Int J Clin Exp Med 2014;7(12):5784-5789
www.ijcem.com /ISSN:1940-5901/IJCEM0002579

Original Article

Associations of the pre-pregnancy BMI and gestational BMI gain with pregnancy outcomes in Chinese women with gestational diabetes mellitus

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Received September 17, 2014; Accepted November 24, 2014; Epub December 15, 2014; Published December 30, 2014

Abstract: Background: Pre-pregnancy body mass index (BMI) and weight change in women with gestational diabetes mellitus (GDM) during pregnancy likely have an effect on pregnancy outcome. However, limited clinical evidence is available to support the correlation. Aims: To investigate the relationship of pre-pregnancy BMI and gestational BMI gains and their effect on pregnancy outcome among Chinese women with GDM. Materials and Methods: Data were collected from 1418 pregnant patients with GDM who received antenatal care and performed delivery in our hospital. Patients were categorized into groups based on pre-pregnancy and gestational BMI in order to evaluate the risk of pregnancy complications. After being diagnosed with GDM during pregnancy, every subject received advice on lifestyle modification and learned how to self-monitor glucose and administer insulin if needed. Results: LBW is likely to occur in underweight women with low pre-pregnancy BMI (ORs 2.96, $P < 0.01$). Obese women are more vulnerable to hypertension, macrosomia and preterm labor (ORs are 5.92, 2.92, 1.79 respectively; $P < 0.05$). Similar result is observed in overweight women (ORs are 2.72, 1.64, 1.45 respectively; $P < 0.05$). The prevalence of LBW was higher in gestational BMI gain of < 4 team and the teams of BMI gain > 6 were vulnerable to macrosomia. Conclusion: An appropriate maternal pre-pregnancy BMI (18.5-24) followed by adequate gestational BMI gain (4~6) could reduce the risk of the maternal and infant complications.

Keywords: Gestational diabetes mellitus, body mass index (BMI), pregnancy outcomes, pre-pregnancy weight, gestational weight gain (GWG)

Introduction

With the improvement of prenatal and peripartum care, pre-pregnancy BMI and weight change in women with GDM during pregnancy are gradually gaining attention. GDM is a common metabolic complication during pregnancy that may resolve in twelve weeks postpartum [1-3]. Women with GDM, if not intervened, are at higher risk for adverse maternal and neonatal outcomes when compared with the people with no history of diabetes [4, 5]. However, nutritional and insulin treatment can significantly reduce the risk. In recent years, we find that in addition to the high risk conferred by GDM, excessive gestational weight gain (GWG) and obesity in pre-pregnancy have further adverse risks [7-10], including preeclampsia, eclampsia, cesarean delivery, macrosomia, etc [6]. GWG prevalence is now higher than ever before because of increasing living standards, with approximately 40% of pregnant women gaining more weight than is recommended [6]. So limiting GWG in GDM women, especially in overweight and obese pre-pregnancy women has been associated with improved pregnancy outcomes [10, 12, 13]. Several measures for maternal optimal weight gain have been proposed. The Institute of Medicine (IOM) in the United States revised the guidelines again in 2009 which recommended an optimal weight gain range for women based on their pre-pregnant BMI, upon which excessive weight gain during pregnancy could be defined [11].

Materials and methods

We retrospectively reviewed the medical records of all recruited subjects, who were diagnosed with GDM and subsequently received

Table 1. Characteristics of the study population

In total N=1418 (%)	Underweight 108 (7.6)	Normal 769 (54.2)	Overweight 363 (25.6)	Obese 178 (12.6)	*P* value
Age (y, mean ± SD)	29.22±3.85	30.96±4.94	31.70±4.83	31.12±4.97	< 0.01
Age (y, n, %)					
≤ 25	16 (14.8)	99 (12.9)	36 (9.9)	19 (10.7)	/
26~30	54 (50.0)	297 (38.6)	136 (37.5)	67 (37.6)	/
31~35	31 (28.7)	225 (29.3)	105 (28.9)	54 (30.3)	/
> 35	7 (6.5)	148 (19.2)	86 (23.7)	38 (21.4)	
Height (cm)	161.5±5.06	160.0±5.06	160.4±5.12	160.1±6.81	0.084
gestational age of OGTT (week)	24.45±7.5	26.66±3.92	26.04±4.50	25.51±5.14	< 0.01
OGTT (mmol/L)					
0 h	5.61±2.12	5.44±1.45	5.97±1.61	6.23±1.65	< 0.01
1 h	10.91±1.69	11.44±2.40	12.08±2.51	12.69±6.22	< 0.01
2 h	9.14±3.16	9.97±3.12	10.34±2.89	10.57±2.67	< 0.01
birth weight (g)	3229±504	3333±524	3424±556	3511±641	< 0.01
GWG (kg, mean ± SD)	13.88±6.06	13.89±7.48	11.49±5.21	9.59±7.27	< 0.01
GWG (n, %)					
< 8	14 (12.96)	82 (10.7)	82 (22.6)	60 (33.7)	/
8~16	60 (55.6)	474 (61.6)	219 (60.3)	96 (53.9)	/
> 16	34 (31.5)	214 (27.8)	61 (16.8)	22 (12.4)	/
LBW (n, %)	13 (12.0)	34 (4.4)	20 (5.5)	9 (5.1)	< 0.05
Macrosomia (n, %)	7 (6.5)	80 (10.4)	58 (16)	45 (25.3)	< 0.01
Preterm labor(n, %)	9 (8.0)	70 (9.1)	47 (12.9)	27 (15.2)	< 0.05
Gestational hypertension (n, %)	3 (2.8)	17 (2.2)	21 (5.8)	21 (11.8)	< 0.01

