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Associations of Gestational Weight Gain with Preterm Birth among Underweight and Normal Weight Women

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Abstract

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Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Studies report increased risk of preterm birth (PTB) among underweight and normal weight women with low gestational weight gain (GWG). However, most studies examined GWG over gestational periods that differ by term and preterm which may have biased associations because GWG rate changes over the course of pregnancy. Furthermore, few studies have specifically examined the amount and pattern of GWG early in pregnancy as a predictor of PTB. Within one integrated health care delivery system, we examined 12,526 singleton pregnancies between 2000 and 2008 among women with a body mass index $<25 \text{ kg/m}^2$, who began prenatal care in the first trimester and delivered a live-birth >28 weeks gestation. Using self-reported pregravid weight and serial measured antenatal weights, we estimated GWG and the area under the GWG curve (AUC; an index of pattern of GWG) during the first and second trimesters of pregnancy (<28 weeks). Using logistic regression adjusted for covariates, we examined associations between each GWG measure, categorized into quartiles, and PTB (<37 weeks gestation). We additionally examined associations according to the reason for PTB by developing a novel algorithm using diagnoses and procedure codes. Low GWG in the first and second trimesters was not associated with PTB [aOR 1.11, (95 % CI 0.90, 1.38) with GWG <8.2 kg by 28 weeks compared to pregnancies with GWG >12.9]. Similarly, pattern of GWG was not associated with PTB. Our findings do not support an association between GWG in the first and second trimester and PTB among underweight and normal weight women.

Keywords

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

Preterm birth (<37 weeks of gestation) is the leading predictor of infant death and long-term neurological disabilities in children [1]. With one of every eight infants in the United States born preterm, it is important to identify potentially modifiable risk factors to prevent preterm birth.

Several studies have reported an association between low gestational weight gain (GWG) and increased risk of preterm birth particularly among leaner women [2, 3]. However, a recent simulation study demonstrated that conventional measures of GWG historically examined (i.e., total GWG or average rate of GWG) may have biased observed associations between GWG and preterm birth due to the inherent correlation between GWG and gestational age [4]. GWG is not linear throughout pregnancy. Instead, it is slower during the first trimester and then increases at a relatively linear rate in the second and third trimesters [5]. Thus, a woman who delivers earlier will have a lower total and average rate of GWG than a woman who delivers later. Most studies have been limited by the availability of only two weight measures (pregravid or early pregnancy weight and weight at delivery) and therefore have examined total GWG or average rate of GWG across the entire pregnancy [2]. To reduce bias associated with gestational age, some studies have examined rate of GWG in the second and third trimesters only by assuming a constant GWG in the first trimester among all pregnancies. This, however, also assumes that first trimester gain is less informative and few studies have specifically examined first trimester GWG. An alternative approach to resolve the inherent bias with gestational age is to examine GWG up to a given gestational week achieved by all pregnancies and determine whether GWG differs among

those who eventually delivered pre-term or at term. Furthermore, it has been suggested that the pattern and timing of GWG over the course of pregnancy, not just the total amount, may be an important predictor of preterm birth, particularly for spontaneous preterm labor [6, 7]. Few studies, however, have used serial weight measures to examine GWG patterns throughout pregnancy [6–9].

The objective of this study was to use serial antenatal weights to examine whether low GWG in the first and second trimesters is associated with preterm birth among women with a pregravid body mass index (BMI) $<25 \text{ kg/m}^2$. We additionally examined whether associations differed between spontaneous and medically-indicated pre-term births.

Methods

Participants

We conducted a retrospective cohort study using data from electronic medical records from Kaiser Permanente Northwest (KPNW), a large nonprofit prepaid, federally certified, Joint Commission-accredited, integrated health care delivery system with approximately 475,000 members in western Oregon and Washington State. Members include individuals and families covered by commercial group and individual self-pay health plans, Washington State Basic Health Plan (subsidized, Washington State only), Medicare Advantage, and Medicaid (Oregon and Washington State). This study was approved by the Centers for Disease Control and Prevention and the KPNW Institutional Review Boards.

