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Original Research

Influence of pre-pregnancy body mass index and gestational weight gain in twin pregnancies on blood glucose, serum lipid and perinatal outcomes

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Summary

Objective: To explore the influence of pre-pregnancy body mass index (pBMI) and gestational weight gain (GWG) on maternal outcomes in twin pregnancies. *Methods*: Clinical data of women with twin pregnancies delivered in Women's Hospital School of Medicine Zhejiang University from January 2014 to December 2014 were collected and retrospectively analyzed. The women were classified into three groups according to pre-pregnancy body mass index based on WHO guidelines, and gestational weight gain based on the Institute of Medicine (IOM) classification. The characteristics, blood glucose, serum lipid and obstetrical outcomes were compared among the groups of women. *Results*: Three hundred and twelve eligible women with twin pregnancies were identified. Fifty-nine of the women were underweight, 226 had a normal weight, and 27 were overweight or obese. Fasting blood glucose, OGTT-1H, glycosylated hemoglobin, triglycerides in second and third trimester in overweight or obese group were significantly higher when compared with the normal weight group. Overweight or obese increased the risk of hypertension (OR2.86; 95% CI, 1.15-7.13) and intrahepatic cholestasis (OR, 4.01; 95% CI, 1.51-10.84) compared with normal weight. GWG among women with twin pregnancies was low (n = 125), moderate (n = 143) or high (n = 43) based on pBMI. High GWG increased the risk of preterm birth (< 32weeks gestation) (OR, 5.49; 95% CI 1.47-20.44) while low GWG increased the risk of low birth weight (< 2500 g) (OR, 1.95; 95% CI, 1.20-3.19).Multivariate linear analysis showed gestational weeks, GWG and gestational hypertension had effects on birth weight ($P < 0.05$). *Conclusion*: Pre-pregnancy overweight or obese in women with twin pregnancies adversely influence glucose levels, serum lipid concentrations and perinatal outcomes. Preterm and birth weight are adversely influenced by excessive or insufficient GWG.

Key words: Pre-pregnancy body mass index; Gestational weight gain; Twin pregnancies; Blood glucose; Serum lipid; Birth weight; Preterm birth.

Introduction

The prevalence of obesity has risen dramatically in recent years, not only in developed countries, but also in developing countries especially China. This increase in prevalence of obesity has been linked to a change in lifestyle. Obesity in women of reproductive age is a significant health concern, contributing to increased risks of adverse pregnancy outcomes. With the development and increasing utilization of assisted reproductive technology (ART), the rate of multiple pregnancies has increased over time. Compared with singleton gestation, twin pregnancies are associated with greater risks of perinatal complications and adverse pregnancy outcomes. Therefore, weight management of women with twin pregnancies is crucial for obstetricians, particularly in women with abnormal pre-pregnancy weight. Based on pre-pregnancy body mass index (pBMI), the Institute of Medicine (IOM) [1] recommended an optimal range of gestational weight gain (GWG) in 2009. GWG has been suggested to be associated with pregnancy outcomes. While excessive GWG increases the rate of pregnancy complications and often results in long-term chronic metabolic diseases in offspring, insufficient GWG has been shown to increase the rate of preterm birth.

During pregnancy, metabolism and body composition of women change in order to accommodate fetal nutritional demands. Pregnant women in China are more likely to consume a high calorie diet and less likely to engage in physical activity due to traditional customs. Therefore, weight management during pregnancy may be a challenge.

The aim of this study was to assess the impact of pBMI and GWG during twin pregnancies on blood glucose, serum lipids and pregnancy outcomes, in order to highlight the importance of weight management during pregnancy for Chinese women with twin pregnancies.

