Association of pre-pregnant body mass index and gestational weight gain with timing of delivery

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Abstract

Objective. *To evaluate the effect of both pre-pregnant body mass index and gestational weight gain on preterm delivery.* ***Design.*** *Retrospective study using the pregnancy risk Assessment Monitoring System Phase IV data.* ***Setting.*** *Centers for Disease Control and Prevention and 22 state health departments.* ***Sample.*** *Women having delivered a live birth were randomly sampled using stratified systematic sampling.* ***Methods.*** *Women were asked to complete a self administered questionnaire, merged with the respective birth certificate. Those with multiple pregnancies, preterm premature rupture of fetal membranes, and those presenting with several indications for medically induced preterm birth were excluded. A multinomial logistic regression model and the Wald's test were used to estimate and compare adjusted odds ratios associated with risk factors for preterm delivery and potential confounders.* ***Main outcome measure.*** *Gestational age at delivery.* ***Results.*** *The sample included 30,108 women representing a population of 1,495,474. The risk of very preterm birth (<33 WG) was significantly increased when compared to the risk of moderate preterm birth (33-37 WG) in women with either low or excessive weight gain, regardless of body mass index (BMI). Age <18 years, African American origin, Medicaid insurance, no prenatal care, smoking during pregnancy, or a large for gestational age fetus were associated with a significantly increased risk of very preterm birth compared to the risk of moderate preterm birth.* ***Conclusions.*** *Variations and interactions between the rates of pre-pregnant body mass index and weight gain during pregnancy impact preterm delivery. Their effects appear to be interactively related with the risk of preterm delivery and hence should not be studied separately.*

Keywords: *body mass index, weight gain, preterm delivery, pregnancy*

Abbreviations:
BMI = body mass index
SGA = small for gestational age newborn
LGA = large for gestational age newborn
WG = weight gain

Introduction

In 1990, the Institute of Medicine published recommended ranges of maternal weight gain (WG) for singleton term deliveries, by pre-pregnant body mass index (BMI)[1]. Since rate of WG in singleton pregnancies is considered linear from around 20 weeks to term, the WG ranges may be used to assess whether women delivering preterm achieve the target weight gain for any specific gestational age.

In the literature, maternal pre-pregnant BMI and gestational WG have been associated with preterm delivery[2,3]. It has been shown that suboptimal maternal WG is related to an increase in very preterm delivery[4,5], while excessive WG is associated with a higher rate of preterm delivery in African American women[3]. A recent survey concluded that excessive WG, regardless of maternal BMI, could be related to a higher preterm delivery risk, but that this relationship "deserves further investigations"[2].

The aim of the present study is to evaluate the effect of both pre-pregnant BMI and WG during pregnancy on the risk of preterm delivery, using data from a large U.S.A. survey sample.

Methods

The Pregnancy Risk Assessment Monitoring System (PRAMS, Phase IV) data for live births (2000-2001) was used for the analysis. PRAMS is a surveillance project

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implemented by the Centers for Disease Control and Prevention (CDCP) and 22 state health departments[6-8]. In each state, women having recently delivered a live birth were randomly sampled using stratified systematic sampling and asked to complete a self administered questionnaire. All states provided an incentive for participation and over sampled women who were at risk of adverse pregnancy outcomes. The completed surveys were merged with the respective birth certificates. The data was weighted to adjust for survey design, non-coverage, and non-response, and is representative for all state resident women delivering a live birth in the state[6]. Each participant was assigned a sample weight enabling survey sample data to be extrapolated to the entire state population. Stata 9.2 (Stata Corporation, Lakeway Drive, College Station, Texas, USA) was employed for all analyses. The study was approved by the Medical University of South Carolina Institutional Review Board.