GWG: gestational weight gain; OGTT: oral glucose tolerance test; LBW: low birth weight; $P < 0.05$ indicates a significant difference by chi-squared test or Fisher's exact test.

prenatal care and successfully delivered their baby in the First People's Hospital of Shanghai from January 2010 to December 2012. The number of ethical approval document is 20-14KY099.0 wing to the nature of retrospective study, informed consent was not obtained. Women with the following conditions were excluded in our study: autoimmune disease, heart disease, chronic hypertension, bleeding disorder, endocrine disease and other complications; women with the history of smoking or drinking; women without insulin treatment or diet modification during pregnancy. Women with missing information on height, weight before pregnancy, intrapartum weight and the time of delivery were also excluded from our sample. Every subject received advice on lifestyle modification and learned how to self-monitor glucose and administer insulin if needed. Every subject's blood glucose was reviewed on every pre-natal care visit. When blood glucose was beyond the following thresholds on more than three successive days, insulin was suggested: fasting glucose 5.1 mmol/L or a 2 h postprandial glucose 6.8 mmol/L. Demographic characteristics of the pregnant women were collected: pre-pregnancy BMI, age, height, oral glucose tolerance test (OGTT), gestational age of OGTT, GWG, and birth weight. Weight was measured at the last prenatal visit prior to delivery and was used to calculate gestational weight gain and intrapartum BMI (maternal weight in kg/height^2, while pre-pregnancy weight and height reported by each subject were used to calculate pre-pregnancy BMI. Gestational age was estimated from the last menstrual period, and this was confirmed or corrected by ultrasonography during early pregnancy. On the basis of the pre-pregnancy BMI, they were categorized into four groups: underweight (BMI < 18.5), normal-weight (18.5 ≤ BMI < 24), overweight (24 ≤ BMI < 28) and obesity (BMI ≥ 28). These categories were based on the definition of prevention and control guidelines of overweight and obesity among Chinese adults. In every group, according to the BMI increased during

Table 2. Unadjusted odds ratio (OR) of pregnancy complications by pre-pregnancy body mass index (BMI)

Pregnancy outcomes	In total N=1418						
	underweight OR (95% CI)	*P* value	Normal OR (95% CI)	overweight OR (95% CI)	*P* value	obese OR (95% CI)	*P* value
LBW	2.958 (1.51~5.8)	0.001	1.0	1.261 (0.72~2.22)	0.423	1.151 (0.54~2.44)	0.714
Macrosomia	0.597 (0.27~1.33)	0.202	1.0	1.637 (1.14~2.36)	0.007	2.915 (1.93~4.39)	< 0.00001
Preterm labor	0.908 (0.44~1.88)	0.794	1.0	1.486 (1.00~2.20)	0.047	1.786 (1.11~2.88)	0.016
gestational hypertension	1.264 (0.36~4.39)	0.7121	1.0	2.717 (1.41~5.21)	0.002	5.917 (3.05~11.49)	< 0.00001

LBW: low birth weight; $P < 0.05$ indicates a significant difference by chi-squared test or Fisher's exact test.