Materials and Methods

Study population

Three hundred and twelve women with twin pregnancies and two live births at the Women's hospital school of Medicine Zhejiang University China between January

Table 1. — *Maternal characteristics by pBMI (underweight, normal and overweight or obese) in twin pregnancies*

	Underweight (n = 59)	Normal weight (n = 226)	Overweight (n = 27)	*P* value
Maternal age (yrs)	29.04 ± 3.05	30.50 ± 4.05	32.00 ± 3.40	0.013
Maternal age ≥ 35yrs[a]	3 (5.08)	34 (15.04)	5 (18.52)	> 0.05
Nulliparous[a]	47 (79.7)	173 (76.6)	21 (77.8)	> 0.05
ART[a]	21 (35.6)	86 (38.1)	11 (40.7)	> 0.05
GWG	17.06 ± 4.40	17.70 ± 5.05	15.56 ± 5.30	> 0.05
Low GWG[a]	20 (33.9)	95 (40.0)	10 (30.0)	> 0.05
Moderate GWG[a]	30 (50.9)	101 (44.7)	12 (44.4)	> 0.05
High GWG[a]	9 (15.3)	30 (13.3)	5 (18.5)	> 0.05
Pregnancy week (wks)	35.28 ± 1.84	35.64 ± 1.99	35.04 ± 1.97	> 0.05

[a]: reported as N (%)

Table 2. — *Obstetric outcomes and birth weight by pBMI*

	Underweight (n = 59)	Normal weight (n = 226)	Overweight (n = 27)	Underweightvs. Normal weight OR (95%CI)	*P*	Overweightvs. Normal weight OR(95%CI)	*P*
GDM	10(16.9%)	51(22.6%)	10(37.0%)	0.70(0.33,1.48)	> 0.05	2.02(0.87,4.68)	> 0.05
FBG (mmol/L)*	4.37 ± 0.33	4.49 ± 0.45	4.68 ± 0.52	-	-	-	-
OGTT-1H (mmol/L)*	7.82 ± 1.55	8.27 ± 1.55	9.11 ± 1.67	-	-	-	-
OGTT-2H (mmol/L)	6..75 ± 1.45	6.89 ± 1.33	7.28 ± 2.02	-	-	-	-
HbA1c (%)*	4.82 ± 0.34	4.92 ± 0.33	5.06 ± 0.57	-	-	-	-
≥ 2abnormalvalues in OGTT*	2(3.4%)	15(6.6%)	5(18.5%)	-	-	-	-
Gestational hypertension	6(10.2%)	29(12.8%)	8(29.6%)	0.77(0.30,1.95)	> 0.05	2.86(1.15,7.13)	0.041
ICP	8(13.6%)	18(8.0%)	7(25.9%)	1.81(0.75,4.40)	> 0.05	4.04(1.51,10.84)	0.009
Preterm birth < 32w	4(6.8%)	9(4.0%)	1(3.7%)	1.75(0.52,5.91)	> 0.05	0.93(0.11,7.62)	> 0.05
Preterm birth < 35w	16(27.1%)	52(23.0%)	5(18.5%)	1.25(0.65,2.39)	> 0.05	0.76(0.27,2.11)	> 0.05
Mode of delivery by C-section	58(98.3%)	218(96.5%)	25(92.6%)	2.13(0.26,17.36)	> 0.05	0.46(0.09,2.28)	> 0.05
Mean weight of twins	2.34 ± 0.36	2.40 ± 0.43	2.44 ± 0.40	-	-	-	-
weight of twins (2500-3999g)	14(23.7%)	68(29.7%)	11(40.7%)	0.72(0.37,1.40)	> 0.05	1.60(0.71,3.62)	> 0.05
weight of twins (< 2500g)	30(50.9%)	90(39.3%)	10(37.0%)	1.56(0.88,2.78)	> 0.05	0.89(0.39,2.03)	> 0.05
Average weight of the heavier twin	2.46 ± 0.39	2.53 ± 0.46	2.59 ± 0.39	-	-	-	-
Average weight of the lighter-twin	2.22 ± 0.37	2.23 ± 0.43	2.23 ± 0.42	-	-	-	-

*: $P < 0.05$.

2014 and December 2014 were included in this study. Women who delivered before 28 weeks, had major congenital anomalies, pre-existent diabetes or hypertension, incomplete or missing documentation of maternal pregnancy data were excluded.

