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Maternal body mass index and daughters' age at menarche

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Abstract

Background—The role of inter-generational influences on age at menarche has not been explored far beyond the association between mothers' and daughters' menarcheal ages. Small size at birth and childhood obesity have been associated with younger age at menarche, but the influence of maternal overweight or obesity on daughters' age at menarche has not been thoroughly examined.

Methods—In a follow-up study of the prospective Collaborative Perinatal Project grown daughters were asked in 1987-1991 for their age at menarche. Data from the original Collaborative Perinatal Project (1959-1966) included their mothers' height and pre-pregnancy weight. In the follow-up study, 597 of 627 daughters had complete menarche and maternal data available and were included in the present analysis. We used polytomous logistic regression to examine the association between maternal overweight (body mass index [BMI] = 25-29.9 kg/m²) or obesity (BMI ≥ 30) and daughter's age at menarche (< 12, 12, 13, > 13 years).

Results—Compared with those whose mothers had a BMI less than 25, daughters of obese mothers experienced younger age at menarche (OR for menarche at < 12 years=3.1 [1.1 - 9.2]). This association remained after adjusting for maternal age at menarche, maternal parity, socioeconomic status, race, and study site (OR=3.3 [1.1 - 10.0]). Effect estimates for maternal overweight were close to the null. There was limited evidence of mediation by small-for-gestational age or BMI at age 7.

Conclusions—Maternal obesity is associated with younger menarcheal age among daughters in this study, possibly via unmeasured shared factors.

INTRODUCTION

Whether the average age at menarche in the U.S. is continuing to decrease is controversial.¹⁻⁴ Early puberty has been associated with later life glucose intolerance, high blood pressure, depression and breast cancer.⁵⁻⁸ Discussion about a possible trend toward

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younger pubertal age has focused on the increase in obesity prevalence among children.^{9, 10} Previous studies have noted an association of childhood obesity with earlier menarche and with breast and pubic hair development.^{4, 11, 12} Additionally, a variety of prenatal factors has been associated with pubertal timing. Small size at birth has been associated with early menarche, although not consistently.¹³⁻¹⁷ Several studies have found fetal growth restriction with rapid growth during childhood to be associated with younger menarche.^{18, 19} Age at menarche has inter-generational or genetic underpinnings as well, in that age at menarche is correlated across generations.^{20, 21}

Despite the focus on child growth and body size in relation to pubertal timing, there has been less attention to whether maternal body size plays a role in pubertal timing for the offspring. Maternal pre-pregnancy body size is positively correlated with offspring body size in that obese women are less likely to give birth to a small infant,²² and the children of obese women are more likely to be overweight.²³ If maternal obesity is associated with earlier menarche among the offspring, it may be through a pathway different from the one involving small-for-gestational age (SGA) infants, who experience rapid catch-up growth and subsequent earlier menarche.

Previous studies have not thoroughly examined the association between maternal body mass index (BMI) and pubertal timing among offspring. In a few studies, taller maternal height has been associated with later menarche among daughters, but less is known about the possible relationship with maternal weight or BMI.^{14, 24} We used data from the Collaborative Perinatal Project to address the hypothesis that high maternal pre-pregnancy BMI is associated with younger age at menarche among daughters.

METHODS

The Collaborative Perinatal Project enrolled women (55,000 pregnancies) at the first prenatal visit at 12 U.S. sites (1959-1965).²⁵ Women were followed prospectively through delivery, and their offspring were followed to age 7 or 8. We refer to the pregnant women enrolled in the study as “mothers” and their offspring as “daughters.” A sample of daughters from two sites was recontacted in 1987-1991 when they were ages 22-32 years. Study staff interviewed 627 daughters (the subjects for the present study) who reported having had at least one pregnancy lasting through at least 20 weeks’ gestation. The design and methods of this follow-up study have been described previously.²⁶ This study was ruled exempt from Institutional Review Board review by the NIH Office of Human Subjects Research.

Interviewers recorded a health history of mothers at the first prenatal visit, including the age (in years) at menarche, number and outcome of all prior pregnancies, and pre-pregnancy weight. Maternal parity was defined as the number of non-aborted pregnancies of 20+ weeks’ gestation that occurred before the conception of the daughter in the present study. Parity categories were defined as 0, 1-2, and 3+ prior pregnancies. Maternal age at menarche was categorized by quartiles (< 12, 12, 13, > 13 years).

