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Prepregnancy obesity status and risks on pregnancy outcomes in Shanghai

A prospective cohort study

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Abstract

Obesity in women of reproductive age is not only associated with numerous adverse maternal and fetal effects prenatally but also exerts a negative influence on female fertility. The aim of this study was to investigate the situation of prepregnant obesity in Shanghai and explore the impact of prepregnant obesity on gestational weight gain as well as other pregnancy outcomes. A prospective hospital-based pregnant women cohort was established in Shanghai since January 2015. All pregnant women who were registered and expected to deliver in this hospital were included in the cohort. Nearly one fourth of pregnant women in Shanghai were overweight/obese and the prevalence of overweight/obesity was more common among women with advancing age ($P < .001$). Women prepregnancy overweight/obesity was associated with 3.5-fold higher risk of excessive gestational weight gain (odds ratio, OR 3.58; 95% confidence interval, CI, 2.82–4.55; $P < .001$). Women prepregnancy BMI was statistically related to pregnancy outcomes as macrosomia (OR 2.24; 95% CI, 1.55–3.23; $P < .001$), cesarean delivery (OR 2.04; 95% CI, 1.60–2.62; $P < .001$), maternal complications (OR 1.53; 95% CI, 1.18–1.98; $P < .001$). Prepregnancy obesity is associated with a much higher risk of excessive gestational weight gain and pregnancy outcomes in Shanghai. Further interventions targeting maternal obesity, especially prepregnancy obesity are required.

Abbreviations: BMI = body mass index, CIs = confidence intervals, GDM = gestational diabetes mellitus, GHO = Global Health Observatory, HR = hazard ratio, IM = intestinal microbiota, IOM = Institute of Medicine, LGA = large for gestational age, MD = mean difference, OR = odds ratio.

Keywords: cohort study, gestational weight gain, pregnancy outcomes, prepregnany obesity

1. INTRODUCTION

Obesity has become a global epidemic, affecting more than 650 million adults worldwide.[1] Global health observatory (GHO) data released by WHO in 2017 showed that 67.9% of adult Americans were overweight and 36% obese. In contrast, the prevalence of obesity in China has increased from 0.5% to 6% between 1975 and 2016.[2]

The worldwide increasing trend of obesity has been dramatic, now affecting more than 20% of American women of reproductive age.[3] It was estimated that 50% of childbearing women in the United Kingdom were overweight/obese in 2006.[4] Obesity in women of reproductive age is not only associated with numerous adverse maternal and fetal effects prenatally but also exerts a negative influence on female fertility_EN REF_1.[5] Obese pregnant women are at increased risk of maternal complications. Maternal-related pregnancy complications (diabetes, preeclampsia, and cesarean delivery) and fetal or neonatal complications (preterm birth, large for gestational age [LGA], macrosomia, fetal growth restriction, and stillbirth) are more common in obese pregnant women.[6–10]

Moreover, accumulating evidence indicated that prepregnancy obesity was associated with severe maternal morbidity. Mortality data from California in 2015 suggested that the recent increasing maternal mortality in the United States is related to maternal obesity.[11] A population-based retrospective cohort study over a 10-year period (2004–2013) in Washington State showed that there were statistically significant increases in risk of severe maternal morbidity among women with obesity.[12]

In the past decade, great attention has been paid on obesity. American Medical Association even voted in 2013 to define obesity as a disease. However, effective strategies to prevent obesity pandemic are still in urgent need. Owing to the significant difference in obesity by race, ethnicity and district, specific preventions should be applied according to local conditions. Thus, local prepregnancy obesity status and its risk factors are indispensible to warrant individualized intervention strategies.

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However, little is known about the prepregnancy obesity status in China, while most of the researches on the risks of prepregnancy obesity in China were of retrospective nature or meta-analysis. In this study, we conducted a prospective, hospital-based pregnant women cohort in Shanghai to explore the local obese pregnancy women situation and the association of prepregnancy overweight/obesity with excessive gestational weight gain and other pregnancy outcomes. With our first-hand prospective data, we expect to provide evidence for further targeting interventions to prevent local pregnant obesity.