Study design

This was a retrospective cohort study. Women's height and pre-pregnancy weight were recorded to calculate pBMI. Participants were classified into three according to pBMI based on WHO guidelines: underweight (BMI ≤ 18.5 Kg/m^2), normal weight (BMI 18.5–24.9 Kg/m^2), overweight or obese (BMI ≥ 25 Kg/m^2).

According to the Institute of Medicine (IOM) guidelines, adequate GWG for twin pregnancy in normal, overweight and obese women were 17-25, 13-23 and 11-19 kg respectively. We calculated the range of weekly weight gain (netGWG) by dividing total weight gain by gestational weeks. The ranges of netGWG were 0.45-0.64 kg/week for women with normal pBMI, 0.38-0.61 kg/week for overweight women and 0.31-0.64 kg/week for obese women. Due to a lack of recommendation by IOM for underweight women with twin pregnancies, singleton pregnancy standard measurement of 0.43-0.60 kg/week was selected in this study. Pregnant women in all pBMI groups were classified into low GWG (netGWG less than the lower cutoffs), moderate GWG (netGWG within the normal range) or high GWG (netGWG greater than the upper cutoffs).

We collected information including maternal age, delivery method, fasting blood glucose and 1 h, 2 h blood glucose after a 75 g oral glucose tolerance test (24-28 week), mid-pregnancy (24-28weeks) and third-trimester (within one week before delivery) serum lipid including total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides (TG), neonatal weight.

Table 3. — *Blood glucose, serum lipids during pregnancy by pBMI*

	Underweight (n = 59)	Normal weight (n = 226)	Overweight (n = 27)	*P*
FBG (mmol/L)	4.37 ± 0.33	4.49 ± 0.45	4.68 ± 0.52	0.008
OGTT-1H (mmol/L)	7.82 ± 1.55	8.27 ± 1.55	9.11 ± 1.67	0.002
OGTT-2H (mmol/L)	6..75 ± 1.45	6.89 ± 1.33	7.28 ± 2.02	> 0.05
HbA1c (%)	4.82 ± 0.34	4.92 ± 0.33	5.06 ± 0.57	0.014
≥ 2 abnormal values in OGTT[a]	2 (3.39)	15 (6.64)	5 (18.52)	0.035
Secondtrimester				
TC (mmol/L)	7.03 ± 1.08	6.79 ± 1.13	6.16 ± 1.10	0.004
TG (mmol/L)	2.48 ± 0.79	2.92 ± 1.10	3.28 ± 1.01	0.002
LDL-C (mmol/L)	4.08 ± 0.96	3.91 ± 1.00	3.43 ± 0.87	0.015
HDL-C (mmol/L)	2.38 ± 0.57	2.28 ± 0.49	2.01 ± 0.48	0.009
Thirdtrimester				
TC (mmol/L)	7.07 ± 1.36	6.93 ± 1.44	6.59 ± 1.13	> 0.05
TG (mmol/L)	3.74 ± 1.11	4.53 ± 1.91	4.51 ± 1.72	0.008
LDL-C (mmol/L)	4.17 ± 1.06	3.78 ± 1.17	3.62 ± 0.84	0.038
HDL-C (mmol/L)	1.86 ± 0.45	1.80 ± 0.65	1.66 ± 0.41	> 0.05

[a]: reported as N (%)

