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Rate of Second and Third Trimester Weight Gain and Preterm Delivery Among Underweight and Normal Weight Women

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Abstract

Objectives—Low gestational weight gain (GWG) in the second and third trimesters has been associated with increased risk of preterm delivery (PTD) among women with a body mass index (BMI) < 25 mg/m^2. However, few studies have examined whether this association differs by the assumptions made for first trimester gain or by the reason for PTD.

Methods—We examined singleton pregnancies during 2000–2008 among women with a BMI < 25 kg/m^2 who delivered a live-birth ≥28 weeks gestation (n = 12,526). Women received care within one integrated health care delivery system and began prenatal care ≤13 weeks. Using antenatal weights measured during clinic visits, we interpolated GWG at 13 weeks gestation then estimated rate of GWG (GWG_{rate}) during the second and third trimesters of pregnancy. We also estimated GWG_{rate} using the common assumption of a 2-kg gain for all women by 13 weeks. We examined the covariate-adjusted association between quartiles of GWG_{rate} and PTD (28–36 weeks gestation) using logistic regression. We also examined associations by reason for PTD [premature rupture of membranes (PROM), spontaneous labor, or medically indicated].

Results—Mean GWG_{rate} did not differ among term and preterm pregnancies regardless of interpolated or assumed GWG at 13 weeks. However, only with GWG_{rate} estimated from interpolated GWG at 13 weeks, we observed a U-shaped relationship where odds of PTD increased with GWG_{rate} in the lowest (OR 1.36, 95 % CI 1.10, 1.69) or highest quartile (OR 1.49, 95 % CI 1.20, 1.85) compared to GWG_{rate} within the second quartile. Further stratifying by reason, GWG_{rate} in the lowest quartile was positively associated with spontaneous PTD while GWG_{rate} in the highest quartile was positively associated with PROM and medically indicated PTD.

Conclusions—Accurate estimates of first trimester GWG are needed. Common assumptions applied to all pregnancies may obscure the association between GWG_{rate} and PTD. Further

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research is needed to fully understand whether these associations are causal or related to common antecedents.

Keywords

Pregnancy; Gestational weight gain; Weight gain measures; Preterm delivery

Introduction

Preterm delivery (<37 weeks), the leading cause of neonatal and infant death and neurological disabilities among survivors [6], affects about 1 of every 10 infants born in the United States [4]. The amount of weight a woman gains during pregnancy (i.e., gestational weight gain [GWG]) may be a modifiable risk factor for preterm delivery. Both low GWG, particularly among lean women [5, 23], or high GWG [14] have been associated with preterm delivery; however, studies have been limited by the availability of weight data throughout pregnancy and the ability to account for the heterogeneity of preterm delivery.

GWG is not linear throughout pregnancy; it tends to be slow in the first trimester then increase at a relatively linear rate during the second and third trimesters [7]. Consequently, there is an intrinsic correlation between GWG and gestational age, thus many studies examining associations with GWG have focused on the rate of GWG during the second and third trimesters. Studies using serial antenatal weight data are scant. To estimate second and third trimester GWG rate, many studies have relied on only two weight measures, weight at or near conception and weight at delivery, making an assumption about first trimester gain. The influence of this assumption on associations is unknown. Furthermore, the etiology of preterm delivery is heterogeneous and few studies have examined whether associations between GWG and preterm delivery differ by reason for preterm delivery.

We have previously published findings among lean women demonstrating no association between GWG in the first 28 weeks of pregnancy and preterm delivery [19]. Our first analysis focused on examining the same gestational window for both term and preterm deliveries and GWG early in pregnancy. In this analysis, our objective was to assess whether low or high rate of GWG in the second and third trimesters was associated with preterm delivery as weight gain later in pregnancy may be more influential. We examined whether associations differed based on the method by which first trimester weight gain was estimated (hypothetical weight gain assumption versus measured estimate) and the reason for preterm delivery.

Methods

Participants

We conducted a retrospective cohort study of pregnant women using electronic medical record data from Kaiser Permanente Northwest (KPNW). KPNW is a large integrated health care delivery system serving western Oregon and Washington State. A detailed description of KPNW, its members, and how pregnancies were identified and matched to birth certificate data is described in detail elsewhere [19]. Institutional Review Boards at KPNW and the Centers for Disease Control and Prevention approved the study.

