Maternal Anthropometry and Mammographic Density in Adult Daughters

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abstract

OBJECTIVE: We examined the relation between maternal anthropometry and mammographic density in the adult daughter using prospectively collected data.

METHODS: Our study included a total of 700 mother-daughter dyads participating in an adult follow-up of women born in 2 US birth cohorts: the Child Health and Development Study and the Boston, Massachusetts, and Providence, Rhode Island sites of the National Collaborative Perinatal Project.

RESULTS: We observed an increased percent breast density at a mean age of 43.1 years in the daughters of mothers who gained 5 kg or less during pregnancy compared with mother-daughter pairs in which the mother gained 5 to 10 kg ($\beta = 4.8$, 95% confidence interval: 1.0 to 8.6). The daughters of mothers who were overweight at the time of conception (prepregnancy BMI ≥25) and who gained >5 kg during pregnancy had a lower percent density ($\beta = -3.2$, 95% confidence interval: −6.2 to −0.2) compared with mothers with a BMI <25 at conception who gained >5 kg.

CONCLUSIONS: We did not find any strong and consistent patterns between maternal anthropometry and the daughter's breast density, a strong predictor of breast cancer risk. A modest association between low gestational weight gain and increased breast density 40 years later in the daughter was observed, even after accounting for adult body size, and if confirmed, possible mechanisms need to be further elucidated.

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There is mounting evidence that intrauterine conditions may affect future risk of a number of chronic diseases, including cancer. Most significantly, the risk of breast cancer has been associated with both weight and length at birth.[1,2] A wealth of studies from diverse populations suggests that a high birth weight may increase susceptibility to breast cancer in adulthood (as reviewed in Michels and Xue[3]). To gain a better understanding of the mechanistic underpinnings of the observed associations, exploring the role of antecedents of birth weight is essential.

Two previous studies have explored the relation between maternal anthropometry and the daughter's breast cancer risk.[4,5] Like most studies on early life characteristics and chronic disease outcomes, however, the data in these studies were derived from retrospectively assessed and recalled information obtained decades later from the mothers on their pregnancies, which likely resulted in both nondifferential and differential measurement error of the early life variables. Although other studies on early life factors tried to eliminate this source of bias by generating them on the basis of record linkage data, this method often lacks important covariate information, such as anthropometry, smoking, and alcohol consumption.

Prospective data linking early life data with adult disease outcomes in real time across the life course are difficult to obtain because of the need for lengthy follow-up spanning several decades. We built on the National Collaborative Perinatal Project (Boston and Providence sites) (NCPP) and the Childhood Health and Development Study in California (CHDS) to link prospectively assessed maternal characteristics with daughters' risk of breast cancer. These large prospective pregnancy cohorts collected data on prepregnancy BMI and gestational weight gain (GWG) in mothers of girls born between 1959 and 1967. We conducted an adult follow-up study of these girls (referred to as "daughters") when they were 39 to 49 years old. Although this age range is consistent with a low incidence of breast cancer thus far, we have obtained mammograms for a subset of the NCPP and CHDS participants to estimate daughter's mammographic density in mid-life, one of the strongest independent predictors of breast cancer risk, besides early life irradiation exposure.[6] We therefore examined the relation between the maternal anthropometry and mammographic density in the daughter half a century later in 700 mother-daughter dyads participating in these 2 pregnancy cohorts. This is an important topic because it is an example of a fetal exposure with health implications later in life. By addressing this and other early exposures associated with breast development and breast cancer risk, pediatricians can be engaged in primary breast cancer prevention.

METHODS

Study Population

The Early Determinants of Mammographic Density (EDMD) study is an adult follow-up of women born in 2 US birth cohorts: CHDS, which was conducted in California between 1959 and 1967,[7,8] and 2 sites of the NCPP conducted in Boston, Massachusetts, and Providence, Rhode Island, between 1959 and 1966.[9] Details of the EDMD have been previously published.[10] The final sample included 1134 women: 521 singletons and 296 sibling-sets totaling 613 individuals. Sibling-sets included 277 sets of 2, 17 sets of 3, and 2 sets of 4 siblings. The study was approved by the institutional review boards at Columbia University Medical Center, Kaiser Permanente, Brigham and Women's Hospital, and Brown University.