2. METHODS

2.1. Study population

In Shanghai, all pregnant women are required to register at the hospitals in the twelfth to sixteenth gestational week and then attend to all the pregnant examinations in the registered hospital during the whole pregnant period, until 42 days after the child is born.

We established one hospital-based pregnant women cohort from January 2015 in the department of obstetrics and gynecology, Shanghai Pudong new area healthcare hospital for Women and Children, which is the largest specialized hospital for women and children healthcare in Pudong new area of Shanghai. It boasts more than 3,00,000 outpatients annually, more than 30 percent of whom were pregnant women. The annual number of delivery is about 10,000. All registered pregnant women who hoped to deliver in this hospital were included in the cohort. Pregnant women health records and children health records were collected in detail.

Pregnant women health records start within the first 12 weeks of pregnancy and include general information (age, place of domicile, height, weight, date of first antenatal visit, numbers of pregnancy, numbers of infants, last menstrual period, expected delivery date, and complications during pregnancy), pregnancy outcomes (near delivery weight, gestational weeks of labor, delivery modes, maternal postpartum hemorrhage, and labor complications). Children health records comprise of information from newborns (date of birth, sex, gestational weeks of birth, birth weight, birth recumbent length, Apgar score, and neonatal complications).

We collected 6492 records of pregnant women registered in the hospital between January 2015 and May 2016, 2612 of whom were followed up to delivery and both records of mothers and their new-born babies were collected as mother-child pairs. The major reason for loss of follow-up were delivering elsewhere (mostly returning to their native towns for delivering) and not yet delivered. Women who delivered more than one infant or lack of anthropometric data were excluded. A total of 2292 women met the eligibility criteria and were included in this study. A flow diagram of the study population is presented in Figure 1.

This study uses secondary data obtained from a prospective pregnant women cohort study, evaluating the role of genetic risk factors of pregnant women with venous thromboembolism in China. The present study was approved by the Ethics Committee of Shanghai Institute of Planned Parenthood Research (No. PJ2014–11).

2.2. Data collection

Specially trained gynecologists did all the measurement using same devices. The prepregnancy weight was measured at first antenatal visit. Final pregnancy weight was measured at the last antenatal visit or the time of delivery. Weight and height were measured in light clothing without shoes using a beam balance scale (RGZ-120, Jiangsu Suhong Medical Instruments Co., Changzhou, Jiangsu Province, China). Birth weight was measured to the nearest 0.001 kg using an electronic baby scale (DY-1, Shanghai Guangzheng Medical Equipment Co., Shanghai, China). Baby length was measured to the nearest 0.1 centimeter (cm) using infant radiation radiators (HKN-90, Ningbo David Medical Device Co., Ningbo, Zhejiang Province, China).

Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. Prepregnancy BMI

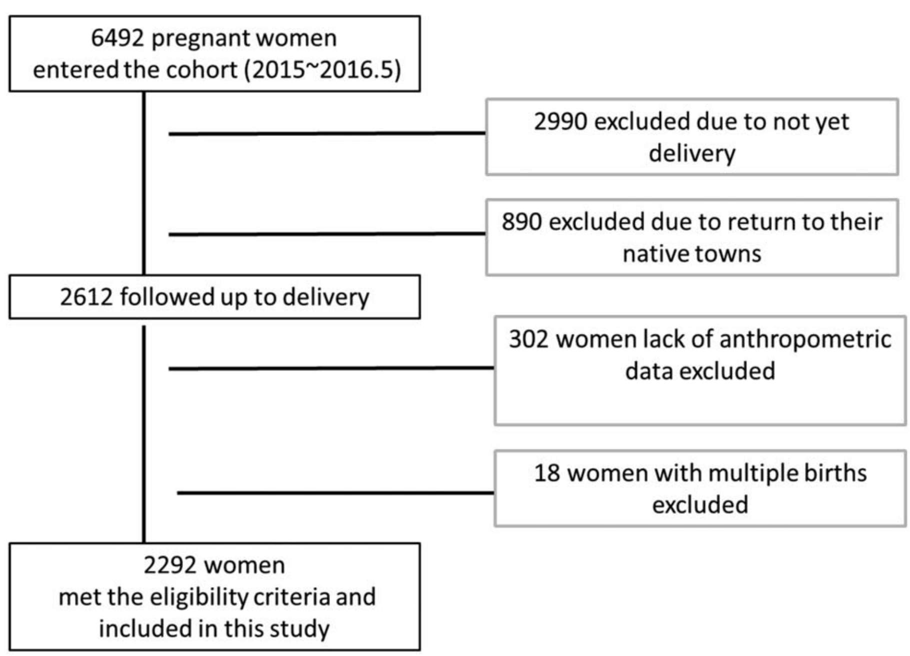

Figure 1. Flow diagram of the study population.

was categorized into 4 groups using the standard of Working Group on Obesity in China: underweight ($BMI < 18.5\,kg/m^2$), normal-weight ($18.5\,kg/m^2 \leq BMI \leq 23.9\,kg/m^2$), overweight ($24\,kg/m^2 \leq BMI \leq 28\,kg/m^2$), and obesity ($BMI > 28\,kg/m^2$).

The gestational weight gain during pregnancy was calculated as the weight difference between first and last antenatal visit. The recommended weight gain in Chinese women by BMI categories were defined as 15.5 to 22 kg (prepregnancy $BMI < 18.5\,kg/m^2$); 13 to 21 kg (prepregnancy $18.5\,kg/m^2 \leq BMI \leq 23.9\,kg/m^2$); 10 to 18 kg (prepregnancy $24\,kg/m^2 \leq BMI \leq 28\,kg/m^2$); and 9.5 to 17 kg (prepregnancy $BMI > 28\,kg/m^2$). The gestational weight gain above the recommendation was defined as excessive gestational weight gain, within the recommendation as adequate gestational weight gain and below the recommendation as inadequate gestational weight gain.

As defined by WHO, birth weight was divided into 3 categories: low birth weight (<2500 g), normal birth weight (2500–3999 g), and macrosomia (birth weight ≥ 4000 g).

2.3. Statistical analysis

Logical checks and data cleaning were carried out by 2 independent researchers and inconsistencies were returned to original chart. All data were double-checked and cleaned. The difference of proportions between different BMI categories was calculated using R by C Table. For continuous outcomes (such as prepregnancy BMI and gestational weight gain), crude mean difference (MD) were reported, along with their 95% confidence interval (CI). Differences (prepregnancy BMI or gestational weight gain) between age at delivery (< 35 years or ≥ 35 years), parity (1 or ≥ 2 times), maternal complications (with or without), and delivery modes (cesarean or vaginal delivery) were tested using the student t test and difference among offspring birth weight (<2500 g, 2500–3999 g, or ≥4000 g) was tested using ANOVA test. Odds ratio (OR) of prepregnancy obesity associated with various risk factors was calculated using binary Logistic regression models. The same regression model was used for excessive gestational weight gain. After univariate analysis, a multivariate Logistic model was fit for all candidate risk factors that were significant at the $\alpha = 0.05$ level. In the prepregnancy BMI regression model, subjects were grouped into 2 categories: prepregnancy BMI overweight/obese and underweight/normal-weight, while in the gestational weight gain regression model, subjects were grouped into excessive gestational weight gain and adequate weight gain.

All statistical analysis was conducted using SPSS 23.0 and statistical significance was defined as a P-value less than .05.

3. RESULTS

Demographics of study subjects at baseline were summarized in Table 1. A total of 2292 pregnant women who were followed up until delivery have been included in our cohort by May 30, 2016. There were 402 overweight woman and 137 obese women among cohort members, with a crude rate of 17.5% for overweight and 6.0% for obesity.