To identify pregnancies, we used a validated algorithm that links indicators and dates of pregnancies and pregnancy outcomes to create pregnancy “episodes” [10]. Validation of this algorithm by experienced medical record abstractors showed 100 % agreement for live birth outcomes between episodes identified by the algorithm and those identified through medical record reviews. To gather additional demographic information, pregnancies were then matched to live birth certificate records using a scored probabilistic matching method based on mother's name (maiden and married), date of birth, and address, and infant's name, date of birth, and facility of delivery/birth.

Gestational Weight Gain

There were 15,277 pregnancies that met our study inclusion criteria of maternal age ≥ 18 years with a pregravid BMI $<25 \text{ kg/m}^2$ and a singleton, live-birth at >28 weeks gestation delivered within KPNW between January 2000 and December 2008. Pregravid BMI [weight (kg)/height (m^2)] was calculated using weight and height data available in the KPNW data system. For pregravid weight, we preferentially used pregravid weight self-reported at the first prenatal visit because it was available for 88 % of pregnancies. When self-reported pregravid weight was not available, we used weight measured within the first 42 days of pregnancy (available for 39 % of pregnancies); else we used weight measured within -180 to 0 days prior to pregnancy (available for 17 % of pregnancies). For height, we used the median of all heights measured at ≥ 18 years of age. We did not use any biologically implausible weight ($<34 \text{ kg}$), height (<1.2 or >2.0 meters), or calculated BMI ($<12 \text{ kg/m}^2$) data. We assessed agreement between the self-reported and measured pregravid weight by

calculating the intraclass correlation (ICC) for absolute agreement based on a two-way random effects model for a single measure. Self-reported pregravid weight demonstrated good agreement with weight measured within -180 to 0 days prior to pregnancy [ICC = 0.90, 95 % CI (0.87, 0.92), n = 5,967] or within the first 42 days of pregnancy [ICC = 0.95, 95 % CI (0.90, 0.97), n = 2,588]; self-reported weight underestimated measured pre-pregnancy and early pregnancy weight by an average of 1.1 kg (SD = 3.2) and 1.1 kg (SD = 2.2), respectively.

Over 90 % of eligible pregnancies had seven 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; 2,280 pregnancies were excluded for missing required data. To ensure erroneously recorded weights were not included in the analysis, we examined serial weight data (pregravid weight defined above and measured antenatal weights from medical records) using an algorithm to identify improbable weight values. Briefly, we examined the absolute and rate of measurement-to-measurement change, both forward (weight at time_x vs. weight at time_{x+1}) and backward (weight at time_x vs. weight at time_{x-1}) and omitted from analyses any weight indicating a drastic increase in weight gain followed by drastic weight loss, or vice versa. Cleaning of weight data resulted in the exclusion of 0.63 % of the total weight data available and an additional 55 pregnancies which no longer had the weight measures required for study inclusion.

We examined three different GWG measurements. GWG during the first trimester (13 weeks) was estimated by linear interpolation using pregravid weight, the closest weight before 13 weeks if available (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. Similarly, GWG during the first and second trimesters (28 weeks) was interpolated using the closest weights before (mean 25.5 weeks, SD 2.0) and after 28 weeks (mean 29.9 weeks, SD 1.6). The mean gestational age for weights used in interpolations did not differ by preterm status. Finally, we estimated the area under the GWG curve (AUC) with respect to increase during the first and second trimesters using the trapezoid method [11, 12]. The AUC is an index of the kilogram-days gained or lost relative to pregravid weight, thus describing the pattern of GWG. For example, if two women each gained 5 kg by 28 weeks, the woman who gained the weight earlier in pregnancy will have a higher AUC compared to the women who gained the same amount of weight later. Once the GWG measures were created, we examined GWG distributions and identified two pregnancies as extreme outliers across more than one GWG measure. Manual inspection of weight measures confirmed recording errors across two successive weight measures; both pregnancies were excluded.

