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Pregnancy weight gain is not associated with maternal or mixed umbilical cord estrogen and androgen concentrations

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Abstract

The association of maternal weight gain with serum hormone concentrations was explored in 75 women who had healthy, singleton pregnancies. Estradiol, estriol, estrone, androstenedione, testosterone, dehydroepiandrosterone (DHEA) and DHEA sulfate concentrations were measured both in maternal and mixed umbilical cord serum to assess hormone levels in both the maternal and fetal circulation at delivery. Our data show no association of maternal or cord steroid hormone concentrations with pregnancy weight gain. Increased exposure to steroid hormones, especially estrogens, during pregnancy has been hypothesized to play a role in subsequent breast cancer risk for both mother and female offspring. Our results are not consistent with an effect of pregnancy weight gain being mediated by this pathway as reflected by hormone concentrations at the end of pregnancy.

Keywords

Pregnancy; breast cancer; estrogens; androgens

Introduction

Weight gain during adult life is an established risk factor for postmenopausal breast cancer (1–8). Various studies have attempted to identify a critical time period for weight gain that is associated with subsequent breast cancer risk. Weight gain from age 18 to breast cancer diagnosis (6), from age 30 to breast cancer diagnosis (6), weight gain in the decade prior to breast cancer diagnosis (8) and lifetime weight gain (1,3,4,7) have all been associated with increased risk of breast cancer. In addition, weight gain during pregnancy may influence both

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the mother and offspring's subsequent health outcomes, including cancer risk (2,9–12). In a Finnish cohort study, pregnancy weight gain was positively associated with subsequent maternal breast cancer risk independent of weight at time of diagnosis (9).

Estrogens and androgens are substantially elevated in pregnancy although there is significant between woman variation in concentrations. Some of this variation may be explained by weight gain during pregnancy. Pregnancy hormones have been hypothesized to mediate the association of other pregnancy characteristics like preeclampsia (13–16) with breast cancer risk for both mother and offspring (12–14,17–19). Comprehensive data, however, are lacking on the relationship between pregnancy weight gain and the range of steroid hormones in late pregnancy found in both maternal and cord serum samples as most studies have focused mainly on maternal circulating estrogens (20,21). One of these studies focused exclusively on maternal estriol and found no association with pregnancy weight gain, while the other reported a positive association of weight gain up to week 31 with both total estrogens and estradiol, although the associations were not statistically significant.

Materials and Methods

Study population

Participants were a sample from an ongoing study of preeclamptic and uncomplicated pregnancies being conducted at the Magee Womens Hospital, University of Pittsburgh (22). All women attending the Magee Womens Hospital's obstetric practice who had uncomplicated pregnancies, delivered between February 1994 and May 1998 and were 14 years of age or older were invited to participate in the study as controls; 52% agreed to participate. Data on hormone concentrations and pregnancy-related variables in women with uncomplicated pregnancies have been published previously (22). Here we focus the analysis on pregnancy weight gain and steroid hormones from maternal venous and mixed venous and arterial umbilical cord serum samples from uncomplicated pregnancies. Information on maternal age, race/ethnicity, menstrual, reproductive and medical history, pre-pregnancy weight, weight gain during pregnancy, week of gestation and baby's birth weight was obtained by interview and review of subjects' medical records. Self-reported pre-pregnancy weight and last recorded weight measurement prior to delivery was used to determine pregnancy weight gain for all participants. Informed consent for the questionnaire, interview and blood collection was obtained. This study was approved by the University of Pittsburgh Institutional Review Board.

Hormone assays

Maternal venous serum (M) was collected at admission for labor and delivery and mixed venous and arterial cord serum (C) was collected at delivery. The samples were allowed to clot at room temperature, were centrifuged and stored at −80°. Blood samples were analyzed at Quest Diagnostics, San Juan Capistrano, CA. The hormone measurement assay techniques and coefficients of variation for estrone, estriol, estradiol, androstenedione, testosterone, dehydroepiandrosterone (DHEA), and DHEA sulfate have been published previously (22). The coefficients of variation based on blinded quality control samples for maternal hormones were 18.6% for DHEA, 8.5% for DHEAS, 10.2% for androstenedione, 9.6% for testosterone, 13.7% for estradiol, 10.3% for estrone and 6.8% for estriol and 8.1, 6.6, 8.5, 15.2, 10.9, 16.7, and 9.2%, respectively, for hormones in the cord blood.