Maternal pre-pregnancy BMI (weight [kg] / height [m²]) was calculated based on height measured at the first visit and self-reported pre-pregnancy weight. Categories of underweight or normal weight (BMI < 25), overweight (BMI = 25.0-29.9) and obese (BMI ≥ 30) were constructed. A continuous socioeconomic index, developed by the Census Bureau, was applied that incorporated education level and occupation of the head of household and family incomes.^{27,28}

Birthweight and gestational age of the daughters were measured at birth, and daughters participated in a visit around the age of 7 years.²⁶ At the later visit, height was measured to the nearest 0.5 centimeters using a standardized backboard, and weight was recorded in

pounds to the nearest 0.25 pounds or grams to the nearest 100 grams using scales calibrated semiannually.²⁶ For this analysis, daughters' childhood BMI-for-age z-scores were calculated based on the Centers for Disease Control and Prevention growth charts for daughters who were aged 6 years, 9 months to 8 years, 3 months at the age 7 visit.²⁹ We excluded from our mediator analysis involving BMI at age 7, those daughters who missed the age 7 study visit, were missing anthropometrics, or attended the visit when they were older than 8 years, 3 months (n=103; 17.3%).

Daughters' age at menarche is the outcome of interest for this study. As part of the follow-up study of daughters during adulthood, interviewers asked, "how old were you when you had your first period?" and "do you remember what grade you were in?". We relied on the stated age for 617 daughters. Four daughters provided a grade but no age, and we converted seventh grade to 12 years old and eighth grade to 13 years old. Six daughters were missing both age and grade information. Thus, 621 daughters (99 percent) had menarcheal age reported. Daughters were also asked to identify their race. When missing, race recorded during childhood was used. Analytic categories of race were established as Black and all others.

There were 597 of 627 interviewed daughters (95 percent) with complete data for age at menarche and their mother's pre-pregnancy BMI. These were included in the main analysis and a mediator analysis involving SGA status. The 494 daughters with a calculable BMI at age 7 were included in a mediator analysis involving childhood BMI.

We used SAS version 9.1 for all statistical analyses.³⁰ Associations between covariates and the exposure and outcome were evaluated using the mean score statistic. We used polytomous logistic regression to examine the relationship between daughters' age at menarche and maternal pre-pregnancy BMI. The categories of maternal obesity and overweight were compared with a reference of normal/underweight. Socioeconomic index, maternal parity, maternal age at menarche, and daughter's race were identified as potential confounders a priori and were included in the adjusted models. No covariates were found to be notable effect modifiers. Because of the sampling procedures, a variable for study site was included in models. We conducted a mediator analysis to examine to what extent BMI-for-age Z-score at age 7 or being born SGA might mediate the association between maternal BMI and age at menarche.³¹ To test for mediation by BMI-for-age Z-score at age 7, we built 3 regression equations: BMI-for-age Z-score on maternal BMI, menarcheal age on maternal BMI, and menarcheal age on both maternal BMI and BMI-for-age Z-score. BMI-for-age Z-score would be a mediator if all of the following hold in the expected direction: maternal BMI is associated with BMI-for-age Z-score, maternal BMI is associated with daughter's menarcheal age, and BMI-for-age Z-score is associated with daughters' menarcheal age (in the third equation), plus the association between maternal BMI and menarcheal age is attenuated when BMI-for-age Z-score is included in the model. We repeated this to examine SGA as a potential mediator.

RESULTS

Table 1 describes the relationships between mothers' and daughters' characteristics and mothers' pre-pregnancy BMI. Parity was positively associated and maternal age at menarche was negatively associated with maternal BMI. Black race was associated with higher maternal BMI. Mothers' pre-pregnancy BMI and daughters' age-7 BMI were positively correlated.

The participant characteristics examined in relation to daughters' menarcheal age are displayed in Table 2. The mean age at menarche was slightly older for daughters than

mothers (mean for daughters=12.8 years; mean for mothers=12.6, paired $t=2.2$, $P=0.03$). Daughters' BMI-for-age at age 7 was inversely associated with age at menarche, and Black race was associated with younger age at menarche among daughters.

Results from the polytomous logistic models are reported in Table 3. The odds of menarche at less than 12, or at 12 or 13 years, compared with greater than 13 years, was not different for daughters of overweight mothers compared with daughters of normal or underweight mothers. Daughters of obese mothers had an increased odds of menarche at less than 12 years (3.3 [95% CI = 1.1 - 10.0]) compared with daughters of normal or underweight mothers. The odds of menarche at 12 or 13 years for daughters of obese mothers compared with daughters of normal or underweight mothers were also elevated but progressively closer to the null.

To evaluate whether the effect seen for maternal BMI might be due to maternal height, we evaluated the association between maternal height and daughters' age at menarche; we observed no clear association (adjusted OR for menarche at < 12 years for > 65 inches compared with < 62 inches=1.2 [95% CI = 0.7 - 2.1]). After accounting for the potential mediating role of childhood BMI, the observed association between maternal obesity and daughters' age at menarche was not attenuated (adjusted OR for < 12 years=3.2 [1.0 - 9.8]). Similar results were observed for the mediator analysis for SGA status (adjusted OR for < 12 years=3.4 [1.1 - 10.2]). In addition, BMI-for-age Z-score and SGA status were associated with daughters' age at menarche in models that included maternal BMI and other covariates (ORs ranged from 0.8 to 1.2). Thus, BMI-for-age Z-score at age 7 and SGA status do not appear to play a notable mediating role.