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 birth was defined as delivery <37.0 weeks gestation. We additionally categorized preterm type using an algorithm based on *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD9-CM) diagnosis and procedure codes recorded within 30 days prior to or

10 days after birth. A listing of all ICD9-CM codes found for the study sample was reviewed by obstetrician/gynecologists (KKV, CJB, WMC) to determine diagnosis codes that could be used to identify medical indication for delivery (Table 1). Among pregnancies with a preterm delivery, preterm type was coded as: (1) premature rupture of membranes (PROM) (658.1×, 658.2× or 761.1×); (2) spontaneous (644.2× [early onset of delivery] and no induction codes (73.01, 73.1, or 73.4), or no induction or cesarean section codes (74.0–74.2, 74.4, or 74.9) and no identifiable medical indication; or (3) medically indicated, if delivery included an induction or cesarean section and a medical indication, or an induction but no identifiable medical indication. Postoperative charts for pregnancies with a cesarean section without identifiable medical indication (n = 16) were reviewed to determine the appropriate preterm type. Seven were determined to be spontaneous onset of labor with six of these a breech presentation. Eight were medically indicated and were predominately repeat cesareans in the 36th week. Preterm type could not be determined for one pregnancy and therefore it was excluded from the preterm type analyses.

Other Variables

We evaluated several maternal characteristics as potential confounders. 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 if missing on the birth certificate they were obtained from the medical record. Pregnancies missing data on maternal characteristics were excluded from the study (n = 414).

Statistical Methods

Underweight (BMI < 18.5 kg/m²) and normal weight women (BMI 18.5–24.9 kg/m²) were analyzed together because only 5.6 % of the eligible sample was underweight. We assessed the characteristics of pregnancies in the study compared with those who were excluded. We also compared characteristics of those in the study sample by preterm versus term status using Chi square statistics for proportions and ANOVA for continuous variables. We compared GWG measures by preterm versus term using least squares means and generalized estimating equations (GEE) which account for correlations introduced by including more than one pregnancy to the same mother. We then fit logistic regression models for preterm (all preterm types combined) versus term and for each preterm type separately versus term using GEE to examine associations between the three GWG measures separately and preterm birth while adjusting for potential confounders selected a priori. We examined associations using GWG categorized into quartiles where we used the highest quartile as the referent. To assess the robustness of associations, we performed sensitivity analyses excluding women with any diagnosis of diabetes or hypertension (determined by ICD9 code or indication on birth certificate) as GWG and risk of PTB may differ among women with these conditions. We additionally examined associations stratified by early to moderate preterm delivery (28–33 weeks gestation) or late preterm delivery (34–36 weeks gestation). Statistical significance was set at $p < 0.05$. Statistical analyses were run in Statistical Analysis Software (SAS) version 9.2 (SAS Institute, Cary, NC).

Results

Our study sample included 12,526 pregnancies to 10,810 mothers. Pregnancies excluded from analysis ($n = 2,751$) occurred more frequently among women who had preterm births, were younger, were of a race/ethnicity other than non-Hispanic white, were less educated, were on Medicaid, were parous, and smoked during pregnancy (Table 2). Among pregnancies included in the analysis, 5.8 % ended with a preterm delivery. Of these, 88.8 % were late preterm deliveries (34–36 weeks gestation). Pregnancies with a term delivery had more antenatal weights measured during pregnancy compared to those with a preterm delivery [10.6 (SD 2.6) vs. 9.1 (SD 2.9), $p < 0.0001$]. There were also fewer days between the last measured weight to delivery among pregnancies with a term delivery [4.6 (SD 3.9) vs. 7.1 (SD 6.6), $p < 0.0001$]. Compared to pregnancies with a term delivery, those with a preterm delivery were more likely to be among women who were either younger or older, non-Hispanic black or Hispanic, less educated, nulliparous, and smoked during pregnancy (Table 3). Pregnancies with preterm delivery were also more likely to be diagnosed with diabetes or hypertension during pregnancy.