Adult Data Collection

Women who agreed to participate in the adult follow-up completed a telephone interview.[10] The adult follow-up ascertained information on sociodemographic characteristics (age at mammogram, race), BMI, current smoking status, first-degree family history of breast cancer, and reproductive events (age at menarche, menopausal status, hormonal birth control use, and pregnancy history). For race, women who self-identified as non-Hispanic white were referred to as white and women who self-identified as non-Hispanic black, Hispanic, or non-Hispanic Asian Pacific Islander/other were referred to as nonwhite. Interviews also collected a detailed history of alcohol intake.

Baseline Maternal and Childhood Data

The CHDS and NCPP cohorts enrolled pregnant mothers and followed them prospectively throughout their pregnancy. At the clinic visits, study staff asked women to report prepregnancy weight, smoking during pregnancy, and maternal education at registration. Weight during pregnancy was measured repeatedly by study staff during clinic visits. Maternal GWG was calculated by using self-reported prepregnancy weight and measured weight at the end of pregnancy (for details see refs 8, 9, and 11). Gestational age was calculated by subtracting the date of the last menstrual period from the date of delivery. In the NCPP, the pediatrician examined the neonate in the delivery room. Trained clinical staff measured childhood height and weight at 8 months or 12 months, and at 4 years or 7 years of age.[9] In the CHDS, serial growth measurements were abstracted from medical records until age 5.[11]

Mammographic Density Data

Detailed information on the procurement and assessment of the mammogram data have been published previously.[8,10] Of the 1134 women in the sample, 87% (n = 981) had a previous mammogram or planned to obtain a mammogram, and 91% of these participants consented to providing their mammogram for density assessments in this study (n = 893). Mammograms for 23 participants could not be retrieved, 51 mammograms were of poor quality, and 119 participants had only digital mammograms available. As the sensitivities for digital and film mammograms may differ, we restricted our sample to those with film mammograms. The remaining 700 women were included in the present analysis.

We assessed mammographic density through Cumulus (University of Toronto, Toronto, Ontario, Canada), a computer-assisted threshold program.[12] We measured total breast area, total dense area (cm^2), and percent density (dense area divided by breast area multiplied by 100). We calculated nondense (fat tissue) area as total breast area minus total dense area. All craniocaudal and mediolateral oblique films that were available for a participant were read in 1 batch and all sibling-sets were read within the same batch. Each batch included films from NCPP and CHDS cohorts. Films were read in batches of approximately 50, and 10% of the films had repeated readings from the same batch. We repeated an additional 10% of films in every batch to estimate batch-to-batch variability. The overall within-batch correlation coefficient was 0.96 for percent density and the intraclass correlation coefficient for between-batch reliability was 0.95.[10]

Statistical Analyses

We examined the associations between maternal characteristics and mammographic density, measured as percent density and absolute dense area, using multivariable linear regression models with generalized estimating equations to account for correlations in density between siblings. We first assessed the association between the exposure of interest and each mammographic density measure adjusting for age at mammogram, site, and adult BMI. We additionally adjusted for maternal education, maternal race, prenatal smoke exposure, and maternal prepregnancy BMI (in the GWG analysis only) to examine their influence on the association of interest. We tested for additive interaction by site by using cross-product terms.

GWG was categorized into 4 groups: ≤5 kg, >5 and <10 kg, >10 kg and <15 kg, or ≥15 kg, and was also examined as a continuous variable. Maternal prepregnancy BMI was similarly categorized into 4 groups: <23, 23 to <25, 25 to <30, or ≥30, and was also examined as a continuous variable. Tests for trend for categorical models were performed using ordinal variables across categories.