DISCUSSION

This study examined the relationship between maternal pre-pregnancy BMI and daughters' menarcheal age. Maternal obesity was found to be associated with an increased odds of menarche at less than 12 years of age in daughters, while overweight had no effect. The association for maternal obesity could operate via several possible pathways. First, maternal obesity could increase the risk of obesity among offspring via shared lifestyle or genetic factors, and then obesity during childhood itself lowers the menarcheal age. Second, unmeasured shared genetic or postnatal factors could underlie both maternal obesity and daughters' age at menarche. Third, in utero exposure to biologic factors stemming from maternal obesity such as leptin, a marker for both maternal and fetal adiposity, could alter the timing of daughters' sexual maturation years later.³² During pregnancy, leptin appears to be involved in diverse processes including regulation of energy transfer to the fetus and fetal growth, stimulation of the hypothalamic-pituitary axis, and endometrial function.^{32, 33} Leptin also appears to be important in pubertal timing and fertility.¹⁰

The current study indicates that BMI at age 7 was not an important mediator of the association, which would suggest less of an influence of a pathway working through childhood obesity. Being born SGA could also be a mediating influence, although most studies have found obese women to be less like to have a SGA infant and so it is unlikely to be an important explanation. SGA status was not found to be a mediator of the association between maternal BMI and menarcheal age. Future research could evaluate whether biologic factors related to maternal obesity is a reasonable explanation, or if unmeasured confounding factors explain the association.

In this sample, the mean age at menarche for the daughters was slightly older than for the mothers. This may be explained by the slightly different methods used to assess menarcheal age for mothers and daughters (interview during first prenatal visit versus in-person

interview sometime after a first pregnancy) or the differences in the length of recall (mean number of years between first menstruation and the interview was 11.1 years for mothers vs 13.8 years for daughters).

There are few studies that have focused on the association between maternal BMI and daughters' age at menarche. However, a recent study,³⁴ which was based partly on the data used in the present analysis (focused on maternal smoking and demographic characteristics and their associations with offspring menarche), included maternal BMI as a covariate. The authors observed a lower mean age at menarche as maternal BMI increased but did not use standard classifications for overweight and obesity; they also did not assess the potential mediating role of SGA or childhood BMI.³⁵

Our study is subject to several limitations. Age at menarche was based on recall in adulthood, which may be less accurate than recall closer to the event.^{36, 37} Maternal report of pre-pregnant weight may be prone to underestimation, but this would not account for the association because this bias would tend to draw the effect estimates toward the null.^{38, 39} Also, information about breast development and pubic hair were not collected; it is possible that maternal obesity could have differing effects on these markers. This study was limited to daughters who reported having had at least one pregnancy lasting 20 or more weeks, thus potentially excluding those with menstrual disorders to the extent that such disorders might compromise the ability to conceive or carry a pregnancy to term. Finally, the sample size limited our ability to more closely examine effects at the ends of the spectrum of age at menarche. Also, the prevalence of obesity was relatively low among women in the Collaborative Perinatal Project, so the number of exposed daughters was small. This sample of mothers was slightly shorter and lighter than the general U.S. population at the time.⁴⁰

This study has several strengths. The Collaborative Perinatal Project and its follow-up component is one of very few studies that have followed mothers and their daughters from the start of prenatal care to the daughters' adulthood. Thus, the study did not rely on proxy reports for the exposure, outcome and covariates. Also, the study had complete data for the exposure and outcome for more than 95 percent of the eligible participants. The sample size for the present study is larger than some previous studies of prenatal factors and pubertal timing.

Maternal obesity pre-pregnancy may be associated with earlier at menarche among daughters, independent of daughters' own childhood BMI. However, these associations remain to be examined in larger, and possibly more representative and contemporary, samples. Additional research into the early life and inter-generational factors underlying menarcheal age, including the possible role of maternal obesity, may enhance understanding of later-life disease processes and secular trends.

