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Role of Prenatal Characteristics and Early Growth on Pubertal Attainment of British Girls

Mildred Maisonet, PhD^{a,b}, Krista Yorita Christensen, PhD^b, Carol Rubin, DVM, MPH^a, Adrienne Holmes, MPH^a, W. Dana Flanders, MD, DSc^{a,b}, Jon Heron, PhD^c, Ken K. Ong, MD^d, Jean Golding, PhD^e, Michael A. McGeehin, PhD^a, and Michele Marcus, PhD^{a,b}

^aNational Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia ^bEpidemiology Department, Rollins School of Public Health, Emory University, Atlanta, Georgia ^cDepartment of Social Medicine, University of Bristol, Bristol, England ^dMRC Epidemiology Unit, Institute of Metabolic Science, Cambridge, England ^eCentre for Child and Adolescent Health, Department of Community Based Medicine, University of Bristol, Bristol, England

Abstract

OBJECTIVES—The objective of this study was to explore the influence of maternal prenatal characteristics and behaviors and of weight and BMI gain during early childhood on the timing of various puberty outcomes in girls who were enrolled in the Avon Longitudinal Study of Parents and Children.

METHODS—Repeated self-assessments of pubertal development were obtained from ~4000 girls between the ages of 8 and 14. Data on prenatal characteristics and weight at birth and 2, 9, and 20 months of age were obtained from questionnaires, birth records, and clinic visits. Infants' weights were converted to weight-for-age and BMI SD scores (SDSs; z scores), and change values were obtained for the 0- to 20-month and other intervals within that age range. We used parametric survival models to estimate associations with age of entry into Tanner stages of breast and pubic hair and menarche.

RESULTS—Maternal initiation of menarche at age <12, smoking during pregnancy, and primiparity were associated with earlier puberty. A 1-unit increase in the weight SDS change values for the 0- to 20-month age interval was associated with earlier ages of entry into pubertal outcomes (0.19–0.31 years). Increases in the BMI SDS change values were also associated with earlier entry into pubertal outcomes (0.07–0.11 years).

CONCLUSIONS—Many of the maternal prenatal characteristics and weight and BMI gain during infancy seemed to have similar influences across different puberty outcomes. Either such early factors have comparable influences on each of the hormonal processes involved in puberty, or processes are linked and awakening of 1 aspect triggers the others.

Address correspondence to Mildred Maisonet, PhD, Emory University, Rollins School of Public Health, Department of Epidemiology, 1518 Clifton Road NE, Atlanta, GA 30322. mmaison@sph.emory.edu.

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Keywords

ALSPAC; puberty; Tanner stages; postnatal growth; obesity

Puberty marks the transition from childhood into adolescence, during which secondary sexual characteristics appear and reproductive maturity is achieved. In the developed world, reproductive maturity occurs at an earlier age today than in the past. It seemed that the secular trend in average age of menarche attainment had leveled off at the middle of the 19th century in the United States and some Northern European countries.^{1,2} In contrast, recent studies from the United States and Europe have noted that onset of breast development is occurring at younger ages in girls, thus suggesting a continued trend.^{3,4} Early pubertal development has potentially important implications for an adolescent's behavior. It is associated with earlier age of sexual debut and cigarette and alcohol use.^{5,6} It is also associated with higher risk for metabolic diseases and cancer later in life.^{6,7}

Obesity, genetics, race, and exposures to environmental pollutants with endocrine-disrupting properties are suggested to be associated with earlier pubertal attainment in girls at ages when puberty is considered normal (age on onset 8 years).^{8–11} Rapid weight gain in infancy also seems to be associated with earlier menarche attainment.^{12–14} Previous analyses conducted in our target population, girls enrolled in the Avon Longitudinal Study of Parents and Children (ALSPAC), reported that higher weight gain during infancy was associated with a higher risk for menarche attainment in girls who are younger than 12 in comparison with older girls.¹⁴

Puberty processes depend on the reactivation of the hypothalamic-pituitary-gonadal axis causing the releases of luteinizing and follicle-stimulating hormones from the pituitary, which in turn induces gonadal maturation.¹⁵ In parallel, adrenal androgen secretions that are associated with the development of the zona reticularis of the adrenal glands stimulates the growth of androgen-dependent hair and development of apocrine glands.¹⁶ The factors that lead to androgen production by the adrenal gland are unknown; however, it seems to be a separate process that may be regulated independently.^{15,16}

In girls, breast development and growth of pubic hair are the first external signs of pubertal development that result from these endocrine changes. Menarche is a later event in the pubertal continuum and represents the attainment of reproductive maturity. The study of determinants of the timing of pubertal milestones in a general population may help to explain secular trends toward earlier puberty. We have expanded previous analyses of early childhood growth in ALSPAC girls to assess the influence of maternal prenatal characteristics and behaviors and weight and BMI gain on menarche and timing of breast and pubic hair development.