We explored the potential interaction between GWG and maternal prepregnancy BMI by categorizing these exposures into 4 groups (for maternal prepregnancy BMI based on cut-offs of <25 kg/m^2 vs 25 kg/m^2 or greater and for GWG based on cut-offs of <10 kg or >10 kg).

Participants with missing data on the exposure of interest, either GWG (3.5%) or maternal prepregnancy BMI (7.7%), were excluded. We used Markov Chain Monte Carlo multiple imputation to impute missing covariate data for adult BMI (2.0%), maternal education (<0.01%), and prenatal smoke exposure (3.1%), by using all available information on these variables as well as mammographic density, age at mammogram, site, maternal race, and maternal prepregnancy BMI or GWG as inputs in the imputation model. Maternal prepregnancy BMI was imputed when examined as a covariate in the GWG analysis only. Multivariate linear regression models using generalized estimating equations were conducted in each of the 5 imputed data sets and results were recombined. The effective amount of missing information for the association between the exposure of interest and mammographic density was estimated to be <2% in all analyses.

We conducted a difference-in-difference analysis to investigate whether the association between GWG and mammographic density remained after considering fixed family-level effects. We randomly chose 2 siblings from families with >2 siblings enrolled, for a total sample of 254 siblings. We subtracted the values of the younger sibling from the older sibling for continuous predictors. We used multivariable linear regression to assess the association between the difference in GWG and mammographic density between siblings, controlling for differences in age, maternal age at registration, and BMI. For this analysis, participants with missing covariate data were excluded (8.6%).

RESULTS

A total of 700 mother-child dyads from the NCPP and the CHDS were included in this study (Table 1). The mean prepregnancy BMI was 23.3 kg/m^2 and the mean GWG was 9.2 kg. There were some differences across the sites: mothers from the NCPP were on average younger, had a lower prepregnant BMI, and were less likely to be nonwhite. NCPP mothers were less educated and more likely to smoke during pregnancy. Adult daughters were also different by site, with NCPP daughters more likely to be older, have a lower BMI, and higher dense area. Maternal prepregnancy BMI and GWG were inversely correlated (Fig 1).

TABLE 1 Descriptive Characteristics of Study Sample by Site and Overall, EDMD Study, $n = 700$

	Overall			NCPP			CHDS			*P*
	n	Mean/*n*	Std/%	*n*	Mean/*n*	Std/%	*n*	Mean/*n*	Std/%	
Maternal variables										
Maternal age at registration	700	26.2	5.9	352	25.6	6.0	348	26.8	5.7	.004
Maternal prepregnant BMI	656	23.3	3.8	322	22.9	3.9	334	23.6	3.8	.03
Maternal GWG, kg	675	9.2	4.0	335	9.0	4.0	340	9.4	4.0	.13
Maternal race										
Non-Hispanic white	—	577	82.4	—	322	91.5	—	255	73.3	.001[a]
Non-Hispanic black	—	82	11.7	—	29	8.2	—	53	15.2	
Non-Hispanic API and other	—	16	2.3	—	1	0.3	—	15	4.3	
Hispanic	—	25	3.6	—	—	—	—	25	7.2	
Maternal education at registration										
Less than high school	—	180	25.9	—	124	35.8	—	56	16.1	<.0001
High school graduate	—	289	41.6	—	164	47.4	—	125	35.9	
Some college/technical/trade school or college graduate	—	225	32.4	—	58	16.8	—	167	48.0	
Prenatal smoke										
Prenatal smoke	—	272	40.1	—	176	50.3	—	96	29.3	<.0001
No prenatal smoke	—	406	59.9	—	174	49.7	—	232	70.7	
Daughters' adult variables										
Age at menarche, y	696	12.7	1.6	349	12.8	1.6	347	12.7	1.6	.25
BMI	686	27.5	6.4	345	26.9	5.5	341	28.1	7.2	.02
Age at interview, y	700	44.1	1.8	352	44.5	1.9	348	43.7	1.6	<.0001
Age at mammogram, y	700	43.1	2.3	352	43.1	2.5	348	43.0	2.1	.48
Percent density	700	31.8	18.7	352	32.2	17.4	348	31.4	19.9	.58
Dense area, cm^2	700	35.8	22.0	352	37.6	21.9	348	33.9	21.9	.02
Breast area, cm^2	700	137.8	74.0	352	139.2	73.0	348	136.4	75.0	.62

API, Asia and Pacific Islanders.