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Table 1

Participant characteristics by maternal pre-pregnancy body mass index, Collaborative Perinatal Project, 1959-1965 and 1989-1991

	Maternal BMI (kg / m ²)		
	< 25 (n=466) No. (%)	25.0-29.9 (n=94) No. (%)	≥ 30 (n=37) No. (%)
Maternal socioeconomic index ^a			
< 27 (low)	97 (21)	24 (26)	6 (16)
27-39	104 (22)	26 (28)	8 (22)
40-52	135 (29)	24 (26)	18 (49)
> 52	115 (25)	18 (19)	4 (11)
Missing	15 (3)	2 (2)	1 (3)
Maternal parity			
0	131 (28)	16 (17)	3 (8)
1-2	189 (41)	32 (34)	12 (32)
> 2	145 (31)	46 (49)	22 (59)
Missing	1 (<1)		
Maternal age at menarche (years)			
< 12	107 (23)	27 (29)	14 (38)
12	110 (24)	24 (26)	10 (27)
13	140 (30)	19 (20)	6 (16)
>13	106 (23)	24 (26)	7 (19)
Missing	3 (1)		
Daughter race			
Black	314 (67)	74 (79)	31 (84)
All others	152 (33)	20 (21)	6 (16)
Daughter BMI-for-age percentile ^b			
< 85 th	343 (74)	67 (71)	26 (70)
85 th to less than 95 th	26 (6)	10 (11)	4 (11)
≥ 95 th	10 (2)	3 (3)	5 (14)
Missing	87 (19)	14 (15)	2 (5)
Daughter SGA status			
SGA	124 (27)	21 (22)	7 (19)
Not SGA	342 (73)	73 (78)	30 (81)

^aBased on the mothers' socioeconomic status at the time of the first prenatal visit

^bBased on CDC growth charts for BMI at age 7 among girls

Table 2

Participant characteristics and daughters' age at menarche

	Daughters' age at menarche (years)			
	<12 (n=121) No. (%)	12 (n=158) No. (%)	13 (n=147) No. (%)	>13 (n=171) No. (%)
Maternal socioeconomic index ^a				
< 27 (low)	20 (17)	33 (21)	37 (25)	37 (22)
27-39	34 (28)	45 (28)	26 (17)	33 (19)
40-52	41 (34)	40 (25)	40 (27)	56 (33)
> 52	23 (19)	35 (22)	40 (27)	39 (23)
Missing	3 (2)	5 (3)	4 (3)	6 (4)
Maternal parity				
0	33 (27)	43 (27)	36 (24)	38 (22)
1-2	48 (40)	63 (40)	58 (39)	64 (37)
> 2	40 (33)	52 (33)	52 (35)	69 (40)
Missing			1 (1)	
Maternal age at menarche (years)				
< 12	37 (31)	46 (29)	28 (19)	37 (22)
12	31 (26)	39 (25)	39 (27)	35 (20)
13	27 (22)	44 (28)	39 (27)	55 (32)
>13	26 (21)	27 (17)	40 (27)	44 (26)
Missing		2 (1)	1 (1)	
Daughter race				
Black	90 (74)	127 (80)	99 (67)	103 (60)
All others	31 (26)	31 (20)	48 (33)	68 (40)
Daughter BMI-for-age percentile ^b				
< 85 th	82 (68)	113 (72)	108 (73)	133 (78)
85 th to less than 95 th	12 (10)	9 (6)	9 (6)	10 (6)
≥ 95 th	6 (5)	10 (6)	1 (1)	1 (1)
Missing	21 (17)	26 (16)	29 (20)	27 (16)
Daughter SGA status				
SGA	35 (29)	42 (27)	36 (24)	39 (23)
Not SGA	86 (71)	116 (73)	111 (76)	132 (77)

^aBased on the mothers' socioeconomic status at the time of the first prenatal visit^bBased on CDC growth charts for BMI at age 7 among girls

Table 3

Crude and adjusted odds ratios (polytomous logistic regression models) for daughters' age at menarche

Maternal BMI (kg/m ²)	Daughters' age at menarche (years)											
	<12			12			13			>13 ^c		
	No. (%)	Unadjusted ^a OR (95% CI)	Adjusted ^b OR (95% CI)	No. (%)	Unadjusted ^a OR (95% CI)	Adjusted ^b OR (95% CI)	No. (%)	Unadjusted ^a OR (95% CI)	Adjusted ^b OR (95% CI)	No. (%)	Unadjusted ^a OR (95% CI)	Adjusted ^b OR (95% CI)
≥ 30	12 (10)	3.1(1.1, 9.2)	3.3(1.1, 10.0)	13 (8)	2.5(0.9, 7.2)	2.7(0.9, 8.3)	7 (5)	1.5(0.5, 4.9)	1.8(0.5, 5.8)	5 (3)	1.0	1.0
25.0-29.9	22 (18)	1.1(0.6, 2.1)	1.1(0.6, 2.1)	23 (15)	0.8(0.5, 1.5)	0.8(0.4, 1.5)	22 (15)	0.9(0.5, 1.7)	0.9(0.5, 1.6)	27 (16)	1.0	1.0
< 25 ^c	87 (72)	1.0	1.0	122 (77)	1.0	1.0	118 (80)	1.0	1.0	139 (81)	1.0	1.0

^a Adjusted for study site.^b Adjusted for study site, socioeconomic index, maternal parity, maternal age at menarche and daughter's race.^c Reference category.