Gestational Weight Gain

A total of 15,277 pregnancies delivered between January 1, 2000 and December 31, 2008 met study inclusion criteria of maternal age ≥18 years, a pregravid BMI < 25 kg/m^2, and a singleton, live-birth at ≥28.0 weeks of gestation. A detailed description of the pregravid and antenatal weights and data cleaning are described elsewhere [19]. Briefly, over 90 % of eligible pregnancies had 7 or more antenatal weight measurements. To be included in the analysis, pregnancies had to have a weight measured between 9 and 16 weeks gestation and within 4 weeks of delivery. We preferentially used pregravid weight self-reported at the first prenatal visit because it was available for 88 % of pregnancies. If not available, we used weight measured in the medical office within the first 42 days of pregnancy or weight measured in the medical office within the 180 to 0 days prior to pregnancy. Previous analyses demonstrated self-reported pregravid weight had good agreement with measured weights (intraclass correlation coefficient (ICC) = 0.90, 95 % CI (0.87, 0.92) for weight measured 180–0 days prior to pregnancy; ICC = 0.95, 95 % CI (0.90, 0.97) for weight measured within the first 42 days of pregnancy) and underestimated measured pre-pregnancy and early pregnancy weights by an average of 1.1 kg (SD = 3.2) and 1.1 kg (SD = 2.2), respectively [19].

We estimated the weekly rate of second and third trimester GWG in two ways to examine whether the association between rate of GWG and preterm delivery differed based on the method by which first trimester weight gain was estimated (hypothetical weight gain assumption versus measured estimate). The first rate estimate used the assumption that all women gained 2 kg (4.4 lbs) in the first trimester [7]. Rates of GWG were then calculated as [(Last measured weight (within 4 weeks of delivery) – (prepregnancy weight + 2.0 kg))/(gestation age at last measured weight −13.0 weeks)]. The second rate estimate used linear interpolation to calculate mother's weight at 13.0 weeks of gestation by using pregravid weight, the closest weight measured before 13 weeks (mean 11.9 weeks, SD 1.8), and the closest weight measured after 13 weeks (mean 16.6 weeks, SD 2.2). At least one weight measured between 9 and 16 weeks was used. Rate was then calculated as [(Last measured weight (within 4 weeks of delivery) – (interpolated weight at 13.0 weeks))/(gestation age at last measured weight −13.0 weeks)]. The mean gestational age for weights used in interpolations did not differ by preterm status.

Outcomes

Gestational age at birth was determined using the estimated due date, documented by the clinician in the medical record, and the date of delivery. Preterm delivery was defined as delivery between 28 weeks 0 days and 36 weeks 6 days gestation. We excluded very preterm deliveries (<28 weeks gestation) as there were few in this cohort, and there would be almost no third trimester data for this group. We additionally categorized preterm type as either premature rupture of membranes (PROM), spontaneous labor, or medically indicated using an algorithm described elsewhere [19]. Preterm type could not be determined for one pregnancy.

Covariates

Maternal age and Medicaid enrollment were obtained from the electronic medical record. Parity and tobacco use during pregnancy were obtained from the birth certificate. Race/ ethnicity and mother's educational attainment were obtained primarily from the birth certificate, but when missing they were obtained from the medical record. Pregnancies missing data on maternal characteristics (primarily maternal education, parity and smoking status) were excluded from the study (n = 414). A detailed description of the study cohort and a comparison between pregnancies included and excluded from the study is described elsewhere [19].

Statistical Methods

Only 5.6 % of the eligible sample was classified as underweight (BMI < 18.5 kg/m^2), therefore all women were analyzed together. We compared rate of GWG by preterm versus term using least squares means and generalized estimating equations (GEE) to account for more than one pregnancy to the same mother. The study sample included 12,526 pregnancies to 10,810 mothers. Using logistic regression with GEE, adjusting for potential confounders, we assessed the associations between rate of GWG and preterm delivery for all preterm versus term and for each preterm type separately versus term. We examined associations using GWG categorized into quartiles where we used the second quartile as the referent as the rates included in this quartile were closest to current GWG recommendations [7]. We conducted two sensitivity analyses. To examine the influence of first trimester gain on associations between rate of second and third trimester GWG and preterm delivery, we additionally adjusted models for interpolated GWG at 13 weeks. To examine the influence of preeclampsia on excess GWG among pregnancies categorized as medically indicated preterm delivery [7], we performed a sensitivity analysis excluding women with an *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD9-CM) code indicating a diagnosis of mild/unspecified or severe preeclampsia, eclampsia, or pre-eclampsia or eclampsia superimposed on pre-existing hypertension (ICD-9-CM codes 642.4–642.7, respectively). All analyses used Statistical Analysis Software (SAS) version 9.2 (SAS Institute, Cary, NC) with statistical significance defined as $p < 0.05$.