Using pre-pregnant weight and height measures, women were assigned to one of four pre-pregnant BMI classifications: underweight (<19.8 kg/m^2), normal weight (19.8-26 kg/m^2), overweight (OW = 26.1-29 kg/m^2) and obese (OB >29 kg/m^2)[1]. For each pre-pregnant BMI category, the expected ideal WG range for term singletons was determined based on the Institute of Medicine 1990 recommendations (12.7-18.1 kg for underweight women, 11.3-15.9 kg for normal weight women, and 6.8-11.3 kg for both overweight and obese women). Women who gained less than the minimum were classified as low WG, those who gained more than the maximum were classified as excessive WG and all others were classified as adequate WG.

Women who delivered preterm were not expected to gain as much weight as those who delivered at term, weight gain categories were therefore calculated for each gestational age to adjust for preterm birth. Since the Institute of Medicine rate of ideal WG differs from the first half to the second half of pregnancy, the WG expected in the first 20 weeks was considered separately from that expected in the second 20 weeks. Firstly, for each BMI, the Institute of Medicine average WG at 20 weeks (5.7 kg for underweight women, 4.8 kg for normal weight women, and 3.1 kg for overweight and obese women) was subtracted from the minimum and maximum WG at term. These remainders were then equally apportioned across the following 20 weeks to obtain the minimum and maximum WG range expected at each gestational age from 20 weeks to term. Finally, each delivery was categorized as low, adequate or excessive WG and adjusted for gestational age and pre-pregnant BMI. For WG analyses only, deliveries over 41 weeks were omitted (the assumption that WG continued linearly beyond 41 weeks could not be confirmed). For other analyses, all gestational ages were included.

The following demographic characteristics were obtained from both the PRAMS database and birth certificates: maternal age, maternal race, type of medical insurance, prenatal care, maternal blood pressure disorders and presence of diabetes mellitus, participation in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC Program), pregnancy intention, and mode of delivery. Data concerning birth weight and gestational age at delivery were collected from birth certificates and used to calculate fetal growth status. The variable "prenatal care" is an indicator that combines the pregnancy trimester when prenatal care began and the number of prenatal visits during pregnancy[9].

Women presenting with multiple pregnancies were excluded from the analysis due to the particular likelihood of preterm labor, as were those presenting with preterm premature ruptures of membranes, placental abruption and placenta previa, due to the close relationship between these conditions and the occurrence of preterm birth. In addition, women presenting with an indication for a potential medically induced preterm birth (i.e. blood pressure disorders, diabetes or small for gestational age fetus) were also excluded.

Statistical analysis

The primary outcome was gestational age at delivery, defined by three levels: term birth (>37 weeks gestation), very preterm birth (<=32 weeks gestation[10]), and moderately preterm birth (33-37 weeks gestation[11]). The univariate relationship between timing of delivery and potential risk factors or confounders was studied using the Chi square test. All factors for which the univariate relationship with preterm delivery was characterized by a P<0.2 were included in a multivariate analysis, using the multinomial logistic regression model to allow for simultaneous comparison of very preterm and moderate preterm birth risks to that of delivery at term[12]. The Wald's test was further used to perform an additional comparison between risks for very preterm and

Table 1 Characteristics of women included in the survey sample

	Entire population (100%)	UW women (16.4%)	NW women (56.2%)	OW women (11.2%)	OB women (16.2%)
Weight gain					
LWG	22.4	28.6	22.3	12.2	23.4
NWG	35.1	44.3	36.8	25	26.5
EWG	42.5	27.1	40.8	62.8	50.1
Age (years)					
<18	3.8	6.2	3.9	2.8	1.6
18-35	83.9	86	82.7	82.4	86.8
>35	12.3	7.9	13.4	14.8	11.6
Race					
White	78.1	80.7	79.2	76.2	73.1
Black	16.8	12.4	15.8	19.4	23.2
Asian	3.2	5.3	3.4	2.3	1.2
Indian	1	0.8	0.8	1.2	1.7
Other	0.9	0.8	0.9	1	0.8
Smoking					
No	90.5	88.8	91.2	90.5	89.9
Yes	9.5	11.2	8.8	9.5	10.1
Insurance					
Private	66.7	62.9	69.4	67.8	60.5
Medicaid	33.3	37.1	30.6	32.2	39.5
Pregnancy intention					
Yes	90.3	91.2	91.4	89.7	85.8
No	9.7	8.8	8.6	10.3	14.2