[a] *P* value only for comparing distribution of white and black race between sites.

We examined the association between maternal anthropometric pregnancy characteristics and the daughter's mammographic density in multivariable linear regression models simultaneously adjusting for the age at mammogram, BMI at mammogram, study site, and, in second models, additionally for race, maternal education, and maternal smoking during pregnancy. In these models, maternal prepregnancy BMI was not related to the daughter's mammographic breast density for both percent density and dense area (Table 2). When the top 2 categories were collapsed, the results did not appreciably change (prepregnancy BMI ≥25: percent density: β = −2.3, 95% confidence interval [CI]: −5.7 to 1.1; dense area: β = −1.6, 95% CI: −7.1 to 3.9). No statistically significant effect modification by geographic site was observed (data not shown).

The association between GWG in pregnancy and the daughter's mammographic breast density was also examined in multivariable linear regression models for both percent density and dense area (Table 3). We found an increased percent breast density in the daughter among mothers who gained ≤5 kg during pregnancy compared with mother-daughter pairs in which the mother gained 5 to 10 kg. This association only became statistically significant after adjusting for maternal prepregnancy BMI and maternal smoking during pregnancy (β = 4.8, 95% CI: 1.0 to 8.6). GWG of ≥15 was inversely associated with percent density, although this association was not statistically significant (β = −3.5, 95% CI: −7.8 to 0.8). There was no association between GWG and dense area. The association between GWG and either measure of mammographic breast density was not modified by geographic site (data not shown).

We examined the differences between continuous measures of prepregnancy BMI and GWG and

TABLE 2 Regression Coefficients (β) and 95% CIs for the Association Between Maternal Prepregnancy BMI and Mammographic Density in the Daughter in 656 Women Participating in the EDMD Study

	n = 656	Percent Density		Dense Area	
		Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
		β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Prepregnancy BMI					
<23.0	368	0.0 (−2.9 to 2.8)	0.0 (−2.7 to 2.8)	−3.2 (−7.6 to 1.3)	−2.8 (−7.2 to 1.5)
23.0 to <25.0	124	0.0 (Ref)	0.0 (Ref)	0.0 (Ref)	0.0 (Ref)
25.0 to <30.0	120	−2.4 (−6.0 to 1.3)	−2.5 (−6.1 to 1.2)	−2.6 (−8.3 to 3.1)	−2.7 (−8.4 to 3.0)
≥30.0	44	−1.5 (−7.4 to 4.5)	−1.7 (−7.6 to 4.1)	1.1 (−9.3 to 11.5)	1.7 (−8.7 to 12.0)
P for trend		0.24	0.18	0.34	0.39

[a] Adjusted for age at mammogram, site, and adult BMI.
[b] Adjusted for age at mammogram, site, adult BMI, maternal education, race, and maternal smoking.