METHODS

Participants

The ALSPAC enrolled pregnant women who were from 3 health districts of the county of Avon, Great Britain, and had an expected delivery date between April 1991 and December

1992. A total of 14 062 children enrolled in the cohort at birth. There were 11 972 singleton active cohort members by age 14, 5842 (49%) of which were girls. Details of recruitment methods are described elsewhere.¹⁷

Pubertal Status

Repeated self-assessments of pubertal development were obtained from the girls between the ages of 8 and 14. Details of data collection methods and management are described elsewhere.¹⁸ Briefly, respondents were asked to examine line drawings and accompanying descriptions of the 5 Tanner stages for breast size and pubic hair developed by Morris and Udry¹⁹ and to record which drawing most closely resembled their stage of development. Each time, they were asked whether they had had their first menstrual period and, if so, the month and year it started. Of the 5842 eligible girls, 4738 (81%) returned at least 1 completed pubertal self-assessment between 8 and 14 years of age. Girls with inconsistent responses were excluded from the analyses. After these exclusions, 3703 singleton girls from the initial cohort had valid data on pubertal status.

Maternal Prenatal Characteristics and Behaviors

Self-reported data on prenatal characteristics and behaviors were collected from the mother during pregnancy. We evaluated variables that were identified a priori from the literature as being potentially related to^{9,12,20–24} pubertal development in girls. We assessed potential associations of the following maternal variables: educational level; social class; age at menarche; prepregnancy BMI; race; age at delivery; season of delivery; previous live births; presence of sugar in urine in third trimester; and smoking, alcohol, coffee, and tea consumption in pregnancy. Data collection instruments and methods have been described in detail elsewhere.¹⁷

We assigned maternal prepregnancy weight status according to the Centers for Disease Control and Prevention adult BMI classification: underweight (<18.5), normal (18.5–24.9), overweight (25.0–29.9), and obese (≥30.0). We conducted analyses of the association of maternal prenatal characteristics on puberty timing on data from 2661 girls.

Postnatal Weight Gain and Growth

Birth weight and gestational age were abstracted from medical records. We assessed associations of fetal growth on girls who were born at term (37–42 weeks of gestation), classifying them as small for gestational age when they had a birth weight <10th percentile of weight for gestational age. Referent weight percentiles were estimated by using weight and gestational age data of singleton girls from the full ALSPAC cohort. Weight and length were measured at ages 2, 9, and 20 months. These measures were made by health professionals as part of the routine infant health surveillance program. We converted the infant's weights to weight-for-age SD scores (SDSs; *z* scores) and BMI SDSs (weight-for-height²) by using the girls' 1990 British growth reference.²⁵ We assessed the change in weight and BMI for the following age intervals: birth to 2 months, 2 to 9 months, 9 to 20 months, and birth to 20 months. The weight SDS change value for each age interval was obtained by subtracting the weight SDS for the age at the beginning of the interval from the score for the age at the end of the interval. The same procedure was used to obtain the BMI

SDS change values. We assessed associations for weight and BMI gain and puberty timing on 1316 girls.

Statistical Analysis

To describe the study group, we estimated means, SDs, and interquartile ranges for weight and BMI SDSs by age and weight and BMI SDS change values by age interval; Pearson correlation coefficients for weight and BMI change values and birth weight; and frequency distributions of maternal prenatal characteristics. Bivariate analyses were conducted to test prenatal characteristics, whereby each variable was fitted separately to assess its association with the study outcomes. The study outcomes were stages 2 and 3 of breast, stages 2 and 3 of pubic hair development, and menarche. The following characteristics were not associated with any puberty outcome and therefore were not included in subsequent analyses: social class; presence of sugar in urine in third trimester; alcohol, coffee, and tea consumption; and season of delivery (data available on request).