	Entire population (100%)	UW women (16.4%)	NW women (56.2%)	OW women (11.2%)	OB women (16.2%)
WIC Program					
No	60.7	58.1	63.9	61.9	51.5
Yes	39.3	41.9	36.1	38.1	48.5
Prenatal care					
Adequate	75.2	73.5	75.6	76.7	74.4
Intermediate	19.4	20.5	19.2	18.7	19.3
Inadequate	5	5.5	4.8	4.2	5.8
None	0.4	0.5	0.4	0.4	0.5
Preterm birth					
No	90.3	88.3	90.5	90.5	91.5
Moderate	9.2	11.1	9.1	9	8
Very preterm	0.4	0.6	0.4	0.6	0.6
Delivery					
Vaginal	71.3	77.5	71.4	70	65.8
Forceps	2.3	3	2.4	2	1.2
Vacuum	4.8	5.3	5.1	4.3	3.3
VBAC	2.3	1.6	2.2	2.6	3.2
Primary CS	10.8	7.9	10.8	12.7	12.4
Repetitive CS	8.5	4.8	8	8.6	14
Fetal growth					
Normal	91.2	94.2	91.6	89.7	88
LGA	8.8	5.8	8.4	10.3	12

Abbreviations: UW - underweight, NW - normal weight, OW - overweight, OB - obese women; LWG - low weight gain, AWG - adequate weight gain, EWG- excessive weight gain during pregnancy; WIC Program - participation in the Special Supplemental Nutrition Program for Women, Infants, and Children; VBAC - vaginal delivery after cesarean section; Primary CS - primary cesarean section; Repetitive CS - repetitive cesarean section; LGA - large for gestational age newborn

Table 2 Relationship between pre-pregnant body mass index, gestational weight gain and the likelihood of moderate and very preterm birth (multinomial logistic regression model; adjustment made for maternal age, maternal race, pregnancy intention, medical insurance, prenatal care, WIC-pregnancy, smoking during pregnancy and birth weight)

	Moderate preterm birth	**Very preterm birth**	**Wald's test**
	ORa (95%CI)	ORa (95%CI)	P
NW and NWG	1	1	
NW and LWG	1.1 (0.90-1.4)	3.1 (2.0-4.8) *	<0.001*
NW and EWG	0.98 (0.80-1.2)	1.7 (1.1-2.7) *	0.04 *
UW and NWG	0.93 (0.71-1.2)	0.60 (0.32-1.1)	0.23
UW and LWG	1.8 (1.4-2.3) *	3.8 (2.4-6.1) *	<0.001*
UW and EWG	1.5 (1.1-2) *	4.2 (2.5-7.0) *	<0.001*
OW and NWG	1 (0.68-1.6)	1.8 (0.82-3.9)	0.35
OW and LWG	1.4 (0.89-2.3)	3.5 (1.6-7.4) *	0.002 *
OW and EWG	0.87 (0.66-1.1)	2.3 (1.3-4.3) *	0.01 *
OB and NWG	0.81 (0.57-1.2)	0.49 (0.21-1.2)	0.15
OB and LWG	0.82 (0.57-1.2)	2.4 (1.2-4.7) *	0.02 *
OB and EWG	0.87 (0.67-1.1)	2.7 (1.7-4.5) *	<0.001*

*Abbreviations: UW - underweight, NW - normal weight, OW - overweight, OB - obese women; LWG - low weight gain, NWG - normal weight gain, EWG - excessive weight gain during pregnancy; * - statistically significant*

moderate preterm birth, and the results were expressed as P-values. In the multivariate model, potential confounders were entered individually and excluded from the model where their associations were characterized by P>0.2. Significance was defined as P<0.05. Potential interactions in the model were tested and pre-pregnant BMI was found to modify the relationship between WG and both very preterm and moderate preterm birth (P<0.001). A 12-level variable was subsequently introduced, combining the four classes of pre-pregnant BMI with the three classes of weight gain, the reference class being that of normal weight women with adequate WG intake.