TABLE 3 Regression Coefficients (β) and 95% CIs for the Association Between GWG and Mammographic Density in the Daughter, in 675 Women Participating in the EDMD Study

	n = 675	Percent Density		Dense Area	
		Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
		β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Gestational weight gain, kg					
≤5	79	3.4 (−0.3 to 7.2)	4.8 (1.0 to 8.6)	4.7 (−1.0 to 10.4)	3.7 (−1.9 to 9.4)
>5–10	335	0.0 (Ref)	0.0 (Ref)	0.0 (Ref)	0.0 (Ref)
>10–15	222	1.9 (−0.8 to 4.5)	1.8 (−0.8 to 4.4)	3.3 (−0.3 to 6.9)	2.8 (−0.7 to 6.4)
>15	39	−3.4 (−7.9 to 1.0)	−3.5 (−7.8 to 0.8)	−0.7 (−9.5 to 8.2)	−1.0 (−9.5 to 7.4)
P for trend		.34	.14	.92	.98

[a] Adjusted for age at mammogram, site, and adult BMI.
[b] Adjusted for age at mammogram, site, adult BMI, maternal education, maternal prepregnancy BMI, race, and maternal smoking.

mammographic density. There was no significant interaction between the 2 maternal anthropometric indicators (Wald test for fully adjusted models: $P = .35$ for percent density; $P = .83$ for dense area) a model with the 2 main effects was fit. There were no statistically significant associations for maternal weight indicator and the daughters' density either as overall percent or as dense area measures when these exposure constructs were measured by using continuous variables (Table 4).

Because GWG recommendations depend on prepregnancy BMI, we considered the joint effect of maternal prepregnancy BMI and gestational weight on the daughters' mammographic density (Table 5). The daughters of mothers who were overweight at the time of conception (prepregnancy BMI of ≥25) and who gained >10 kg during pregnancy had a lower percent density (β = –5.0, 95% CI: –9.9 to –0.6) compared with mothers with a BMI of <25 at conception who gained >10 kg. Overall, all maternal weight combinations resulted in lower percent density and dense area relative to a prepregnancy BMI

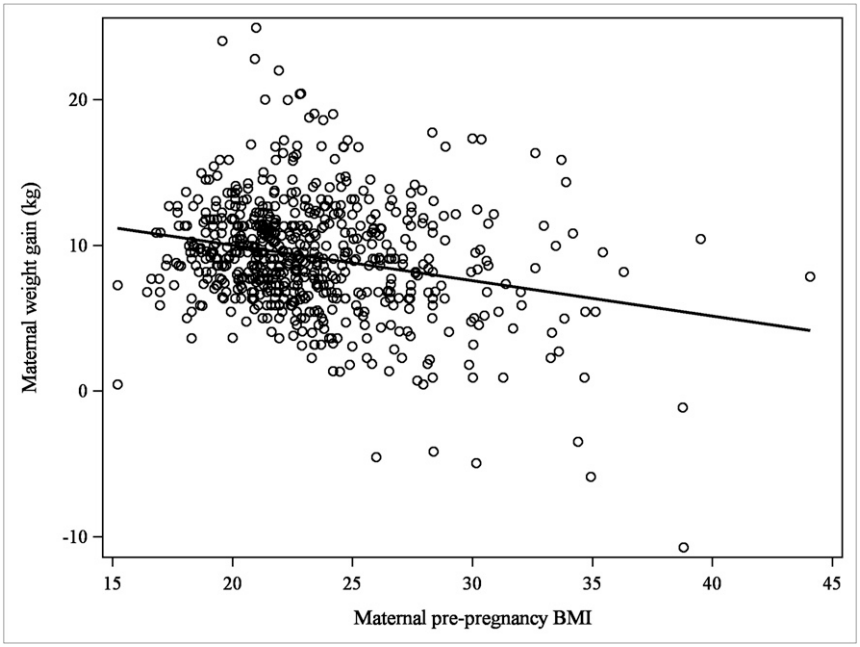

FIGURE 1
Distribution of maternal prepregnancy BMI and GWG in the study population; *n* = 700.

TABLE 4 Regression coefficients (β) and 95% CIs for the Association Between Maternal Prepregnancy BMI, GWG, and Mammographic Density in the Daughter, in 646 Women Participating in the EDMD Study

	Percent Density		Dense Area	
	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Maternal prepregnancy BMI	−0.3 (−0.7 to 0.0)	−0.4 (−0.7 to 0.1)	0.3 (−0.2 to 0.8)	0.2 (−0.3 to 0.7)
GWG, kg	−0.2 (−0.5 to 0.2)	−0.2 (−0.5 to 0.2)	0.1 (−0.4 to 0.7)	0.1 (−0.4 to 0.6)

[a] Adjusted for age at mammogram, site, and BMI.
[b] Adjusted for age at mammogram, site, BMI, maternal education, race, and maternal smoking.