We modeled the associations of weight and BMI change, adjusting by prenatal characteristics that were associated with each outcome, and reported differences in median age of transition into a stage and 95% confidence interval. We present results from multivariable models in which the weight or BMI change values that were obtained for each interval were modeled separately. We also modeled values together to address the influence that the change in weight or BMI during 1 interval may have on other intervals. Finally, we present results with adjustment for birth weight and length. For the analyses of breast and pubic hair development, we used interval-censored parametric survival models assuming a normal distribution by using PROC LIFEREG in SAS.²⁶ Human subject protection was assessed and approved by the ALSPAC law and ethics committee, the local research ethics committees, and the Centers for Disease Control and Prevention institutional review board.

RESULTS

Median ages of entry into stages 2 and 3 of breast and pubic hair development and menarche were very similar among subgroups for analyses of prenatal factors and weight and BMI gain (Table 1). No departures in the frequency distributions of maternal prenatal characteristics and behaviors were observed between analysis subgroups (Table 2).

Associations With Maternal Prenatal Characteristics

Daughters of obese and overweight mothers attained breast stages and menarche earlier when compared with daughters of women who reported a normal prepregnancy weight. On the contrary, pubic hair timing did not seem to be associated with maternal weight. Maternal age at menarche <12 and primiparity were associated with earlier entry into puberty outcomes, and differences in age of entry seemed to be comparable across the various puberty outcomes. Smaller differences in age of attainment were reported for maternal smoking. In comparison with other prenatal characteristics, neither maternal education nor maternal age at delivery seemed to have consistent associations across puberty outcomes. A lower maternal education seemed to be related to an earlier age of attainment of breast stages but not with other outcomes. Maternal age at delivery was not associated with

pubertal outcomes except for entry into stage 3 of breast development (Table 3). Daughters of nonwhite mothers also entered puberty earlier; however, results were limited by the small sample size on which these estimations were based (data not shown).

Fetal Growth

The mean $\pm$ SD for weight at birth was 3.42 ± 0.44 kg, at 2 months was 4.83 ± 0.58 , at 9 months was 8.87 ± 0.98 , and at 20 months was 11.49 ± 1.41 . The mean $\pm$ SD birth weight in the group of all girls with puberty data was 3.39 ± 0.49 and for the subgroup of girls with data on prenatal characteristics was 3.40 ± 0.48 , which were similar to those of the subgroup of girls used for the weight gain analyses.

Mean BMI increased up to 9 months of age and decreased afterward. The mean weight SDS change value for the entire age interval (0–20 months) under study was 0.19, whereas the BMI SDS value for the same interval was -0.19 (Table 4). Mean weight change values for individual intervals suggest a slightly higher pace of change in the 2- to 9-month age interval compared with the national reference. Weight change values were inversely correlated with birth weight and between intervals (Table 5). BMI change values displayed similar correlations (data not shown). Neither birth weight nor birth length was associated with puberty outcomes (Table 6). There is some evidence that girls who were small for gestational age may be more likely to enter breast, pubic hair, and menarche at an earlier age.

Postnatal Weight Gain and Growth

A 1-unit increase in the weight SDS change value estimated for the 0- to 20-month age interval was associated with earlier ages of entry into breast and pubic hair development and menarche (Table 6). When age intervals were modeled separately, associations seemed to be of similar magnitude across intervals of the study outcomes. After adjustment for the weight gain of previous age intervals, the magnitude of the coefficients shifted farther away from the null value, showing an earlier age of attainment. Adding birth weight and length to the model had a similar effect.

For BMI, a 1-unit increase in the SDS change value for the 0- to 20-month age interval was associated with earlier ages of entry into breast and pubic hair development and menarche. When age intervals were modeled separately, BMI was associated with earlier entry into breast stages and menarche but not pubic hair development. After adjustment for scores of previous age intervals, the magnitude of the coefficients shifted farther away from the null value. Adding weight and length at birth to the models had a similar effect on pubic hair development but not on breast development or menarche attainment (Table 7).

DISCUSSION

Initiation of menarche before age 12, smoking during pregnancy, and primiparity were maternal prenatal characteristics that were associated with early entry into breast and pubic hair Tanner stages and menarche. The relationship between an earlier maternal age at menarche and the daughter's early entry into breast stage and menarche is in agreement with other studies.^{27–29} Approximately half of the variation in menarche timing is attributable to genetic factors.¹¹ Some studies of risk factors for menarche have reported an association

with being the firstborn child.^{12,24} Firstborn children have a higher risk for low birth weight and are more likely to undergo rapid weight gain during infancy. Concentrations of sex hormones in umbilical cord blood have been found to be higher in firstborn children than in later born children who were closely spaced in relation to their next-older siblings.³⁰ Perhaps a more intense exposure to maternal sex hormones among firstborn children explains the association of parity with earlier breast and pubic hair development.