Table 3. Unadjusted odds ratio (OR) of pregnancy outcomes by gestational BMI gain (ΔBMI) according to different categories of the body mass index (BMI)

In total N=1418		Pregnancy outcomes							
		LBW OR (95% CI)	P	Macrosomia OR (95% CI)	P	Preterm labor OR (95% CI)	P	gestational hypertension OR (95% CI)	P
I	<4 (n=25)	1.12 (0.24~5.12)	0.89	3.91 (0.34~45.5)	0.24	1.96 (0.36~10.5)	0.43	0	0.65[a]
	4~6 (n=46)	1.0	/	1.0	/	1.0	/	1.0	/
	> 6 (n=37)	1.28 (0.34~4.81)	0.71	5.46 (0.58~5.0)	0.10	1.26 (0.24~6.67)	0.78	2.57 (0.22~29.4)	0.43
II	< 4 (n=201)	2.46 (1.08~5.59)	0.03	0.21 (0.08~0.55)	0.005	1.57 (0.87~2.84)	0.13	1.26 (0.33~4.75)	0.73
	4~6 (n=314)	1.0	/	1.0	/	1.0	/	1.0	/
	> 6 (n=254)	1.12 (0.45~2.80)	0.81	1.59 (0.98~2.59)	0.06	1.05 (0.57~1.92)	0.89	2.02 (0.65~6.25)	0.22
III	< 4 (n=170)	4.32 (0.95~19.7)	0.04	0.84 (0.43~1.61)	0.59	1.08 (0.53~2.21)	0.83	2.60 (0.71~9.53)	0.14
	4~6 (n=115)	1.0	/	1.0	/	1.0	/	1.0	/
	> 6 (n=78)	4.72 (0.93~23.81)	0.04	1.20 (0.57~2.54)	0.63	1.18 (0.51~2.76)	0.70	3.68 (0.92~14.7)	0.05
IV	< 4 (n=93)	1.17 (0.28~4.89)	0.83	0.50 (0.22~1.13)	0.09	1.50 (0.58~3. 89)	0.40	0.62 (0.22~1. 71)	0.35
	4~6 (n=54)	1.0	/	1.0	/	1.0	/	1.0	/
	> 6 (n=31)	0	0.30[a]	2.44 (0.97~6.14)	0.06	0.72 (0.17~3.01)	0.65	0.85 (0.23~3.10)	0.81

LBW: low birth weight; CI: confidence interval; [a]: Fisher's exact test; $P < 0.05$ indicates a significant difference by chi-squared test or Fisher's exact test.

pregnancy (ΔBMI), women were categorized as low (ΔBMI < 4), medium (4 ≤ ΔBMI ≤ 6), high (ΔBMI > 6). We analyzed the effects of pre-pregnancy BMI and gestational BMI gains on perinatal outcomes in women with GDM, and these were analyzed on the basis of above-mentioned maternal and neonatal complications. The following complications were noted: gestational hypertension, preterm delivery (gestational weeks < 37 weeks), a low birth weight (LBW, birth weight < 2500 g), macrosomia (birth weight > 4000 g). Gestational hypertension diagnosis is based on blood pressure (BP) ≥ 140/90 mmHg on at least two occasions more than 6 hours apart in women. GDM is diagnosed using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, if met one of the three categories: a fasting blood glucose of ≥ 5.1 mmol/L, plasma glucose levels at 60 min of ≥ 10.0 mmol/L or at 120 min of ≥ 8.5 mmol/L following a 75 g oral glucose tolerance test (OGTT) during 24-28 weeks gestation [14, 15].

Statistical analysis

We used SPSS 21.0 Version (IBM, Chicago, IL) for all statistical analyses. Demographic data are presented as the mean ± SD by analysis of the variance (ANOVA). Differences in proportions of categorical variables were compared using Fisher's exact test or the chi-square test. We estimated the odds ratios (ORs) for the above-mentioned complications. Medium BMI gain (4 ≤ ΔBMI ≤ 6) and normal weight BMI (18.5 ≤ BMI < 24) were used as reference groups. *P*-values less than 0.05 represents significant difference and ORs are presented with the 95% confidence intervals (CIs).

Results

A total of 1418 cases were enrolled in our study. In the whole cohort, 108 subjects (7.6%) were underweight (BMI < 18.5) as group I,769 (54.2%) were normal (18.5 ≤ BMI < 24) as group II, 363 (25.6%) were overweight (24 ≤ BMI < 28) as group III, and 178 (12.6%) were obese

(BMI ≥ 28) as group IV. We divided each group further into three small sub-groups depending on the BMI gain during pregnancy (< 4, 4~6, > 6). **Table 1** outlines the clinical characteristics for these women. Significantly, overweight and obese women were older than those in the normal weight and underweight women (29.22 ±3.85, 30.96±4.94, 31.70±4.83, 31.12±4.97 years, respectively, P < 0.01). The mean gestational age of OGTT and the mean infant birth weight were in normal range. The mean weight gain from conception until delivery in the whole cohort was 13.88±6.06 kg for underweight, 13.89±7.48 kg for normal, 11.49±5.21 kg for overweight, 9.59±7.27 kg for obese women respectively. We further analyzed the effects of pre-pregnant BMI and BMI gain during pregnancy on pregnancy outcomes in the whole cohort.