TABLE 5 Regression Coefficients (β) and 95% CIs for the Joint Effects of Maternal Prepregnancy BMI and GWG on Mammographic Density in the Daughter, in 646 Women Participating in the EDMD Study

	n = 646	Percent Density		Dense Area	
		Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
		β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
GWG and maternal prepregnancy BMI, categorized					
Maternal prepregnancy BMI <25 and gestational weight gain ≤10 kg	284	−1.4 (−4.1 to 1.4)	−1.7 (−4.4 to 1.0)	−3.5 (−7.4 to 0.5)	−3.3 (−7.1 to 0.5)
Maternal prepregnancy BMI ≥25 and gestational weight gain ≤10 kg	110	−2.1 (−6.1 to 1.8)	−2.4 (−6.2 to 1.5)	−0.3 (−6.2 to 5.6)	−0.3 (−6.1 to 5.6)
Maternal prepregnancy BMI <25 and gestational weight gain >10 kg	198	0.0 (Ref)	0.0 (Ref)	0.0 (Ref)	0.0 (Ref)
Maternal prepregnancy BMI ≥25 and gestational weight gain >10 kg	54	−4.5 (−9.4 to 0.4)	−5.0 (−9.9 to −0.6)	−2.9 (−9.9 to 4.0)	−3.4 (−10.4 to 3.7)

[a] Adjusted for age at mammogram, site, and adult BMI.
[b] Adjusted for age at mammogram, site, adult BMI, maternal education, maternal prepregnancy BMI, race, and maternal smoking.

<25 and GWG of >10 kg, but none was statistically significant.

Our sibling set analysis included 116 sets of siblings with a total of 232 individuals. Table 6 summarizes the results of the sibling differences in mammographic breast density by the difference in maternal GWG. Models were adjusted for sibling differences in age at interview, maternal age at registration, and adult BMI. Prepregnancy BMI was highly correlated across pregnancies within mothers; therefore, we did not include this variable in the regression models. The regression coefficient represents the difference in percent density and dense area in the sisters for a 1-kg difference in GWG for the respective pregnancies (Table 6). We observed a 0.4 or 0.5 lower percent density and dense area per kg difference between siblings in GWG, respectively, implying that the sister with the higher GWG had a lower percent density after adjusting for differences in age at interview,

TABLE 6 Relation Between Difference in Maternal GWG and Difference in Mammographic Density Between Siblings, EDMD Study, *n* = 232 (116 Sets)

	Percent Density[a]	Dense Area[a]
	β (95% CI)	β (95% CI)
Difference in GWG, kg	−0.4 (−1.3 to 0.6)	−0.5 (−1.8 to 0.9)

[a] Adjusted for differences in age at interview, maternal age at registration, and adult BMI.

maternal age at pregnancy, and adult BMI and fixed-level family effects by design. Although there was generally a lower percent density or dense area the higher the difference in GWG, these differences were not statistically significant.

DISCUSSION

In this prospective analysis of NCPP and CHDS participants, we did not find an overall association between maternal pregnancy anthropometry and the daughter's mammographic density. We did, however, observe a statistically significantly higher percent dense mammary tissue, but not absolute dense area, independent of their own BMI among daughters whose mothers gained <5 kg during pregnancy. Among overweight mothers, a GWG of >5 kg was also associated with a lower percent density among the daughters. The patterns for dense area were similar but not statistically significant.