In our study, higher maternal prepregnancy weight BMI seemed to influence puberty outcomes differently. The magnitude of the differences in age of entry into breast stages was approximately twice the size of that for menarche and was not associated with pubic hair timing. Daughters of obese or overweight mothers were more likely to be so themselves, and higher body fat was previously associated with breast development onset.^{27,28} Overestimation of breast stage is more common in overweight girls, and this may explain some of the larger differences in age of entry into breast development observed.³¹

Consistent with the literature, birth weight or length alone did not influence puberty timing.^{12,13} The greatest variations in rates of weight gain are usually seen in the first 2 years of life, when infants show accelerated or diminished growth to compensate for intrauterine restraint or enhancement of fetal growth.³² We found that higher weight gain during infancy led to an earlier puberty attainment. Overall, our results suggest similar magnitude of the associations across puberty outcomes and across age intervals of the specific outcomes. Another study suggested that associations between rapid weight gain during infancy and menarche may vary with age. Associations of early menarche with rapid weight gains were reported in the 4-month to 1-year age interval but not earlier.¹³ Whether associations between rapid weight gain and puberty varies by age is difficult to establish. In our study, age intervals were not established a priori but determined by the available data. In addition, comparison of results between studies is limited by the differences in the age intervals analyzed.

Higher BMI gain during infancy also led to an earlier puberty attainment. These associations also exhibited similar magnitudes across puberty outcomes and age intervals. When compared with results for weight gain, these associations seem to be of a smaller magnitude. Adiposity increases in the first year of life and subsequently decreases.³³ Our results confirm an adiposity decrease after the first year in ALSPAC girls. Less variability in the individual BMI SDSs arising from this decrease may explain the smaller magnitudes observed. An alternative explanation is that, during infancy, other factors that are associated with growth act independent from obesity on timing of puberty.

Rapid weight gain during infancy has been associated with higher body mass in ALSPAC children at age 5 and higher circulating androgen concentrations at age 8.^{32,34,35} Childhood obesity, resulting from restricted intrauterine growth, may explain the association between rapid weight gain and early pubertal development. Obesity leads to insulin resistance and compensatory hyperinsulinemia, which in turn may act in various organs to increase sex steroid bioavailability.³⁶ Alternatively, the drive to obesity, most likely through greater appetite, may appear early in growth-restricted individuals who live in an obesogenic environment. Children with precocious puberty are more likely to have higher BMIs than

prepubertal children of similar age.^{8,37} The growing global childhood obesity epidemic, which has increased more dramatically in economically developed countries, may explain the secular trends toward earlier puberty observed in developed countries.³⁸

A caveat of our study is that weight gain data were not available for all girls. Only 36% of the girls with puberty data had weight gain data. Our results could be biased if exclusion of girls with missing data was differential. Comparison of median age of entry into puberty outcomes and determinants between the group of girls with valid puberty data and the subgroup with weight data suggests that bias does not explain our results. Another limitation of our analyses is that we assessed study associations on term girls. Our measures of growth excluded girls with a shorter course of gestation.³⁹

Our results are based on self-assessed pubertal status. Self-assessment of Tanner stage is considered a practical and valid choice, particularly for longitudinal studies with repeat assessments.⁴⁰ We used the drawings of pubertal stages developed by Morris and Udry,¹⁹ which showed good correlations between clinician and self-reporting of Tanner stage (breast: $r = 0.63$; pubic hair: $r = 0.81$) and had been successfully used in previous studies.^{10,41} As the girls became older, more of them completed the questionnaires by themselves. By age 14, 83% of girls with valid puberty data self-assessed. Of those who did not, most reported being helped by parents. We assume that the mother is the parent more likely to collaborate with the girl.

Good correlations between mother-physician ($r = 0.85$) and mother-daughter ($r = 0.77$) pairs have been reported.⁴² Sources of errors that affect the accuracy of an adolescent's self-assessment include obesity, the adolescent's actual Tanner stage, and the setting where the instrument is administered.^{31,43}

The influence of infancy weight gain on specific thresholds of early menarche was previously analyzed using earlier data on these ALSPAC girls, where rapid weight gain was associated with a higher risk for menarche at <12 years.¹⁴ Our assessment of rapid weight gain on the wider distribution of menarche by using parametric survival models yielded similar results.