In **Table 2**, it can be observed that a higher pre-pregnancy BMI increased the risk of macrosomia, preterm labor, gestational hypertension. Relatively, a lower pre-pregnancy BMI increased the risk of LBW infant. According to the pre-pregnancy BMI, LBW is more likely to occur in underweight women compared to others (ORs 2.96, P < 0.01). Obese women are more at risk for hypertension, macrosomia and preterm labor (ORs are 5.92, 2.92, 1.79 respectively); the differences are all statistically significant P < 0.05. The above-mentioned complications also occur in overweight women frequently (ORs are 2.72, 1.64, 1.45 respectively), the difference is significant (P < 0.05).

Table 3 shows pregnancy outcomes according to the gestational BMI gain in different categories. In group II and III, the prevalence of LBW was higher in BMI gain < 4 subgroup (ORs 2.46 and 4.32 respectively), and the difference was significant (P < 0.05). Macrosomia, on other hand, tends to be higher with women's BMI gain in group II, III and IV, and the subgroup of BMI gain > 6 were more vulnerable to macrosomia. The rates of preterm labor and gestational hypertension, however, were no longer significantly different in the BMI gain in different subgroups.

Discussion

As is known to all, maternal hormone secretion increases significantly during pregnancy, and these hormones are antagonistic to insulin in peripheral tissue. The insulin is relatively insufficient, and it makes normal pregnancy women be women with GDM. During the last decade, the population of women with GDM has been growing at an alarming rate. Diet modification is the primary choice of treatment for GDM, with insulin therapy when diet modification fails. As living standards have been rising quickly in recent years, the number of overweight and obese women has increased dramatically. Simas et al. [16] found that a third of pregnant women are about overweight or obese. Since obesity and GDM can lead to adverse pregnancy outcome, blood glucose monitoring and weight control for women with GDM during pregnancy are crucial to reduce maternal and infant mortality and complications.

It is very important to have an appropriate weight gain during pregnancy. The recommendation from IOM showed that optimal weight gain in pregnancy is 12.5-18 kg for underweight women (pre-pregnant BMI < 18.5), 11.5-16 kg for normal women (18.5 ≤ pre-pregnant BMI ≤ 24.9), 7-11.5 kg for overweight women (25 ≤ pre-pregnant BMI ≤ 29.9), and 5-9 kg for obese women (pre-pregnant BMI ≥ 30) [12]. However, there is no recommendation for GDM women's weight gain during pregnancy in the world. Due to the varying heights of women, BMI is more individualized than weight monitoring. So our study used BMI as the observational index of pregnancy complications.

In our study, we found that women with a pre-pregnancy BMI of < 18.5 showed less likelihood for pregnancy complications than women with pre-pregnancy BMI of > 24. Wataba et al. [17] also found that Japanese women with a pre-pregnancy BMI ranging from 18 to 23.9 had the least pregnancy related complications. But underweight women have a higher risk of low birth weight infants, thus increasing the rate of infant hospitalization [18].

Overweight and obese women seem more likely to give birth to a macrosomia than women with normal weight. Larsen et al. [19] showed that the frequency of macrosomia increases with a high BMI. The risk of macrosomia depends not only on the BMI before pregnancy [20] but also on weight gain during pregnancy [21]. Ducarne et al. [22] found that the birth weight of infants was influenced by the maternal BMI, and a greater number of children who were macrosomic have obese mothers. Besides, a study by

Kabali and Werler [23] proved that the risk of macrosomia was much higher for women who were overweight and obese before pregnancy and for those who gained excessive weight during pregnancy.

In fact, the rate of hypertension was very significant in overweight and obese women. In our study, overweight and obese women in pre-pregnancy significantly increased the probability of gestational hypertension, there was a significant difference as shown by our data. Some reports have shown that gestational hypertension is associated with an increased pre-pregnancy BMI and high GWG [11, 24, 25].

Our study found that preterm labor is also associated with pre-pregnancy BMI. The incidence of preterm labor was much higher in overweight and obese women.

In conclusion, our study shows that pregnancy complications in women with GDM increase with pre-pregnancy BMI and antepartum BMI gains. An appropriate maternal BMI (18.5-24) at conception followed by appropriate gestational BMI gain (4~6), however, could reduce the risk of maternal and infant complications. Therefore, we suggest that obstetrician should pay attention to GDM women's BMI gain during pregnancy after blood glucose is within the normal range. If their blood glucose or BMI is beyond normal range, we should adjust the treatment accordingly.

Acknowledgements

This study was supported by the Department of Obstetrics and Gynecology, First People's Hospital of Shanghai.

Disclosure of conflict of interest

None.

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