Results

In the analytic sample, 5.8 % (n = 721) pregnancies ended with a delivery <37 weeks of gestation. Pregnancies with a preterm delivery occurred more frequently among women who were either younger or older, non-Hispanic Black or Hispanic, less educated, nulliparous, smoked during pregnancy, and diagnosed with diabetes or hypertension during pregnancy (data not shown; refer to [19]).

Mean rate of GWG in the second and third trimesters did not differ by method used to estimate first trimester weight gain or by preterm status (Table 1). However, the overall range of weekly gain was wider when first trimester gain was estimated to be 2.0 kg (Table 2).

When examining the association between rate of GWG and preterm delivery, although strength of associations differed depending on the estimate of rate used, the patterns were similar. When first trimester gain was assumed to be 2.0 kg, rate of GWG was not significantly associated with preterm delivery overall. In contrast, when first trimester gain was interpolated using measured weight data, GWG in both the lowest quartile and the highest quartile, compared to the second quartile, was associated with increased odds of preterm delivery. (Table 3) Similarly, after stratifying by type of preterm, GWG in the lowest quartile was associated with increased odds of spontaneous preterm delivery while GWG in the highest quartile was associated with increased odds of both PROM and medically indicated preterm delivery. For both GWG measures, the associations among medically indicated preterm deliveries were no longer significant after excluding pregnancies with preeclampsia. With this exclusion, associations among pregnancies with PROM remained unchanged (data not shown), while the lowest quartile among pregnancies with spontaneous delivery became slightly stronger (OR 1.42, 95 % CI 1.06, 1.89). Adjusting for first trimester GWG resulted in relatively no change to associations.

Discussion

In this study, we examined the association between rate of second and third trimester GWG and preterm delivery among women with a BMI < 25 kg/m^2. When first trimester gain was interpolated using measured weight data, our results suggest a U-shape relationship, with both low and high rates of second and third trimester GWG having a positive association with preterm delivery. This U-shaped relationship has been observed in other studies [23, 24, 18, 2]. Notably, the lowest odds of preterm delivery were observed in the quartile of GWG rate most consistent with current GWG recommendations (0.44–0.58 kg/week for underweight women and 0.35–0.50 kg/week for normal weight women) [7].

Why there was no association between preterm delivery and rate of gestational weight gain when assessing the association using an assumed weight gain in the first trimester may be due substantial variability in weight accumulation during that time. Typically, first trimester GWG is assumed to be 2 kg (range 1–3 kg) on average for underweight and normal weight women [7]. Our previous analysis using this cohort found that first trimester GWG based on interpolation of measured weights was 2.4 kg on average, but there was high variability with over 50 % of pregnancies gaining outside the assumed 1–3 kg range [19]. The wide variability in first trimester GWG has been corroborated by other studies [13, 8, 1]. Our study results further demonstrate the limitation of using an assumed average first trimester GWG for all women as doing so results in misclassification of exposure, biasing measured associations toward the null.

One question is whether low or excessive weight gain at a particular time in pregnancy is more influential on pregnancy outcomes than cumulative GWG. In our previous analysis, we found no association between total GWG in the first and second trimester of pregnancy and preterm delivery between 28 and 36 completed weeks' gestation [19]. However, with an observation period including the second and third trimester, we did find an association between rate of gestational weight gain and preterm delivery. We propose two possible explanations for these findings. First, it may be patterns of weight change later in pregnancy that are associated with preterm delivery or, second, that the divergence in pattern is not detectable until later in pregnancy. Nevertheless, the biological mechanism explaining the association between GWG and preterm delivery remains unclear and likely differs by reason for preterm delivery. For example, the positive association between rate of GWG < 0.65 kg/week (the highest quartile) and medically indicated delivery in our study was attenuated and no longer significant after excluding pregnancies with a diagnosis of a preeclampsia. Preeclampsia is associated with both edema and preterm delivery [11]; thus, it is possible that hypertensive disorders are the common antecedent of both excess GWG (due to edema) and preterm delivery and the GWG-preterm delivery association is not causal. However, excess weight gain is also known to increase systemic inflammation and oxidative stress, risk factors for hypertensive disorders and spontaneous labor [12, 16]. To fully understand whether excess GWG precedes preeclampsia or is a consequence of preeclampsia, large prospective studies with detailed data on GWG as well as timing of onset of signs or symptoms of medical conditions are needed.