Statistical analysis

Selected maternal, fetal and gestational characteristics were compared across tertile of pregnancy weight gain using analysis of variance for continuous variables and χ^2 tests for categorical variables. Mean maternal and cord hormone concentrations were compared by tertile of pregnancy weight gain using analysis of variance with logarithm-transformation of

all hormones. Geometric means and 95% confidence intervals are presented. The association of weight gain with hormones also was evaluated using Spearman rank correlations and linear regression modeling with the hormones as dependent variables and weight gain as a continuous, independent variable. Maternal age, gestational week, parity, days from last weight measurement to birth and baby's birth weight were included as independent variables. Statistical significance was defined at the $p<0.05$ level and all analyses were performed using Statistical Analysis Systems (SAS) software package PC SAS 9.1 (SAS Corp., Cary, NC).

Results

Selected maternal, gestational and fetal characteristics for 75 uncomplicated pregnancies are presented by tertile of pregnancy weight gain (Table 1). Maternal pre-pregnancy weight, race, and parity, and offspring gender, gestational length, and birth weight did not significantly differ across tertiles of pregnancy weight gain. There was no trend in weight gain by maternal age but women who gained the least weight (tertile 1) tended to be the oldest ($p=0.01$ and $p=0.17$ compared with tertiles 2 and 3, respectively). None of the unadjusted correlations between continuous measures of maternal or cord hormone concentrations and weight gain were statistically significant (data not shown). In addition, there were no trends in any of the hormone concentrations by tertile of pregnancy weight gain (data not shown). Subsequent analyses using linear regression models and adjusting for maternal age, gestational week, parity, birth weight, and days from last weight measurement to delivery, also demonstrated no significant associations of the hormones measured in either maternal or mixed cord serum samples with pregnancy weight gain (Table 2). Adding maternal pre-pregnancy weight to the model outlined above did not substantially affect the results although the association of pregnancy weight gain with maternal testosterone levels approached statistical significance ($p=0.10$.)

Discussion

These data suggest that pregnancy weight gain is not associated with selected estrogen and androgen concentrations measured in maternal or in mixed cord serum collected at delivery. Pregnancy weight gain across the population was wide, ranging from 0.3%–73.7% of pre-pregnancy weight. In addition, 55% of this population had gained greater than the 16 kg of recommended weight gain for normal weight women (23) demonstrating that even weight gain in excess of the current recommendations was not associated with increased hormone concentrations in the estrogen or androgen pathways measured at the time of delivery in this study.

The size of the present study was small and it would be useful to confirm these findings in a larger sample, in particular because the association of pregnancy weight gain and testosterone concentrations approached statistical significance once maternal pre-pregnancy weight was included in the model The hormone concentrations were measured at delivery thus representing levels when weight gain is greatest and the only feasible sampling time for cord concentrations. As the critical exposure period for breast cancer risk is unknown for both mother and daughter, it would be useful to characterize hormones and other biomarkers earlier in the pregnancy as well.

Several factors related to pregnancy have been evaluated for their associations with maternal breast cancer risk, with some such as twinning associated with increased risk, while others such as preeclampsia associated with reduced risk (12). Pregnancy weight gain also is associated with increased maternal breast cancer risk, independent of weight at time of diagnosis, as indicated by a study of Finnish women (9). The results presented here suggest that an association of pregnancy weight gain with breast cancer risk may be mediated by biological factors other than estrogen and androgen concentrations at delivery. Elevated

estrogen concentrations from aromatization of androgens in adipose tissue is speculated to mediate the excess postmenopausal breast cancer risk in heavier compared with leaner women (2). However, only 20–30% of the 16 kg of pregnancy weight gain for a normal weight woman is attributed to increased adipose tissue (24), suggesting that additional mechanisms by which pregnancy weight gain contributes to breast cancer risk should be considered. In addition, the study of excess pregnancy weight gain also is relevant to future breast cancer risk as weight gain in excess of the recommended guidelines is associated with increased weight retention post-partum (25), which has implications for studies of weight gain across the lifespan.