Nearly one fourth of Chinese pregnant women were overweight/obese and 10% of prepregnant women underweight. The prevalence of overweight/obese increased with advancing age ($P < .001$) in Shanghai. Compared with the standards of Working Group on Obesity in China, the gestational weight gain in Shanghai was at the lower range of normal weight gain level across all different prepregnancy BMI categories, with no difference by age (Table 2).

Table 1

Demographics of study subjects at baseline.

	n	%
Total population	2292	
Age at conception, y		
≤34	2012	87.8
>34	280	12.2
Register		
Native	681	29.7
Non-native	1611	70.3
Height, m		
<1.6	742	32.4
1.6–1.69	1418	61. 9
>1.7	131	5.7
Prepregnancy BMI		
Underweight	242	10.6
Normal	1511	65.9
Overweight	402	17.5
Obese	137	6.0
Parity		
0	1263	55.1
1	1029	44.9
Gravidity		
1	3	0.2
2	443	32.2
3	329	23.9
4	175	12.7
≥5	427	31.0
Gestational weeks, w		
<37	148	6.6
37–42	2108	93.4
Gestational weight gain, kg		
Inadequate	582	25.9
Adequate	969	43.3
Excessive	689	30.8

BMI = body mass index.

The results of univariate and multivariate analysis for prepregnancy BMI on pregnancy outcomes were shown in Table 3. Estimates of the MD for individual risk factors indicated that preregnancy BMI was related with age at delivery, parity, maternal complications, delivery mode, excessive gestational weight gain, and macrosomia ($P < .001$). The results of the multivariate model showed that overweight/obesity before pregnancy was associated with 3.5-fold higher risk of excessive gestational weight gain (OR 3.58; 95% CI, 2.82–4.55; $P < .001$), 2-fold higher risk of macrosomia (OR 2.24; 95% CI, 1.55–3.23; $P < .001$), 2-fold higher risk of cesarean delivery (OR 2.04; 95% CI, 1.60–2.62; $P < .001$), and 1.5-fold higher risk of maternal complications (OR 1.53; 95% CI, 1.18–1.98; $P < .001$) comparing with normal-weight/underweight women.

The results of univariate and multivariate analysis of gestational weight gain for the pregnant women cohort were shown in Table 4. As for the univariate analysis, delivery mode and low offspring birth weight were not significantly associated with gestational weight gain ($P > .05$). In the multivariate model, excessive gestational weight gain was closely related to prepregnancy obesity (OR 3.86; 95% CI, 2.54–5.87; $P < .001$) and prepregnancy overweight (OR 3.26; 95% CI, 2.50–4.25; $P < .001$). Compared with maternal adequate weight gain, excessive gestational weight gain was associated with age (OR

Table 2

Prepregnancy obesity and gestational weight gain in Shanghai.

Prepregnancy BMI, kg/m^2				Gestational weight gain, kg	
Parameter		N (2292)	%	Mean	95% CI
Under weight	< 18.5	242	10.56	15.30	14.51, 16.10
Normal weight	18.5–23.9	1511	65.92	13.64	13.41, 13.87
Overweight	24–28	402	17.54	11.96	11.40, 12.52
Obese	>28	137	5.98	10.39	9.56, 11.22
By age					
Age 20–34		2012		13.47	13.25,13.69
Under weight	< 18.5	227	11.28	15.04	14.31,15.78
Normal weight	18.5–23.9	1331	66.15	13.81	13.56,14.06
Overweight	24-28	337	16.75	12.01	11.45,12.58
Obese	>28	117	5.82	10.65	9.84,11.56
Age 35–44		280		12.35	11.62,13.08
Under weight	< 18.5	15	5.36	19.23	12.51,25.95
Normal weight	18.5–23.9	180	64.29	12.38	11.80,12.96
Overweight	24–28	65	23.21	11.68	9.76,13.61
Obese	>28	20	7.14	8.89	6.14,11.65

BMI = body mass index; CI = confidence interval.

.97; 95% CI, .94– .99; $P=.02$), parity (OR .69; 95% CI, .55– .89; $P<.001$) and high risk of macrosomia (OR 1.49; 95% CI, 1.00–2.19; $P=.04$), and cesarean delivery (OR 1.28; 95% CI, 1.01–1.62; $P=.04$) (Table 4).

