before conception, and three categories were used: nonsmokers, moderate smokers (9 cigarettes per day or less) or heavy smokers (10 or more cigarettes per day). The maternal and neonatal information collected comprised of maternal demographic characteristics: medical and obstetrics histories; and antepartum, intrapartum, postpartum, and neonatal outcomes.

Statistical Analysis

Statistical analyses were undertaken to identify independent predictors of birth weight (as a continuous variable), and risk factors for SGA. Differences in proportion of categorical variables were compared using χ^2. Differences in continuous variables were determined by independent t-test or by the Mann-Whitney-Wilcoxon test for non-normally distributed data, or ANOVA. Multiple logistic regression analyses were performed to identify the risk factors for SGA. The dependent variable was SGA. Logistic regression was used in the multivariable analysis, the measure of effect being the odds ratio (OR) with its 95% confidence interval (CI) and adjusted for two potential cofounders: maternal height and gestational weeks. Differences were considered significant at $p<0.05$. Statistical analysis was carried out with SPSS for Windows, version 12.0 (SPSS Inc, Chicago, Ⅲ,USA).

Ethical considerations

This study was approved by the ethical committees at the University of Tokyo.