CONCLUSIONS

Many of the maternal prenatal characteristics assessed and weight gain and BMI during infancy seemed to exert similar influences across different measures of pubertal development. Either such early factors may have comparable influences on each of the distinctive hormonal processes involved in pubertal development, or processes are linked and awakening of 1 aspect of it triggers the same in the others.

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research scientists, volunteers, managers, receptionists, and nurses. This publication is the work of the authors, and they will serve as guarantors for its contents.

ABBREVIATIONS

ALSPAC Avon Longitudinal Study of Parents and Children

SDS SD score

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WHAT'S KNOWN ON THIS SUBJECT

Rapid growth during infancy and childhood obesity predict earlier puberty attainment.

WHAT THIS STUDY ADDS

Many of the prenatal factors studied and weight and BMI gain during infancy seemed to exert comparable influences in the ages of breast, pubic hair, and menarche attainment assessed in the same girls.

TABLE 1

Median Age of Entry Into Stages of Breast and Pubic Hair Development and Menarche

Stage	Group With Valid Puberty Data (n = 3703)			Group for Analyses of Prenatal Characteristics (n = 2661)			Group for Analyses of Weight Gain and BMI (n = 1316)		
	Median (SE)	95% CI	IQR	Median (SE)	95% CI	IQR	Median (SE)	95% CI	IQR
Breast									
2	10.20 (0.03)	10.14–10.25	9.16–11.23	10.20 (0.03)	10.14–10.27	9.17–11.24	10.18 (0.05)	10.09–10.27	9.16–11.20
3	11.67 (0.03)	11.62–11.72	10.80–12.54	11.66 (0.03)	11.61–11.72	10.80–12.52	11.64 (0.04)	11.56–11.72	10.79–12.50
Pubic hair									
2	10.95 (0.03)	10.90–11.00	9.99–11.91	10.94 (0.03)	10.88–11.00	9.99–11.89	10.94 (0.04)	10.85–11.02	9.99–11.89
3	11.99 (0.03)	11.94–12.04	11.18–12.80	11.98 (0.03)	11.93–12.04	11.17–12.80	11.95 (0.04)	11.87–12.03	11.14–12.77
Menarche	12.85 (0.022)	12.81–12.90	12.07–13.64	12.83 (0.026)	12.78–12.88	12.05–13.61	12.82 (0.036)	12.75–12.89	12.02–13.61

All parameters were estimated with parametric survival models using PROC LIFETEST in SAS assuming a normal distribution. CI indicates confidence interval; IQR, interquartile range.

TABLE 2

Frequency Distribution of Selected Prenatal Characteristics

Variables	Group With Valid Puberty Data (n = 3703)		Group for Analyses of Prenata Characteristics (n = 2661)		Group for Analyses of Weight Gain and BMI (n = 1316)	
	n	%	n	%	n	%
Maternal education						
<0 level	881	24.8	597	22.4	283	21.5
0 level	1256	35.4	952	35.8	494	37.5
>0 level	1415	39.8	1112	41.8	539	40.9
Maternal age at menarche, y						
<12	577	17.8	466	17.5	231	17.6
12–13	1650	51.8	1385	52.1	702	53.3
14	970	30.4	810	30.4	383	29.1
Maternal prepregnancy BMI						
Underweight	170	5.1	133	5.0	62	4.7
Normal	2503	75.1	2006	75.4	982	74.6
Overweight	489	14.7	386	14.5	198	15.1
Obese	172	5.2	136	5.1	74	5.6
Maternal age at delivery, y						
<25	677	18.3	460	17.3	212	16.1
24–29	1502	40.6	1080	40.6	538	40.9
30	1524	41.2	1121	42.1	566	43.0
Previous live births						
1	1935	53.8	1406	52.8	655	49.8
0	1661	46.2	1255	47.2	661	50.2
Smoking during pregnancy						
No	2657	80.4	2167	81.4	1071	81.4
Yes	647	19.6	494	18.6	245	18.6
Intrauterine growth restriction						
No	3204	91.4	1201	91.3	1201	91.3

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Variables	Group With Valid Puberty Data (<i>n</i> = 3703)		Group for Analyses of Prenata Characteristics (<i>n</i> = 2661)		Group for Analyses of Weight Gam and BM (<i>n</i> = 1316)	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Yes	300	8.6	115	8.7	115	8.7

TABLE 3

Adjusted Difference and 95% CIs in Age of Transition Into a Stage 2 and 3 of Breast and Pubic Hair Development and Menarche for Prenatal Characteristics ($n = 2661$)