There were no differences in GWG or AUC for the first and second trimester by preterm status (Table 4). Rate of GWG during the second trimester also did not differ by preterm status (mean 0.56 kg/week, data not shown). In adjusted models with preterm types combined, neither GWG nor AUC during the first and second trimesters was significantly associated with preterm birth (Table 5). More specifically, the odds of preterm birth were not higher among pregnancies with lower GWG compared to pregnancies gaining within the highest quartile. Among pregnancies ending preterm, 22.2 % were categorized as PROM, 56.3 % spontaneous, and 21.5 % as medically-indicated. Results were similar after stratifying by preterm type, excluding women with any diagnosis of hypertension or diabetes, or stratifying by early to moderate preterm and late preterm delivery; neither GWG nor AUC in the first and second trimesters was associated with preterm birth (data not shown).

Comments

In this study, we used serial antenatal weight measurements to examine the association between GWG and preterm birth among women with a BMI < 25 kg/m². Unlike other studies that examined GWG over gestational periods that can differ among term and preterm births [2], our study specifically examined GWG restricted to the first 28 weeks of gestation, a comparable time period regardless of birth outcome, and observed no association between the amount or pattern of GWG and preterm birth.

Results from some studies suggest that the association between GWG and preterm birth differs by the reason for preterm delivery. Two studies have also examined GWG early in pregnancy. Authors of one study observed that low GWG during the second trimester was associated with increased risk of preterm birth due to spontaneous labor or premature rupture of membranes (analyzed together) among women with a BMI ≥ 26 kg/m² [13]. Findings from the second study indicated GWG in the first 18–22 weeks of gestation among women with normal BMI was inversely associated with spontaneous preterm birth (aOR per

0.1 kg/week gain 0.80, 95 % CI 0.66, 0.94), positively associated with medically-indicated preterm birth (aOR 1.22, 95 % CI 1.02, 1.45), but not associated with preterm birth due to PROM [6]. Our study does not corroborate these previous observations as we found no significant associations between GWG in the first two trimesters and preterm birth regardless of the reason for preterm delivery.

Our study also specifically examined GWG in the first trimester. Often researchers have only a pregravid weight and a delivery weight to estimate GWG. Thus, to determine the rate of GWG after the first trimester, first trimester gain is assumed to be about 1–3 kg for underweight and normal weight women [5]. However, few recent studies have specifically measured first trimester GWG to corroborate these estimates. Our estimates of first trimester gain were based on measured weights and were within this range at 2.4 kg. Interestingly, our data also indicate mean GWG in the second trimester, 0.56 kg/week, was higher than the range recommended for normal weight women (0.35–0.50 kg/week) suggesting many women were on track to gain excess gestational weight.

Strengths of this analysis include the use of measured height and measured weight collected over the course of pregnancy providing the ability to calculate trimester specific GWG as well as the pattern of GWG as measured by the AUC. Although pregravid weight was primarily self-reported, we utilized a rigorous data cleaning method to ensure meaningful errors were detected and it is unlikely reporting errors are related to preterm birth. Our data allowed for the examination of GWG over a comparable period regardless of the gestational age at birth. Additionally, GWG in the first and second trimesters is less likely to be influenced by edema and dietary or physical activity modifications (including prescribed bed rest) associated with hypertensive disorders and gestational diabetes, factors which may alter GWG and increase risk of preterm birth. We also used a validated, electronic algorithm to identify all pregnancies and morbidities, which allowed us to categorize type of preterm birth.

Our study is not without limitations. We relied predominately on self-reported prepregnancy weight; comparisons to measured weights suggest GWG in the first trimester may be overestimated by an average of 1 kg. Previous studies have suggested that low GWG among underweight women is more strongly associated with pre-term birth, yet we did not have a large enough study sample to examine this higher risk group separately. Frequency of antenatal visits increases with gestational age, thus the gestational age at last weight measurement was slightly further from delivery for women with a preterm birth compared to those who delivered at term. We did not include preterm births <28 weeks gestation, thus do not know if GWG is associated with extremely preterm births. We also were unable to control for prior history of preterm birth, a strong risk factor for current preterm birth as these data were unavailable. Our study has limited generalizability, as women in our study were predominately non-Hispanic white, normal weight, insured and enrolled in prenatal care during the first trimester. This may explain why our preterm birth rate was lower than the national rate.