Percent density is measured as the total dense area divided by the total breast area, whereas dense area measures the absolute total area of breast tissue in the breast. Higher BMI maps to higher total breast area so mammographic breast density is generally inversely correlated with overall BMI, even though dense area may be weakly positively associated with BMI. Breast density measures must therefore be considered in the

context of BMI at the time the image was taken.

To our knowledge, this is the first study on maternal pregnancy-related anthropometry and the daughter's breast density. The relation of the weight parameters with the daughter's breast cancer risk has been considered in only 2 previous studies.[4,5] In a case-control study in Washington State using recalled data on maternal anthropometry, no overall association with the daughter's breast cancer risk was found.[4] Although no trend was observed across maternal weight gain, women whose mothers gained 25 to 34 lb had a statistically significant increased risk of breast cancer compared with mothers with a GWG of 15 to 24 lb (odds ratio 1.5; 95% CI: 1.1 to 2.0); weight gains of ≥35 lb or <15 lb were not associated with risk. No relation between the mother's prepregnancy BMI and the daughter's breast cancer risk was observed. By using data from the Nurses' Health Study, the Nurses' Health Study II, and the Nurses' Mothers' Cohort, Wilson and colleagues[5] examined whether the mothers' prepregnancy BMI and/or weight gain during pregnancy, both of which were recalled by the mothers when the nurses were adults, affected the risk of breast cancer in the daughter. Using a risk set analysis, they did not identify any association.

Consistent with these previous studies of maternal pregnancy weight gain and daughter's breast cancer risk, we also did not observe any strong patterns with mammographic breast density. We did, however, observe an inverse association between GWG and percent mammographic density, adjusting for the daughter's BMI at the time of mammogram, for mothers who gained little weight during pregnancy (<5 kg). Low GWG has been related to low adolescent body size in the offspring,[13] which has been linked to higher mammographic density.[14] However, in other studies, maternal GWG of <10 lb was associated with adult obesity in the daughter.[15]

GWG and prepregnancy BMI are inversely associated with sex hormone binding globulin levels during pregnancy, which in turn increases levels of bioavailable estrogen.[16,17] A highly estrogenic environment in utero has been suggested to increase the risk of breast cancer,[18] which may be partly mediated by mammographic density.[19] However, GWG is also positively associated with birth weight,[20] which may be positively associated with mammographic density at least in postmenopausal women, although data are limited.[21]

The Institute of Medicine's GWG recommendations base the recommended amount of weight for a woman to be gained during pregnancy on her prepregnancy BMI.[22] It is therefore sensible to consider prepregnancy BMI and GWG as a composite variable. The association between low GWG (<5 kg) and mammographic density was no longer observed when we stratified by maternal prepregnancy BMI resulting in low weight gain (<10 kg) being inversely associated with mammographic density, although these associations were not statistically significant.

Generalization of our results to today's pregnancy conditions has to be done with caution because both prepregnancy BMI and GWG were considerably lower in the EDMD than in today's pregnancy populations. Specifically, both prepregnancy BMI and GWG have increased over time.[22]

In conclusion, we did not find any strong and consistent patterns between maternal anthropometry and the daughter's breast density, a strong predictor of breast cancer risk. A modest association between low GWG and breast density 40 years later in the daughter was observed, even after accounting for adult body size, and if confirmed, possible mechanisms need to be further elucidated. In addition to well-accepted risk factors for breast cancer, such as family history, evidence is growing regarding the role of other potentially modifiable factors (eg, diet, weight throughout life including birth weight, environmental exposures) and windows of susceptibility during the life course.[23] Studying the association between maternal anthropometry and breast density in the adult daughter is important in light of the obesity epidemic and because it is an example of a fetal exposure with health implications later in life. By addressing this and other early life exposures associated with breast development and breast cancer risk, pediatricians can be engaged in primary breast cancer prevention.

ABBREVIATIONS

CHDS: Childhood Health and Development Study in California
CI: confidence interval
EDMD: Early Determinants of Mammographic Density
GWG: gestational weight gain
NCPP: National Collaborative Perinatal Project

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