Variables	Adjusted Differences and 95% CI ^a											
	Breast				Pubic Hair				Menarche			
	Stage 2		Stage 3		Stage 2		Stage 3		Stage 2		Stage 3	
	Diff	95% CI	P	Diff	95% CI	P	Diff	95% CI	P	Diff	95% CI	P
Maternal age at menarche												
<12	-0.35	-0.52 to -0.17	.00	-0.37	-0.52 to -0.22	.00	-0.35	-0.52 to -0.19	.00	-0.36	-0.51 to -0.22	.00
12-13		Reference			Reference			Reference			Reference	
14	0.53	0.38 to 0.67	.00	0.42	0.30 to 0.55	.00	0.39	0.26 to 0.53	.00	0.40	0.27 to 0.52	.00
Previous live births												
Yes		Reference			Reference			Reference			Reference	
No	-0.39	-0.52 to -0.25	.00	-0.33	-0.44 to -0.21	.00	-0.33	-0.45 to -0.20	.00	-0.31	-0.42 to -0.19	.00
Smoking during pregnancy												
No		Reference			Reference			Reference			Reference	
Yes	-0.19	-0.36 to -0.01	.04	-0.19	-0.34 to -0.04	.02	-0.12	-0.29 to 0.04	.14	-0.16	-0.32 to -0.02	.03
Maternal prepregnancy BMI												
Underweight	0.14	-0.16 to 0.43	.36	-0.05	-0.30 to 0.20	.70	-0.08	-0.36 to 0.20	.58	-0.16	-0.41 to 0.08	.19
Normal		Reference			Reference			Reference			Reference	
Overweight	-0.43	-0.62 to -0.25	.00	-0.41	-0.56 to -0.25	.00	-0.14	-0.31 to 0.04	.12	-0.12	-0.28 to 0.04	.14
Obese	-0.70	-1.00 to -0.40	.00	-0.50	-0.75 to -0.25	.00	-0.20	-0.48 to 0.08	.16	-0.13	-0.38 to 0.12	.31
Maternal age at delivery												
<24	-0.13	-0.32 to 0.07	.21	-0.05	-0.22 to 0.12	.56	0.12	-0.06 to 0.30	.20	0.10	-0.07 to 0.26	.27
24-29		Reference			Reference			Reference			Reference	
30	-0.07	-0.21 to 0.07	.34	-0.20	-0.32 to -0.08	.00	-0.11	-0.24 to 0.03	.12	-0.07	-0.19 to 0.05	.23
Maternal education												
<0 Level	-0.30	-0.48 to -0.12	.00	-0.14	-0.30 to 0.02	.09	-0.07	-0.24 to 0.11	.45	-0.02	-0.18 to 0.13	.78
0 Level	-0.11	-0.26 to 0.04	.15	-0.07	-0.20 to 0.06	.27	-0.01	-0.15 to 0.13	.88	0.07	-0.06 to 0.19	.31
>0 Level		Reference			Reference			Reference			Reference	

β Regression coefficients for the difference in median age of transition into stage and its 95% CI when compared with reference value were estimated with parametric survival models by using the LIFEREG procedure in SAS.
Diff indicates difference; CI, confidence interval; 0 level indicates secondary education certification.

TABLE 4Summary Measures of Birth Size and BMI by Age and Age Interval ($n = 1316$)

Variable	Birth			2 mo			9 mo			20 mo		
	Mean (SD)	IQR		Mean (SD)	IQR		Mean (SD)	IQR		Mean (SD)	IQR	
Weight, kg	3.42 (0.44)	3.10 to 3.70		4.83 (0.58)	4.40 to 5.20		8.87 (0.98)	8.20 to 9.50		11.49 (1.41)	10.50 to 12.40	
Weight SDS	0.01 (0.96)	-0.63 to 0.64		0.06 (0.95)	-0.54 to 0.64		0.15 (1.05)	-0.51 to 0.85		0.20 (1.04)	-0.47 to 0.91	
BMI, weight/height ²	13.36 (1.22)	12.60 to 14.10		14.87 (1.38)	13.90 to 15.80		17.40 (1.56)	16.30 to 18.40		16.79 (1.50)	15.70 to 17.70	
BMI SDS	0.21 (1.00)	-0.40 to 0.80		-0.34 (1.11)	-1.00 to 0.43		-0.10 (1.15)	-0.80 to 0.70		0.03 (1.11)	-0.70 to 0.80	
	Birth-2 mo			2-9 mo			9-20 mo			0-20 mo		
Weight SDS change	0.05 (0.77)	-0.46 to 0.54		0.09 (0.94)	-0.52 to 0.64		0.05 (0.68)	-0.39 to 0.47		0.19 (1.17)	-0.55 to 0.92	
BMI SDS change	-0.56 (1.19)	-1.40 to 0.20		-0.24 (1.27)	-0.60 to 1.10		0.12 (1.07)	-0.60 to 0.81		-0.19 (1.35)	-1.00 to 0.70	

IQR indicates interquartile range.