In summary, the amount and pattern of GWG during the first and second trimesters was not associated with preterm birth occurring between 28 and 36 weeks gestation among

underweight and normal weight women. The appropriate range of GWG is a balance between many risk factors including preterm birth and maternal weight retention [5]. If our findings are replicable, it is possible a lower range of GWG would be appropriate for underweight and normal weight women without increasing risk of preterm delivery.

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Abbreviations

AOR	Adjusted odds ratio
BMI	Body mass index
GA	Gestational age

CI	Confidence interval
GWG	Gestational weight gain
ICD9-CM	International classification of diseases, 9th revision, clinical modification

Table 1
International classification of diseases, ninth revision, clinical modification (ICD9-CM)
diagnoses used to identify medically-indicated preterm birth^a

Pregnancy-related ICD9-CM codes	Description
641	Antepartum hemorrhage, abruptio placentae, and placenta previa
642.2	Other pre-existing hypertension complicating pregnancy, childbirth, and the puerperium
642.5	Severe pre-eclampsia
642.6	Eclampsia
642.7	Pre-eclampsia or eclampsia superimposed on pre-existing hypertension
643.1	Hyperemesis gravidarum with metabolic Disturbance
643.2	Late vomiting of pregnancy
643.8	Other vomiting complicating pregnancy
646.7	Liver disorders in pregnancy
648.0	Diabetes mellitus
648.5	Congenital cardiovascular disorders
648.6	Other cardiovascular diseases
655	Known or suspected fetal abnormality affecting management of mother
656.1	Rhesus isoimmunization
656.2	Isoimmunization from other and unspecified blood-group incompatibility
656.3	Fetal distress
656.5	Poor fetal growth
657	Polyhydramnios
658.0	Oligohydramnios
658.4	Infection of amniotic cavity
665.0	Infection of amniotic cavity
<i>Non-pregnancy ICD9-CM codes</i>	
158	Malignant neoplasm of retroperitoneum and peritoneum
193	Malignant neoplasm of thyroid gland
250	Diabetes mellitus
416	Chronic pulmonary heart disease
425.1	Hypertrophic obstructive cardiomyopathy
425.4	Other primary cardiomyopathies
430	Subarachnoid hemorrhage
434	Occlusion of cerebral arteries
436	Acute, but ill-defined, cerebrovascular disease
437.2	Hypertensive encephalopathy
710.0	Systemic lupus erythematosus
760.0	Maternal hypertensive disorders
760.1	Maternal renal and urinary tract diseases
760.2	Maternal infections
760.3	Other chronic maternal circulatory and respiratory diseases
760.4	Maternal nutritional disorders

Pregnancy-related ICD9-CM codes	Description
760.5	Maternal injury
760.6	Surgical operation on mother
761.2	Oligohydramnios
761.3	Polyhydramnios
762.0	Placenta previa
762.1	Other forms of placental separation and hemorrhage
762.3	Placental transfusion syndromes
762.7	Chorioamnionitis
764	Slow fetal growth and fetal malnutrition
852	Subarachnoid, subdural, and extradural hemorrhage, following injury
853	Other and unspecified intracranial hemorrhage following injury

^aICD9-CM codes listed include only those reported in study sample and may not be a comprehensive list of all possible ICD9-CM codes for medical indication for preterm delivery

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Table 2
Comparison of maternal characteristics among pregnancies included and excluded from study