Our findings of a positive association between low rate of GWG and spontaneous preterm delivery have been observed in other studies [24, 18, 21, 25, 22]. What cannot be determined retrospectively is whether it is low caloric intake and poor nutrition that lead to preterm delivery or whether low rate of GWG is only an indicator for abnormal pregnancy physiology. For example, utero-placental insufficiency and poor expansion of plasma volume (a component of GWG) have been associated with preterm delivery [9]. Utero-placental insufficiency is also a risk factor for preeclampsia. Maternal malnutrition has been associated with lower GWG and intriguing data suggests possible biological mechanism whereby nutrient deficiencies can adversely affect immune and inflammatory responses which may activate preterm labor [7]. However, meta-analysis of randomized-controlled trials found no association between energy/protein supplementation and preterm delivery [10] and evidence from micronutrient studies have been conflicting [6, 3].

Few studies have specifically examined preterm PROM, independent of spontaneous labor, in relation to GWG. We found that rate of GWG > 0.65 kg/week (highest quartile) was positively associated with preterm delivery due to PROM. This result is in contrast to other studies that observed no association between GWG and preterm PROM [2, 17] or an increased risk of preterm PROM with rate of GWG < 0.35 kg/week [20]. Similar to spontaneous preterm deliveries, whether rate of GWG is causal or simply a marker for abnormal pregnancy physiology remains unknown.

Strengths of this analysis include the use of serially measured antenatal weight data providing the ability to estimate first trimester weight gain. While pregravid weight was primarily self-reported, we were able to assess reliability of self-reported pregravid weight in a subset of pregnancies and found self-reported pregravid weight to be 1 kg less, on average, than measured weight. Measured weights were collected in the context of clinical care; thus, a 1 kg difference could reflect any combination of reporting error, change in weight between the time of weight measurement and conception, diurnal changes in body weight [15], or weight measured with or without wearing clothes and shoes. Data were rigorously cleaned to ensure meaningful reporting errors with weight data were detected [19]. Given the data were collected prospectively, it is unlikely reporting errors in pregravid weight are related to preterm delivery. We used an algorithm to identify morbidities allowing us to categorize the reason for preterm delivery.

Our study is not without limitations. Previous studies have suggested that the association between low GWG and preterm delivery is stronger among underweight women compared to normal weight women; our study was not large enough to examine underweight women separately. Both very low and very high rate of GWG was associated with preterm delivery overall and the pattern remained similar after stratifying by type of preterm. However, our relatively small sample size for preterm delivery due to PROM or a medical indication may have limited the power to detect significant associations. We did not examine whether GWG is associated with extremely preterm delivery (<28 weeks' gestation). Women in our study were predominately non-Hispanic white, normal weight, insured, and enrolled in prenatal care during the first trimester, thus our findings may have limited generalizability.

Conclusions

In summary, we found both low and high rates of GWG during the second and third trimesters to be positively associated with preterm delivery, although the U-shaped relationship may differ by reason for preterm delivery. In our study, the association of high GWG with medically indicated preterm delivery was driven by the high weight gain among women with preeclampsia. Well powered, prospective studies starting very early in pregnancy and collecting detailed information on maternal diet and body composition, fetus, placenta and pregnancy complications are needed to determine when and whether weight gain is influential on preterm delivery or whether associations are related to common antecedents.

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Abbreviations

AOR	Adjusted odds ratio
BMI	Body mass index
GA	Gestational age
CI	Confidence interval
GWG	Gestational weight gain
ICD-9-CM	International classification of diseases, 9th revision, clinical modification

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Significance

What is already known on the subject?

Gestational weight gain (GWG) may be a modifiable risk factor for preterm delivery; however, few studies have used measured weights collected throughout pregnancy to examine the patterns of GWG that are associated with preterm delivery.

What this study adds?