Table 4. — *Obstetric outcomes of three GWG groups*

	Low GWG (n = 125)	Moderate GWG (n = 143)	High GWG (n = 44)	Low vs. Moderate OR (95%CI)	*P*	High vs. Moderate OR (95%CI)	*P*
Gestational hypertension	16 (12.8%)	19 (13.3%)	8 (18.2%)	0.96 (0.47, 1.96)	0.906	1.45 (0.59, 3.59)	0.419
ICP	16 (12.8%)	14 (9.8%)	3 (6.8%)	1.35 (0.63, 2.90)	0.436	0.67 (0.19, 2.46)	0.764
GDM	30 (24.0%)	27 (18.9%)	14 (31.8%)	1.36 (0.76, 2.44)	0.307	2.01 (0.94, 4.28)	0.07
Gestational week	35.46 ± 1.96	35.72 ± 1.79	35.57 ± 2.28				
Mode of delivery by C-section	119 (95.2%)	139 (97.2%)	43 (97.7%)				
Preterm birth < 32w	4 (3.2%)	4 (2.8%)	6 (13.6%)	1.15 (0.28, 4.69)	0.847	5.49 (1.47, 20.44)	0.016*
Preterm birth < 35w	35 (28.0%)	28 (19.6%)	10 (22.7%)	1.60 (0.91, 2.82)	0.105	1.21 (0.53, 2.74)	0.65
Average weight of twins*	2.31 ± 0.41	2.46 ± 0.38	2.43 ± 0.49				
Weight of twins(2500-3999 g)	31 (24.8%)	46 (32.2%)	15 (34.1%)	0.70 (0.41, 1.19)	0.184	1.09 (0.53, 2.23)	0.812
Weight of twins(< 2500 g)	65 (52.0%)	51 (35.7%)	14 (31.8%)	1.95 (1.20, 3.19)	0.007*	0.84 (0.41, 1.73)	0.639
Average weight of the heavier twin	2.41 ± 0.43	2.60 ± 0.41	2.58 ± 0.50				
Average weight of the lighter twin	2.21 ± 0.40	2.48 ± 0.42	2.28 ± 0.50				

*: $P < 0.05$

Statistical analysis

All statistical analyses were performed using SPSS version 17.0 statistical software. We described continuous variables with normal distribution using mean ± standard deviation, categorical variables were reported as count (percentage). Continuous variables were compared using One-way ANOVA and Chi-Square tests were applied to categorical variables. The maternal and neonatal outcomes were reported as odds ratios (OR) with accompanying 95% confidence intervals (CI). Multiple regression analysis was used to evaluate pBMI and GWG in relation to birthweight of twins. Values were considered statistically significant when the $P < 0.05$.

Results

Three hundred and twelve eligible twin pregnancies with complete data were included in this study. 72.4% had a normal pBMI, 18.9% were underweight and 8.7% were overweight or obese. Demographic characteristicsare summarized in Table 1. The baseline characteristics were similar among the pBMI groups except for age, which was older in overweight group.

Frequency of pregnancy outcomes including gestational diabetes, gestational hypertension and intrahepatic cholestasis (ICP) are summarized in Table 2. The proportion of hypertension and ICP was higher in the overweight group compared with underweight or normal weight groups ($P < 0.05$). In addition, there was an increased risk of hypertension and ICP in overweight group compared with normal weight group (OR 2.86; 95% CI 1.15-7.13 and OR 4.01; 95% CI, 1.51-10.84, respectively).

The prevalence of GDM appeared to increase with increasing pBMI (Table 2), so were levels of FBG, OGTT-1H and glycosylated hemoglobin (Tables 2 and 3). Over-