4. DISCUSSION

Obesity is becoming a worldwide predominant burden and women are assumed to be the predominant burden of our obesogenic environment. Obesity is more common in women than men, especially women at childbearing age, and could cause numerous maternal and fetal complications such as miscarriage, premature labor, stillbirth, and perinatal risks. In our cohort, we found that nearly one fourth of pregnant women in Shanghai were overweight/obese. Owing to the large population of China, the number of Chinese overweight/obesity women of childbearing age might be far beyond our expectation.

According to our data, the risks for prepregnancy overweight/obesity regarding maternal weight gain, macrosomia, and maternal complications were 3.5-fold, 2.24-fold, and 1.5-fold, respectively, higher than pregnant women with normal weight, which was consistent with previous studies.[7,13–15] During our 1.5 years' follow-up, no severe maternal morbidity or fetal stillbirth was observed. Only 594 out of 2292 pregnant women were reported to have maternal complications, mostly Gestational diabetes mellitus (GDM) (152 women). Some studies

Table 3

Impact of prepregnancy BMI on pregnancy outcomes in Shanghai.

	Univariate		Multivariate	
	MD (95% CI)	*P*	Exp (B) (95% CI)	*P*
Age at delivery, y	0.89 (0.51, 1.27)	.00		
<35			1	
≥35			1.02 (0.99, 1.04)	.26
Number of parity	1.06 (0.81, 1.31)	.00		
0			1	
≥1			1.92 (1.50, 2.45)	.00
Maternal complications	−0.85 (−1.16, −0.53)	.00		
Without			1	
With			1.53 (1.18, 1.98)	.00
Delivery	−1.10 (−1.35, −0.85,)	.00		
Vaginal delivery			1	
Cesarean delivery			2.04 (1.60, 2.62)	.00
Gestational weight gain		.00		.00
Inadequate	−0.08 (−0.35, 0.21)	.92	0.661 (0.49, 0.90)	.01
Adequate			1	
Excessive	−1.26 (−1.59, −0.95)	.00	3.58 (2.82, 4.55)	.00
Offspring birth weight, g		.00		.00
<2500	−0.28 (−1.37, 0.75)	.94	1.23 (0.59, 2.59)	.58
2500–3999			1	
≥4000	−1.93 (−2.48, −1.41)	.00	2.24 (1.55, 3.23)	.00

BMI = body mass index; CI = confidence interval; MD = mean difference.
Data is presented in MD by univariate analysis and in OR by multivariate analysis.

Table 4

Impact of gestational weight gain on pregnancy outcomes in Shanghai.

	Univariate		Multivariate	
	MD (95% CI)	P	Exp (B) (95% CI)	P
Age at delivery, y	−1.12 (−1.77, −0.48)	.00		
<35			1	
≥35			0.97 (0.94, 0.99)	.02
Prepregnancy BMI		.00		.00
Underweight	−1.66 (−2.77, −0.55)	.00	0.60 (0.41, 0.87)	.007
Normal			1	
Overweight	1.68 (0.86, 2.50)	.00	3.26 (2.50, 4.25)	.00
Obese	3.25 (2.09, 4.41)	.00	3.86 (2.54, 5.87)	.00
Number of parity	−1.72 (−2.14, −1.30)	.00		
0			1	
≥1			0.70 (0.55, 0.89)	.001
Maternal complications	−0.94 (−1.47, −0.41)	.00		
Without			1	
With			0.79 (0.60, 1.03)	.09
Delivery	−0.18 (− 0.60, 0.25)	.42		
Vaginal delivery			1	
Cesarean delivery			1.28 (1.01, 1.62)	.04
Offspring birth weight, g		.01		.092
<2500	1.25 (−0.83, 3.33)	.37	1.52 (0.65, 3.58)	.34
2500–3999			1	
≥4000	−1.00 (−2.08, 0.78)	.08	1.49 (1.01, 2.19)	.04