Characteristic	Excluded N = 2,751		Included N = 12,526	p value ^a
	n	%	%	
Preterm (<37 weeks)	2,751	8.5	5.8	<0.0001
Age (years)	2,751			
18–24		38.1	26.4	<0.0001
25–29		29.3	33.4	
30–34		21.7	27.6	
35–39		8.8	11.0	
40+		2.1	1.7	
Race/ethnicity	2,663			<0.0001
Non-Hispanic White		69.6	74.4	
Non-Hispanic Black		3.8	2.3	
Hispanic		11.3	7.4	
Asian/Pacific Islander		4.7	3.9	
Other/Unknown/Mixed		10.6	12.0	
Education (years)	2,495			<0.0001
<12		10.5	5.9	
12		32.6	23.2	
>12		57.0	70.9	
Enrolled in Medicaid or Washington basic health plan	2,751	9.6	4.1	<0.0001
Parity	2,553			<0.0001
0		42.6	46.9	
1+		57.4	53.1	
Used tobacco during pregnancy	2,482	13.7	9.0	<0.0001
Diagnosed with pre-gestational or gestational diabetes mellitus	2,751	5.4	5.2	0.74
Diagnosed with any hypertensive disorder during pregnancy	2,750	8.6	8.7	0.80

^a p value based on χ^2

Table 3
Distribution of term and preterm birth by maternal characteristics among pregnancies included in study

Characteristic	Term N = 11,805	Preterm N = 721	<i>p</i> value ^a
	%	%	
Age (years)			0.04
18–24	26.3	27.5	
25–29	33.4	32.3	
30–34	27.7	26.5	
35–39	11.1	10.7	
40+	1.6	3.1	
Race/ethnicity			0.003
Non-Hispanic White	74.7	69.6	
Non-Hispanic Black	2.3	3.7	
Hispanic	7.3	8.7	
Asian/Pacific Islander	3.9	3.2	
Other/Unknown/Mixed	11.8	14.7	
Education (years)			0.03
<12	5.9	7.2	
12	23.0	26.2	
>12	71.1	66.6	
Enrolled in Medicaid or Washington basic health plan	4.2	3.9	0.73
Parity			0.04
0	46.7	50.6	
1+	53.3	49.4	
Used tobacco during pregnancy	8.8	13.2	<0.0001
Diagnosed with pre-gestational or gestational diabetes mellitus	5.0	8.9	<0.0001
Diagnosed with any hypertensive disorder during pregnancy	8.3	16.1	<0.0001

^a *p* value based on χ^2

Table 4
Mean (standard error) gestational weight gain by preterm status and interquartile range of gestational weight gain across all pregnancies

Gestational weight gain (GWG) measure ^a	Term N = 11,805 Mean (SE) ^b	Preterm N = 721 Mean (SE) ^b	Interquartile range
Total GWG in first trimester (kg)	2.4 (0.03)	2.4 (0.11)	0.6-3.9
Total GWG in first and second trimesters (kg)	10.7 (0.04)	10.6 (0.16)	8.2-12.9
AUC for first and second trimesters (kg/days)	761.6 (4.3)	756.7 (17.7)	475.9-1,015.4

kg kilogram, AUC area under the curve

^aTrimesters defined as first: 13.0 weeks, second: 28.0 weeks

^bStandard errors (SE) accounted for clustering of more than one pregnancy within the same mother

Table 5
Associations between gestational weight gain categorized by quartiles and preterm birth

Gestational weight gain (GWG) measure ^a quartile	Adjusted OR ^b	95 % CI	<i>p</i> value
Total GWG in first trimester (kg)			0.28
First	1.13	0.91, 1.39	
Second	0.91	0.74, 1.13	
Third	1.02	0.82, 1.26	
Fourth	1.00	referent	
Total GWG in first and second trimesters (kg)			0.33
First	1.11	0.90, 1.38	
Second	1.11	0.90, 1.37	
Third	0.94	0.75, 1.17	
Fourth	1.00	referent	
AUC for first and second trimesters (kg/days)			0.34
First	1.12	0.90, 1.37	
Second	0.93	0.75, 1.15	
Third	0.96	0.77, 1.18	
Fourth	1.00	referent	

OR odds ratio, CI confidence interval, kg kilogram, AUC area under the curve

^aTrimesters defined as first: 13.0 weeks, second: 28.0 weeks

^bModels 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