Results

The PRAMS IV's sample included 66,250 women with singleton pregnancies, corresponding to a population of 2,677,484 women. The following subject data were excluded from the analysis: 3,373 women with missing pre-pregnant BMI (5.01%) and 4,168 women (6.29%) with missing WG during pregnancy, resulting in a final sample of 30,108 women, representing a population of 1,495,474. The demographic characteristics are presented in Table 1.

Table 3 Factors associated with the likelihood of moderate and very preterm birth (multinomial logistic regression model; adjustment made for the 12 categories of pre-pregnant body mass index and gestational weight gain)

	Moderate preterm delivery	Very preterm delivery	Wald's test
	ORa (95%CI)	ORa (95%CI)	P
Age (years)			
<18	1 (0.75-1.3)	1.7 (1.2-2.4) *	0.01 *
18-35	1	1	
>35	0.98 (0.81-1.2)	1.3 (0.81-2)	0.56
Race			
White	1	1	
Black	1.5 (1.2-1.7) *	3 (2.2-4) *	<0.001*
Asian	1 (0.76-1.3)	1.6 (0.91-2.9)	0.26
Indian	1.4 (0.84-2.2)	0.57 (0.27-1.2)	0.13
Other	1.3 (0.95-1.9)	1.5 (0.89-2.6)	0.10
Pregnancy intention			
Yes	1	1	
No	0.93 (0.76-1.1)	0.81 (0.5-1.3)	0.08
Insurance			
Private	1	1	
Medicaid	1 (0.84-1.2)	1.5 (1-2.2) *	0.12
Prenatal care			
Adequate	1	1	
Intermediate	1.2 (1-1.4) *	1 (0.78-1.4)	0.13
Inadequate	1.4 (1.1-1.9) *	1.4 (0.91-2.2)	0.015 *
None	2.4 (1.1-5) *	10.6 (5.2-21.6) *	<0.001 *
WIC-pregnancy			
No	1	1	
Yes	1.1 (0.90-1.3)	1.1 (0.79-1.5)	0.66
Smoke			
No	1	1	
Yes	1.3 (1.1-1.5) *	1.8 (1.3-2.5) *	<0.001 *
Fetal growth			
Normal	1	1	
LGA	1.9 (1.6-2.4) *	4 (2.5-6.4) *	<0.001 *

*Abbreviations: WIC-pregnancy - participation in the Special Supplemental Nutrition Program for Women, Infants, and Children; LGA - large for gestational age newborn; * - statistically significant*

Weighted analysis showed that among the population providing the sample, the proportion (95% CI) of pre-pregnant normal weight, underweight, overweight and obese women were 56.2% (55.4-57.1), 16.4% (15.7-17.0), 11.2% (10.7-11.8) and 16.2% (15.6-16.8). The rates of women having adequate, low and excessive WG were 35.1% (34.2-35.9), 22.4% (21.7-23.1) and 42.5% (41.7-43.4). The rates of moderate preterm and very preterm birth were 9.2% (8.7-9.7) and 0.46% (0.41-0.52) respectively (Figure 1).

The univariate analysis found that moderate preterm and very preterm birth were significantly associated with maternal BMI, gestational WG, maternal age and race, smoking during pregnancy, medical insurance, prenatal care, pregnancy intention, and large for gestational age fetus. The results of the multinomial logistic regression model are presented in Tables 2 and 3. The risk of very preterm birth was significantly increased when compared to the risk of moderate preterm birth in women with either low or excessive WG, regardless of pre-pregnant BMI. The risk of very preterm birth was also significantly higher than that of moderate preterm birth in women aged <35 years, of African American race, receiving medical insurance, with no prenatal care, smoking during pregnancy, or having a large for gestational age fetus.