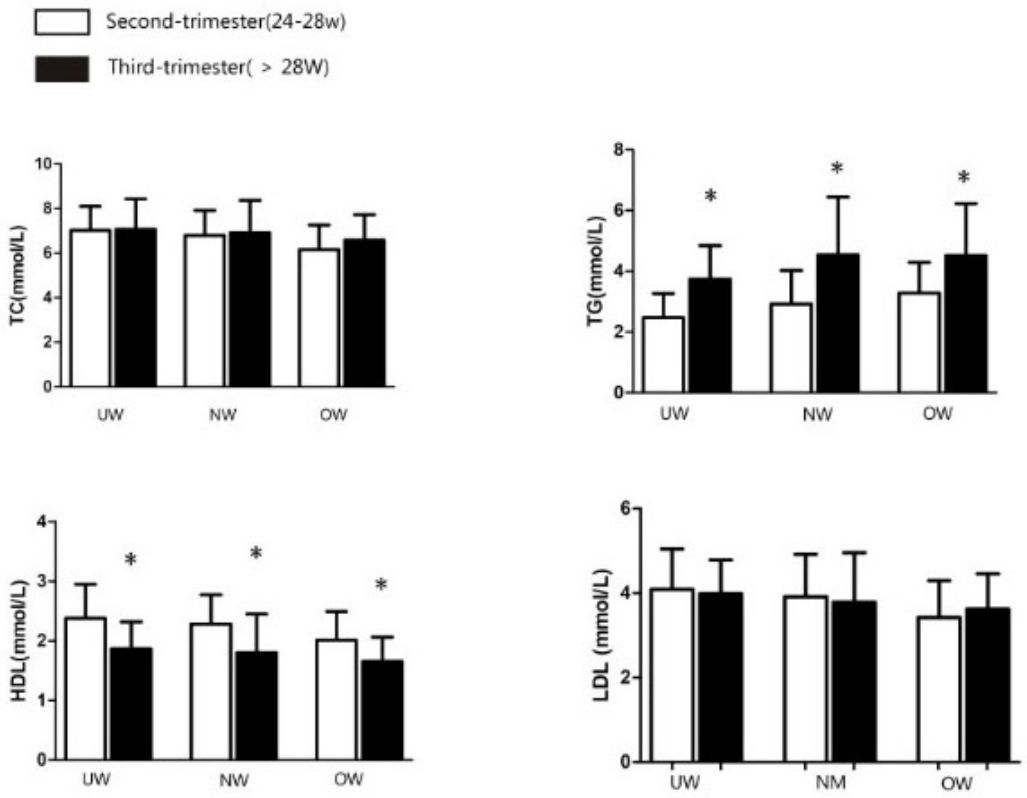

Figure 1. — Mean lipid concentrations during second/third pregnancy trimesters by pre-pregnancy BMI categories. *: $P < 0.05$ (Triglycerides/HDL in third trimester vs second trimester in three groups).

weight or obese increased the odds of two or more abnormal OGTT values when compared with normal weight and underweight group (OR3.20; 95%CI, 1.06-9.64 and OR 6.48; 95%CI, 1.17-35.89, respectively). Overweight women had a higher mean of triglycerides compared to women with normal weight, the difference was statistically significant in both second and third trimesters ($P < 0.01$). Mean total cholesterol, LDL and HDL concentrations were higher in normal weight and underweight than in overweight women, but the difference was significant only in the second trimester of pregnancy ($P < 0.01$).

Triglycerides concentrations were higher in the third trimester compared with the secondtrimester across all pBMI categories. The mean HDL concentrations were significantly lower in the third trimester ($P < 0.05$) (Figure 1).

According to the IOM guideline, 125(40.06%), 143 (45.83%) and 44 (14.10%) women with twin pregnancies were classified as low GWG, moderate GWG and high GWG respectively based on pBMI. There were no significant differences in blood glucose or serum lipid levels across the GWG groups (results not shown).

There were no statistically significant differences in pregnancy outcomes including gestational diabetes, gestational hypertension, ICP and delivery by C-section across all GWG groups. High GWG increased the risk of preterm birth (less than 32 weeks). Insufficient weight gain increased the risk of low birth weight (< 2500 g) in twinscompared with optimalweight gain. In addition, the average weight of twinsin pregnant women with low GWG was lower than the values in pregnant women with moderate GWG ($P < 0.001$).

Multivariate linear and logistic regression analyses showed that gestational weeks, GWG and gestational hypertension had effects on birth weight ($P < 0.05$). For every weekly increase in gestation, birth weight increased by 0.748 grams, and for every one kilogram increase in GWG, birth weight increased by 0.137 grams. A higher probability of low birth weight may occur in women with twin pregnancies with insufficient or adequate weight gain compared with women who gained excessive weight gain during pregnancy (results not shown).

Discussion

For women, pregnancy is a sacred but dangerous thing with hearts full of expectations and joy of the birth of new life, while the fluctuation of various hormones during pregnancy is a major test for maternal body. With the popularization of a two-child policy and assisted reproductive technology in China, the incidence of twins has increased year by year. Women with twins are at higher risk of pregnancy complications compared with singletons. It has been well-known the link between overweight or obesity and ad-

verse pregnancy outcomes thus strict diet control during pregnancy is recommended for this population.