Accurate measures of first trimester GWG are needed. Using measured weights to estimate first trimester GWG, results suggest a U-shape relationship, with both low and high rates of second and third trimester GWG having a positive association with preterm delivery among normal weight women. Whether these associations are causal or related to common antecedents requires further study.

Table 1

Rate of gestational weight gain in second and third trimesters by method to estimate first trimester gain

Gestational weight gain measures	Overall N = 12,526 % or Mean (SE)	Term N = 11,805 % or Mean (SE)	Preterm N = 721 % or Mean (SE)	*P* value[a]
Rate of GWG in second and third trimesters (kg/week), assumes 2 kg gain at 13 weeks	0.56 (0.00)	0.56 (0.00)	0.57 (0.01)	0.23
Rate of GWG in second and third trimesters (kg/week), estimated actual weight at 13 weeks	0.55 (0.10)	0.55 (0.00)	0.56 (0.01)	0.25

Trimesters defined as first: ≤13.0 weeks, second: >13–28.0 weeks, third: >28 to last ambulatory visit within 4 weeks of delivery

kg kilograms, *SE* standard error

[a]Comparison of term vs preterm. Standard errors (SE) accounted for clustering of more than one pregnancy within the same mother

Table 2

Distribution of rates of second and third trimester weight gain with each quartile by method used to estimate first trimester weight gain[a]

Quartile	Rate range (kg/week) when first trimester gain assumed to be 2 kg	Rate range (kg/week) when actual first trimester gain estimated
First	−0.32 to 0.437	−0.04 to 0.435
Second	0.438–0.544	0.436–0.535
Third	0.545–0.682	0.536–0.650
Fourth	0.683–1.94	0.651–1.60

SD standard deviation

[a]Trimesters defined as first: ≤13.0 weeks, second: >13–28.0 weeks, third: >28 to last ambulatory visit within 4 weeks of delivery

Table 3

Adjusted odds ratios for preterm delivery by quartile of gestational weight gain, overall and by preterm type[a]

Gestational weight gain (GWG) measure[b]	Overall		PROM (n = 160)		Spontaneous (n = 405)		Medically indicated (n = 155)		Medically indicated, excluding preeclampsia (n = 113)	
Quartile	**aOR[c]**	**95 % CI**	**aOR[c]**	**95 % CI**	**aOR[c]**	**95 % CI**	**aOR[c]**	**95 % CI**	**aOR[c]**	**95 % CI**
Rate of GWG in 2nd and 3rd trimesters (kg/week), assumes 2 kg gain at 13 weeks										
First	1.18	(0.96, 1.46)	1.05	(0.68, 1.63)	1.23	(0.93, 1.63)	1.23	(0.78, 1.96)	1.36	(0.82, 2.26)
Second	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Third	0.86	(0.68, 1.07)	0.66	(0.40, 1.07)	0.97	(0.72, 1.29)	0.80	(0.48, 1.36)	0.76	(0.42, 1.37)
Fourth	1.19	(0.96, 1.48)	1.25	(0.82, 1.90)	0.98	(0.73, 1.32)	**1.73**	(**1.11**, **2.69**)	1.09	(0.63, 1.87)
Rate of GWG in 2nd and 3rd trimesters (kg/week), interpolated weight at 13 weeks										
First	**1.36**	(**1.10**, **1.69**)	1.51	(0.94, 2.43)	**1.33**	(**1.01**, **1.76**)	1.42	(0.87, 2.32)	1.60	(0.92, 2.79)
Second	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Third	1.00	(0.80, 1.26)	1.21	(0.74, 1.99)	0.95	(0.71, 1.28)	0.99	(0.58, 1.67)	1.19	(0.67, 2.12)
Fourth	**1.49**	(**1.20**, **1.85**)	**1.76**	(**1.11**, **2.81**)	1.19	(0.89, 1.59)	**2.22**	(**1.42**, **3.48**)	1.66	(0.96, 2.87)

aOR adjusted odds ratio, *CI* confidence interval, *kg* kilogram, *PROM* premature rupture of membranes

Significant associations shown in bold

[a]One pregnancy where preterm delivery type could not be determined was excluded

[b]Second and third trimesters defined as, second: >13–28.0 weeks, third: >28 to last ambulatory visit within 4 weeks of delivery

[c]Models included adjustment for mother's age, race, education, Medicaid use, parity and smoking, and accounted for clustering of more than one pregnancy within the same mother