TABLE 5Correlation Matrix for Birth Weight and Change in Weight SDSs ($n = 1316$)

Parameter	Birth Weight	Change in Weight SDS 0–2 mo	Change in Weight SDS 2–9 mo
Change in weight SDS 0–20 mo	–0.54		
Change in weight SDS 0–2 mo	–0.41		
Change in weight SDS 2–9 mo	–0.29	–0.12	
Change in weight SDS 9–20 mo	–0.08	–0.12	–0.20

All Pearson correlations coefficients are significant at a $P < .005$ level

TABLE 6

Adjusted Difference and 95% CIs for Age of Entry Into Stages of Breast and Pubic Hair Development and Menarche for Birth Size and Change in Weight SDS ($n = 1316$)

Variables	Adjusted Differences and 95% CI ^a											
	Breast				Pubic Hair				Menarche			
	Stage 2		Stage 3		Stage 2		Stage 3		Stage 2		Stage 3	
	Diff	95% CI	P	Diff	95% CI	P	Diff	95% CI	P	Diff	95% CI	P
Birth weight ^b	0.00	-0.00 to 0.00	.08	0.00	-0.00 to 0.00	.28	0.00	-0.00 to 0.00	.69	0.00	-0.00 to 0.00	.64
Birth length ^b	-0.02	-0.06 to 0.03	.49	-0.02	-0.06 to 0.01	.29	0.01	-0.03 to 0.06	.51	0.02	-0.02 to 0.06	.29
SGA ^b												
Yes	-0.23	-0.55 to 0.09	.16	-0.17	-0.45 to 0.10	.22	-0.13	-0.44 to 0.17	.38	-0.07	-0.34 to 0.20	.62
No												
Weight change (intervals modeled separately) ^b												
0-20 mo	-0.19	-0.27 to -0.11	.00	-0.16	-0.23 to -0.10	.00	-0.23	-0.30 to -0.15	.00	-0.19	-0.26 to -0.13	.00
0-2 mo	-0.24	-0.36 to -0.12	.00	-0.15	-0.25 to -0.05	.00	-0.18	-0.30 to -0.07	.00	-0.10	-0.20 to -0.00	.05
2-9 mo	-0.03	-0.13 to 0.07	.54	-0.10	-0.18 to -0.02	.02	-0.15	-0.24 to -0.05	.00	-0.16	-0.24 to -0.08	.00
9-20 mo	-0.17	-0.31 to -0.04	.01	-0.09	-0.21 to 0.02	.11	-0.14	-0.27 to -0.02	.03	-0.12	-0.23 to -0.00	.04
Weight change (intervals modeled adjusting for previous intervals) ^b												
0-2 mo	-0.24	-0.36 to -0.12	.00	-0.15	-0.25 to -0.05	.00	-0.18	-0.30 to -0.07	.00	-0.10	-0.20 to -0.00	.05
2-9 mo	-0.06	-0.16 to 0.04	.24	-0.12	-0.21 to -0.04	.01	-0.17	-0.26 to -0.08	.00	-0.18	-0.26 to -0.09	.00
9-20 mo	-0.24	-0.38 to -0.10	.00	-0.16	-0.28 to -0.04	.01	-0.24	-0.37 to -0.11	.00	-0.20	-0.32 to -0.08	.00
Weight change also adjusted by birth weight and length ^b												
0-20 mo	-0.19	-0.29 to -0.10	.00	-0.19	-0.27 to -0.11	.00	-0.31	-0.40 to -0.22	.00	-0.26	-0.34 to -0.18	.00
Weight change also adjusted by birth weight and length (intervals modeled adjusting for prior interval) ^b												
0-2 mo	-0.22	-0.35 to -0.09	.00	-0.13	-0.24 to -0.02	.02	-0.21	-0.34 to -0.09	.00	-0.12	-0.23 to -0.00	.04

Variables	Adjusted Differences and 95% CI ^a											
	Breast				Pubic Hair				Menarche			
	Stage 2		Stage 3		Stage 2		Stage 3		Stage 3		Stage 3	
	Diff	95% CI	P	Diff	95% CI	P	Diff	95% CI	P	Diff	95% CI	P
2–9 mo	–0.05	–0.16 to 0.05	.31	–0.13	–0.22 to –0.04	.00	–0.22	–0.31 to –0.12	.00	–0.21	–0.30 to –0.12	.00
9–20 mo	–0.25	–0.39 to –0.11	.00	–0.18	–0.30 to –0.06	.00	–0.30	–0.43 to –0.17	.00	–0.24	–0.36 to –0.12	.00

Diff indicates difference; CI, confidence interval; SGA, small for gestational age.