BMI=body mass index; CI=confidence interval.
Data is presented in MD by univariate analysis and in OR by multivariate analysis.

indicated that higher prepregnancy BMI plays an important role in the development of GDM.[16,17] Biologically, the metabolic differences between overweight/obese and non-obese women might lead to the potential risks for fetal development and pregnancy outcomes. Children of obese mothers have increased risk of metabolic syndrome (hazard ratio [HR], 1.81; 95% CI, 1.03–3.19) and are more likely to be obese.[18–20]

More and more evidence suggested that prepregnancy obesity may have long-term effects such as obesity, metabolic syndrome and asthma on the offspring.[21–23] However, the molecular mechanism of that maternal obesity might result in an increased risk of childhood obesity and metabolic syndrome remains to be elucidated. A meta-analysis indicated that children with obese mothers during pregnancy were at higher risks of asthma or wheeze.[24] Different dietary patterns or pro-inflammatory states associated with mother obesity may affect fetal immune or pulmonary development, thus leading to asthma. Recently, more and more evidences indicated that offspring overweight/obesity may be a result of intergenerational transmission. Maternal weight, mode of birth delivery and composition of the neonatal intestinal microbiota (IM), which tends to be affected by maternal factors early before the pregnancy, appear to play an increasingly important role.[25] One observational study of 935 infants in a Canadian birth cohort indicated that maternal BMI and cesarean delivery cooperate in shaping the microbial communities of early life, which is associated with the development of overweight /obesity in their offsprings.[26]

Prepregnancy BMI and gestational weight gain were closely related. Pre-pregnant overweight/obese women may be at higher risk of more excessive gestational weight gain than normal weight women. Theoretically, overweight/obese women, with excessive gestational weight gain, could develop more severe maternal and fetal outcomes. It was reported that women with both prepregnancy obesity and excessive gestational weight gain had 2.2 to 5.9 folds higher risks of GDM, pregnancy-induced hypertension, caesarean delivery, LGA, and macrosomia compared with women with normal prepregnancy BMI and adequate gestational weight gain.[27]

Since the close association between prepregnancy obesity and gestational excessive weight gain with increased maternal, pregnancy outcomes, as well as long-term effects such as obesity, metabolic syndrome, and asthma on the offspring has been verified, interventions targeting maternal obesity would enable clinicians to reduce their risks on the offspring and subsequent future generations. To control weight gain during the whole pregnancy was one step. In 1990, the Institute of Medicine (IOM; now known as the National Academy of Medicine) formulated the recommendations for weight gain during pregnancy and updated in 2009. Although guidelines and recommendations on weight gain during pregnancy have been drawn and generalized and some countries even set up domestic guidelines, standard management strategies for pregnant women with obesity, especially prepregnancy obesity have yet been unavailable. Public health preventive interventions such as education promotion are needed to prevent obesity and reduce pregnancy complications.

This study has limitations. We defined maternal obesity according to calculated BMI by height and weight measurement, which can be over-estimated or under-estimated so as to affect the risk estimates. Secondly, we conducted the hospital-based cohort and have up to now, followed up for nearly two years. Short-term follow up data limited us from observation of long-term outcomes and hospital-based data may cause selective bias. In addition, follow-up bias may occur in hospital-based study. Longer follow up and larger pregnancy data resources are required for better analysis. Thirdly, our cohort data was collected from only one hospital, which may cause selective bias and limit the external validity of the results. Multi-centered study is expected to make up above limitations.

In conclusion, we summarized the prevalence of prepregnancy obesity in Shanghai and specifically set up the logistic risk model for the analysis of the impact of prepregnancy overweight/obesity on excessive gestataional weight gain and other pregnancy outcomes and to evaluate the risks associated with prepregnany obesity. Further interventions targeting maternal obesity, especially prepregnancy obesity are required to reduce adverse pregnancy outcomes.

Author contributions

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Software: Jie Shen.
Supervision: Chengfeng Zhang.
Writing – original draft: Jie Shen.
Writing – review & editing: Chengfeng Zhang.

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