Discussion

This study demonstrates that both pre-pregnant BMI and gestational WG are associated with timing of delivery, that their effects are interlinked and hence should not be studied separately. While gestational WG appeared to be closely associated with very preterm birth regardless of BMI, its effect on moderate preterm birth was significant only in underweight women. Furthermore, in women with either low or excessive WG, regardless of BMI, the risk of very preterm birth was significantly greater than that for moderate preterm birth, meaning that the effect of abnormal WG on the likelihood of preterm birth is greater before 32 weeks gestation.

One of the strengths of this study is the use of WG categories based on gestational age, as described above, enabling women having delivered before 38 weeks gestation to be included in the analysis, in addition to term pregnancies. Instead of the classical binary logistic regression model, our statistical analysis employed the multinomial logistic regression model; firstly allowing the investigation of the relationship between an outcome variable with more than two categories and a set of covariates[12], and secondly a comparison of odds ratios corresponding to the same risk factor, using the Wald's test. This made possible an assessment of whether or not the risk for very preterm birth was higher than that for moderate preterm birth, where women presented with a specific risk factor (Tables 2 and 3).

Acute interventions for preterm labor have failed to reduce the prevalence of preterm birth over the past twenty years[11]. In order to identify solutions to this public health problem, further studies are required to provide a better understanding of the causes and epidemiology of preterm birth[13]. The results of this study, based on a national survey, showed that the risk of very preterm birth is increased by both low and excessive WG regardless of pre-pregnant BMI, but is most significant at the extremes of maternal pre-pregnancy BMI. Furthermore, it suggests that programs designed to prevent preterm birth should take into account a woman's WG during pregnancy.

Another recent study, which considered the combined effect of BMI and WG on preterm labor, found that the risk of preterm delivery generally declined with increasing pre-pregnant BMI, with the exception of very low WG (<0.12 kg/week)[2]. We were unable to confirm this tendency in our population, either for very preterm, or for moderate preterm birth. This disagreement may result from differences in definition of preterm delivery and exclusion criteria, leading to potential differences between populations. First, in our sample, women presenting with preterm premature rupture of membranes, placental abruption, placenta previa, blood pressure disorders, diabetes were excluded, due to the fact that these morbidities are not confounders, but strong risk factors for spontaneous and induced preterm delivery. Secondly, in respect to the definition of preterm delivery; in our study, "very preterm birth" and "moderate preterm birth" included the 32nd and the 37th weeks respectively[10,11]. These two factors may explain some of the differences observed in preterm delivery rates between the two studies[2].

Maternal low WG may be associated with several unfavorable co-morbidities that can increase the risk of preterm birth. These associations make difficult to estimate the real and independent effect of low WG on obstetrical or neonatal outcomes, even with multivariate adjustments. In our sample, two health-compromising behaviors, smoking during pregnancy and no prenatal care, significantly increased the risk of very preterm birth when compared to the risk of moderate preterm birth. This risk was similarly increased for women receiving medical insurance, who were likely to have a lower socio-economic status.

It has been shown that fasting during late gestation may be associated with preterm delivery[14] which could be explained by elevated concentrations of corticotropin-releasing hormone[15] present in pregnant women exposed to fasting[16]. Low WG may also be a marker for other preterm birth risk factors such as low vitamin[17] and micronutrient intake[18], in addition to global immunosuppression, which results in greater susceptibility to inflammatory injuries[19]. Further studies are required to explain the mechanisms involved in very preterm delivery in women with low WG.

Furthermore, the relationship between EWG and preterm delivery has been in agreement with our findings[2,20]. The association between preterm delivery <32 weeks and WG >0.79 kg/week, regardless of pre-pregnant BMI, was recently confirmed in a large sample that included women with both intact and preterm premature rupture of membranes[2,21]. Obese women were found to present with higher levels of insulin, leptin and interleukin-6 during the third trimester of pregnancy[22]. This proinflammatory environment may be associated with pathways leading to preterm birth.

Conclusions

This large sample study adds value to our understanding of the relationship between pre-pregnant BMI and WG during pregnancy and preterm delivery. The results obtained therefore lend further weight to the hypothesis that the combined effect of pre-pregnant BMI and WG on preterm birth is real and independent of obstetrical morbidities. ■

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