Many studies pointed that the higher BMI before pregnancy, the less weight gain during pregnancy owing to the medical management and physiological mechanisms [2]. The majority of pregnant women included in the current study had adequate GWG. We also observed no significant differences in GWG across the three pBMI groups. This finding is inconsistent with previous studies which suggested that the higher the pBMI, the lesser the GWG [2].

The prevalence of GDM in our study (22.76%) was higher than reported estimates across many countries. Our observation of a higher prevalence of GDM may be related to an increased risk of GDM among Asians which have been reported in existing literature. There are a number of globally acceptable methods of diagnosing GDM. In this study, we chose the standards issued by the Ministry of Health of China, which were based on women with singleton pregnancy. GDM was defined as having one or more abnormal values measured 1h and 2 h after 75 g OGTT. Our findings showed that blood glucose at each time point of OGTT test increased with increasing pBMI, the difference between groups were statistically significant (except OGTT-2H). Previous studies suggested that pre-pregnancy overweight or obesity were independent risk factors for GDM [3]. Our study showed no differences in GDM across pBMI groups. The proportion of two or more abnormal values were significantly elevated in overweight pregnant women in our study, and accounted for 50% of GDM in overweight or obese women. The conclusion suggested it was it may be are asonable approach to adopt a separate set of criteria for GDM diagnosis in women who are overweight or obese pre-pregnancy.

Our finding for the relationship between GWG and GDM is inconsistent with existing literature. We observed no statistically significant difference in blood glucose level and incidence of GDM in women with twin pregnancies across GWG groups. Dong Beibei *et al*. [4] reported that the incidence of GDM was significantly related to excessive GWG in the first trimester, unrelated to GWG in the second trimester regardless of pBMI. In another report, Moore *et al*. [5] observed that excessive GWG in early pregnancy among overweight women was associated with higher odds of abnormal glucose tolerance and GDM among Latinas. A number of factors may have contributed to the inconsistency stated above. The current study is limited by a relatively small sample size. Additionally, GWG was defined as weight gain during the entire pregnancy which may be affected by treatment or diet, especially in the second and third trimester.

It is well known that overweight or obesity increase the risk of several maternal complications during pregnancy. As excepted [6, 7], gestational hypertension occurred more frequently in women with higher pBMI. Compared with women with normal weight, blood pressure in overweight or obese women was higher at the start of pregnancy, followed by a smaller decrease during the second pregnancy and a higher increase at the end of pregnancy [8, 9]. We found that overweight or obese women were more likely to develop gestational hypertension. Overweight or obese and excessive GWG were associated with an increased risk of ICP. Martineau *et al*. [10] reported that ICP is characterized by increased triglycerides and reduced HDL cholesterol levels. Similar changes were observed in overweight or obese women with twin pregnancies. Literature on the association between GWG and gestational hypertension is inconsistent. Some studies [11, 12] reported increased risk of developing hypertension in pregnant women with excessive GWG. In our study, there was no association between high GWG and gestational hypertension or GDM. Our findings are similar to those reported by Fox *et al*. [13], who observed that excessive weight gain does not appear to be associated with adverse maternal complications in twin pregnancies.

Significant maternal metabolic changes occur during pregnancy, to accommodate fetal growth and development. Previous studies suggested that lipid parameters such as TC, TG, HDL, and LDL were elevated during pregnancy, particularly in the second and third trimesters [14]. Hypercholesterolaemia during pregnancy is a normal physiological change, but there are no reference standards for normal levels of lipid parameters. Our study suggests that the concentration of TC and TG in the third trimester were higher than levels in the second trimester. Across pBMI categories, only the change in triglycerides concentration was significant. We observed significantly lower HDL levels in the third trimester than the second trimester. These findings were consistent with the report by Bartels *et al*. [15], who reported that HDL during pregnancy is always elevated with peak values seen in the second trimester. High HDL concentration is required to maintain the lipid at recommended level throughout pregnancy. Previous studies [10] suggested that the combination of elevated TC, TG, LDL and decreased HDL increase the risk of pregnancy complications such as ICP, GDM and gestational hypertension. Pregnant women with different pre-pregnancy weights share the character that TG increase and HDL decrease in the third trimester, suggesting that clinicians should strengthen monitoring on pregnant women with twin pregnancies to avoid the occurrence and aggravation of complications throughout pregnancy especially in the third trimester.