^aRegression coefficients for the difference in median age of transition into stage and its 95% CI when compared with reference value were estimated with parametric survival models by using the LIFEREG procedure in SAS.

^bResults adjusted by the following maternal prenatal characteristics: maternal age at menarche; previous live birth; maternal race or ethnicity; smoking during pregnancy; maternal prepregnancy BMI; maternal age at delivery; maternal education.

TABLE 7

Adjusted Difference and 95% CIs in Age of Entry Into Stages of Breast and Pubic Hair Development and Menarche and Change in BMI SDS ($n = 1316$)

Variables	Adjusted Differences and 95% CI ^a											
	Breast				Pubic Hair				Menarche			
	Stage 2		Stage 3		Stage 2		Stage 3		Stage 3			
	Diff	95% CI	P	Diff	95% CI	P	Diff	95% CI	P	Diff	95% CI	P
BMI change (intervals modeled separately) ^b												
0–20 mo	–0.13	–0.19 to –0.06	.00	–0.11	–0.17 to –0.05	.00	–0.07	–0.13 to –0.00	.04	–0.07	–0.13 to –0.01	.01
0–2 mo	–0.13	–0.21 to –0.05	.00	–0.07	–0.14 to –0.01	.03	–0.06	–0.13 to 0.01	.10	–0.01	–0.08 to 0.06	.71
2–9 mo	0.01	–0.06 to 0.08	.74	–0.04	–0.10 to 0.02	.18	–0.01	–0.08 to 0.06	.74	–0.04	–0.10 to 0.02	.19
9–20 mo	–0.06	–0.14 to 0.03	.18	–0.03	–0.10 to 0.05	.48	–0.01	–0.09 to 0.06	.72	–0.04	–0.11 to 0.03	.25
BMI change (intervals modeled adjusting for previous interval) ^b												
0–2 mo	–0.13	–0.21 to –0.06	.00	–0.07	–0.14 to –0.01	.03	–0.06	–0.13 to 0.01	.10	–0.01	–0.08 to 0.06	.71
2–9 mo	–0.04	–0.11 to 0.04	.32	–0.08	–0.14 to –0.01	.02	–0.04	–0.11 to 0.03	.29	–0.05	–0.12 to 0.01	.12
9–20 mo	–0.11	–0.20 to –0.02	.02	–0.09	–0.17 to –0.01	.04	–0.05	–0.14 to 0.04	.29	–0.08	–0.16 to 0.00	.04
BMI change also adjusted by birth weight and length ^b												
0–20 mo	–0.10	–0.18 to –0.02	.02	–0.10	–0.17 to –0.03	.01	–0.10	–0.18 to –0.02	.01	–0.11	–0.18 to –0.04	.00
BMI change also adjusted by birth weight and length (intervals modeled adjusting for previous interval) ^b												
0–2 mo	–0.09	–0.18 to –0.00	.04	–0.04	–0.11 to 0.04	.36	–0.09	–0.17 to –0.00	.04	–0.03	–0.10 to 0.05	.46
2–9 mo	–0.02	–0.10 to 0.07	.72	–0.07	–0.14 to 0.01	.07	–0.06	–0.14 to 0.02	.11	–0.07	–0.14 to –0.00	.05
9–20 mo	–0.10	–0.19 to –0.00	.04	–0.08	–0.17 to –0.00	.05	–0.07	–0.16 to 0.02	.12	–0.10	–0.19 to –0.02	.01

Diff indicates difference; CI, confidence interval.

^aRegression coefficients for the difference in median age of transition into stage and its 95% CI when compared with reference value were estimated with parametric survival models by using the LIFEREG procedure in SAS.

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Results adjusted by the following maternal prenatal characteristics: maternal age at menarche; previous live birth; maternal race or ethnicity; smoking during pregnancy; maternal prepregnancy BMI; maternal age at delivery; maternal education.