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Table 1

Maternal, gestational and neonatal characteristics by tertile of pregnancy weight gain.

	Tertile of Pregnancy Weight Gain			
	1 0–14.6 kg n=24	**2 14.7–18.6 n=27**	**3 18.7 + n=24**	**p value***
Pre-pregnancy weight (kg)	73.5 (50.0–118.8)	63.3 (40.8–99.7)	69.6 (47.6–125.0)	0.12
Pregnancy weight (last measurement) (kg)	82.7 (58.9–132.4)	79.9 (57.6–117.6)	95.2 (68.9–145.2)	<0.0001
Weight gain as % of pre-pregnancy weight	13.8 (0.3–24.8)	27.4 (17.5–44.4)	38.8 (16.2–73.7)	<0.0001
Maternal age (y)	29.0 (18–41)	24.4 (15–35)	26.5 (18–37)	0.02
Gestational length (weeks)	37.0 (31–40)	37.7 (34–40)	37.3 (32–41)	0.59
# of previous live births				
0	16 (66.7%)	21 (77.8%)	17 (70.8%)	0.75
1+	8 (33.3%)	6 (22.2%)	7 (29.2%)	
Race				
Caucasian	13 (54.2%)	12 (44.4%)	16 (66.7%)	0.48
African-American	10 (41.7%)	14 (51.9%)	8 (33.3%)	
Hispanic	1 (4.2%)	0	0	
Asian	0	1 (3.7%)	0	
Gender of offspring				
Female	9 (37.5%)	12 (44.4%)	11 (45.8%)	0.56
Male	15 (62.5%)	15 (55.5)	13 (54.2%)	
Birth weight (g)	3158 (1278–4082)	3196 (2210–3954)	3289 (1648–3888)	0.65

Continuous variables listed as mean (range); categorical variables listed as number (percentages).

*Continuous variables evaluated by ANOVA, p value refers to any differences among categories; categorical variables evaluated by χ^2 test.

Table 2

Geometric mean (95% confidence interval) maternal (M) and umbilical cord (C) hormone concentrations at delivery by tertile of pregnancy weight gain

	Tertile of Pregnancy Weight Gain			
	1 0–14.6 kg	**2 14.7–18.6 kg**	**3 18.7 kg +**	**p value***
Estradiol-C (pg/mL)	10622 (7235–15596)	8759 (6648–11541)	7498 (5134–10952)	0.97
Estradiol-M (pg/mL)	19937 (14298–27799)	23002 (18856–28060)	22431 (19114–26324)	0.43
Estriol-C (ng/mL)	207 (158–272)	204 (164–255)	193 (146–255)	0.82
Estriol-M (ng/mL)	15 (11–21)	16 (13–19)	18 (16–21)	0.59
Estrone-C (pg/mL)	30499 (20774–44779)	32730 (27023–39644)	27757 (19111–40316)	0.34
Estrone-M (pg/mL)	6690 (5098–8778)	7752 (5657–10623)	6076 (4408–8372)	0.91
Androstenedione-C(ng/dL)	310 (249–387)	351 (307–400)	324 (266–395)	0.23
Androstenedione-M (ng/dL)	334 (254–439)	366 (300–446)	341 (265–440)	0.45
DHEA-C (nd/dL)	503 (423–598)	502 (438–575)	495 (383–639)	0.47
DHEA-M (ng/dL)	374 (267–524)	598 (450–796)	501 (362–694)	0.31
DHEAS-C (ug/dL)	197 (157–247)	184 (155–218)	191 (143–254)	0.88
DHEAS-M (ug/dL)	77 (57–104)	110 (81–150)	99 (76–129)	0.37
Testosterone-C (ng/dL)	23 (16–32)	20 (16–25)	19 (13–27)	0.99
Testosterone-M (ng/dL)	142 (103–196)	149 (120–184)	156 (122–201)	0.19

* p-values are from multivariate linear regression analysis with weight gain as a continuous variable, adjusted for maternal age, gestational week, parity, birth weight, and days from last weight measurement to delivery