We found that overweight women had higher triglycerides and lower TC, LDL and HDL levels compared with underweight and normal weight women in the second trimester, but in the third trimester, triglycerides levels were higher and LDL levels were lower in overweight compared with under weightwomen. There is inconsistent evidence regarding the relationship between pBMI and lipids during pregnancy. Scifres *et al*. [16] reported that TC and LDL were significantly lower in overweight or obese women compared with normal weight women. Farias *et al*. [17] re-

ported that overweight or obese women had higher triglycerides, total cholesterol and LDL and lower HDL levels during pregnancy compared with normal weight women. These conflicting findings may be related to limited sample sizes and special metabolic regulation of lipid in overweight or obese women. Correlation analysis showed that pBMI was positively correlated with triglycerides, while negatively correlated with TC, LDL-C, and HDL-C (results not shown).

Our finding of no association between pBMI and preterm birth (< 32 w and < 35) is consistent with the findings of Suzuki et al [19], who reported that maternal pBMI based on the IOM cutoffs was not associated with perinatal outcomes in Japanese women with twin pregnancy. Findings in the current study are inconsistent with estimates documented by Al-Obaidly *et al*. [18], who suggested that overweight and obese women with twin pregnancies had a higher risk of preterm delivery compared with normal weight women. Similar findings were noted by Parker et al [20] for medically indicated preterm delivery but not spontaneous preterm delivery. Preterm birth can be divided into medically-induced and spontaneous preterm. Parker [20] reported obesity is only associated with higher risk of medically indicated preterm birth, not spontaneous preterm. Otherwise, the relationship between risk of spontaneous preterm and maternal pBMI may be affected by ethnicity, gestational week and parity [21]. The inconsistent findings in the current study may due to lack of classification of preterm birth into medically indicated and spontaneous preterm births.

Birth weight is an important indicator of fetal growth and development. Insufficient weight gain during pregnancy may indicate nutritional deficiencies. Consistent with previous study [22], we found that birth weight in women with low GWG were significantly lower than those with moderate GWG group, and low GWG was associated with an increased risk of low birth weight. Greenan *et al*. [23] reported that underweight women who achieved weight gain goals may reduce the rate of preterm < 35 w and get greater birth weight. In our study, every 1 kg increase in GWG resulted in 0.137 g increase in birth weight. Therefore, adequate GWG was associated with better perinatal outcomes. The impacts of pBMI on birth weight were different due to race, which was higher in non-Europeans than in Europeans [24]. We found no associations between pBMI and birth weight in women with twin pregnancies. This is consistent with the findings of Farah et al [25]. The results confirmed the role of GWG for fetus birth weight, especially among the women with abnormal BMI before pregnancy.

The current study has several strengths. This is s a relatively comprehensive article of the relationship between various indices during pregnancy, perinatal outcomes and pBMI, GWG in women with twins. Multi-angle and multilayered analysis are used to draw our conclusion.

There are a few caveats that must be noted in the current study. Firstly, we used recommended ranges of GWG for underweight women with singleton due to the deficiency of the current guideline for twin pregnancies. Secondly, we were limited by a small sample size. The small sample size made it impossible to perform analysis stratified by pBMI, particularly in overweight and obese women.

Conclusion

We observed a complex relationship between maternal health status and birth outcomes. Overweight or obesity has adverse influence on glucose levels at each point of OGTT, serum lipid concentration and risk of perinatal outcomes such as gestation hypertension, ICP and very preterm birth in women with twin pregnancies. GWG is correlated with birth weight, therefore, it should be adequately monitored. Excessive weight control must be avoided for the insufficient weight gain which increases the risk of low birth weight. In summary, development of standardized recommendations for GWG throughout pregnancy based on pBMI for women with multiple pregnancies is required, to improve the maternal and fetal outcomes.

Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Women's Hospital, College of Medicine, Zhejiang University (approval number: IRB-20190035-R).

Conflict of Interest

The authors declare no competing interests.

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