Timing of Maternal Depression and Sex-Specific Child Growth, the Upstate KIDS Study

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Objective: Equivocal findings have been reported on the association between maternal depression and children's growth, possibly because of the limited attention to its disproportionate impact by child sex. The relationship between the timing of maternal depression and children's growth was assessed in a population-based prospective birth cohort, with particular attention to sex differences.

Methods: The Upstate KIDS Study comprised 4,394 children followed through 3 years of age from 2008 to 2010. Maternal depression was measured antenatally by linkage with hospital discharge records before delivery and postnatally by depressive symptoms reported from questionnaires. Children's growth was measured by sex- and age-specific weight, height, weight for height, and BMI. Adjusted linear mixed effects models were used to estimate growth outcomes for the full sample and separately by plurality and sex.

Results: Antenatal depression was associated with lower weight for age (\(-0.24\) z score units; 95% confidence interval [CI]: \(-0.43, -0.05\)) and height for age (\(-0.26\) z score units; 95% CI: \(-0.51, -0.02\)) among singleton boys. Postnatal depressive symptoms were associated with higher weight for height (0.21 z score units; 95% CI: 0.01, 0.42) among singleton girls.

Conclusions: The findings of this study suggest that antenatal depression was associated with lower weight and smaller height only for boys, whereas postnatal depressive symptoms were associated with higher weight for height only for girls. The timing of depression and the mechanisms of sex-specific responses require further examination.

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Introduction

Depression is common among reproductive-aged women. In the United States, 14\% to 23\% of women may experience antenatal (during pregnancy) depression (1), and 12\% of women may experience postnatal (within a year after delivery) depression (2). In addition to the considerable impact of depression on the mother's health and social functioning (3), there is also concern that maternal depression impacts offspring development.

Antenatal depression may have adverse effects on the developing fetus through intrauterine pathways (4). For example, antenatal depression may cause a dysregulation of the maternal hypothalamic-pituitary-adrenal (HPA) axis, with corresponding elevated maternal cortisol levels, potentially affecting fetal HPA regulation and infant adiposity (5). Antenatal depression may also increase pro-inflammatory cytokines during pregnancy (6), which have been associated with higher childhood adiposity (7). Postnatal depression has been associated with delays in children's cognitive, mental, and physical development through several mechanisms (8). Mothers with postnatal depression are less likely to engage in earlier initiation or longer duration of breastfeeding (9), both of which are protective against childhood obesity (10). They are also more likely to have

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impaired mother-infant interactions, such as lower responsiveness to infants in needs and difficulties in providing appropriate child care (11,12). Parenting practices related to other child behavioral factors, such as unhealthy diet, food fussiness, low physical activity, and sedentary behaviors, also have been suggested as potential pathways for the impact of postnatal depression (13,14).

Empirical evidence is inconclusive regarding the association between maternal depression and child growth (8,15). Some studies have found that antenatal depression was associated with smaller child size and greater central adiposity (5) and that postnatal depression was associated with higher overall adiposity (5) and an increased risk of having overweight or obesity at 3 years of age (16). However, other studies have found no association between antenatal depression and preschooler growth (4) or postnatal depression and child BMI z scores at the age of 3 years (17). One study documented that postnatal depression was associated with sex- and age-specific child growth; BMI was shown to increase in girls exposed to postnatal maternal depressive symptoms earlier than it increased in boys (18).

The inconsistency in evidence may be partly caused by the differences associated with the timing of maternal depression relative to pregnancy and possible sex-specific growth patterns in offspring of mothers with depression (5,16,18). It has been proposed that fetal sex-specific placental responsiveness to maternal stress and sex hormones may result in sexually dimorphic growth responses in utero and ex utero. Male fetuses need to maintain an accelerated growth pattern; thus, they are more vulnerable to adverse conditions in utero (19). Female fetuses, however, maintain flexible and adaptable growth patterns in response to adverse conditions in utero but may be more vulnerable to adverse conditions ex utero (19). Therefore, this study investigated the relationship between the timing of maternal depression and children’s growth through 3 years of age in a population-based prospective birth cohort, with particular attention to sex-specific differences.

Methods

The Upstate KIDS Study is a population-based birth cohort originally designed to evaluate the impact of infertility treatment on child growth and development through the age of 3 years from 2008 to 2010 (20). By using birth certificates from the 57 counties in New York state (NYS), excepting the five New York city boroughs, infants were oversampled on recorded infertility treatment, with all twins and higher-order infants eligible to participate regardless of conception mode, such as spontaneous or medically assisted conception. The study cohort comprised 4,394 children, including 3,440 singletons and 954 randomly selected siblings from twin pairs for whom growth was measured at least once during follow-up. Full human subjects approval was obtained from all participating institutions (NYSDOH IRB #07-097; UAlbany #08-179), and informed consent was given prior to data collection.

Antenatal depression was derived from the Statewide Planning and Research Cooperative System (SPARCS) (21), a statewide reporting system for discharge data to which the Upstate KIDS Study Cohort was linked to ascertain maternal depression. Maternal records were linked to capture in- or outpatient hospital care 1 to 3 years prior to or after delivery (i.e., 2007-2011) (21). Specifically, mothers were categorized as having antenatal depression if they had any linkable in- or outpatient discharge records with relevant International Classification of Diseases, Ninth Revision, Clinical Modification codes (296.X; 311; 300.4; 648.4X) (22) in the 3 years preceding delivery of the index birth (i.e., “Antenatal depression: SPARCS”). Any in- or outpatient discharge records up to 3 years after delivery from SPARCS were used to define postnatal depression (i.e., “Postnatal depression: SPARCS”). The hospital records from SPARCS data included mothers with depression requiring hospital care, as well as mothers with depression affecting treatment or length of stay that might not be the primary reason for hospital care.

We additionally examined maternal depression by using two other sources of data. Postnatal depressive symptoms were measured with the abridged Edinburgh Postnatal Depression Scale (EPDS), which was administered to mothers when the infants were 4, 12, 24, and 36 months of age. The EPDS encompasses five items assessing emotional experiences over the past 7 days (23). Each item ranges from zero (i.e., absence of symptoms) to three (i.e., maximum severity); thus, total scores range from zero to fifteen (23). A longitudinal measure for severe postnatal depressive symptoms was defined as a score ≥ 8 (23) that was scored at 4, 12, 24, and 36 months after delivery (i.e., “Severe postnatal depressive symptoms: EPDS”). Finally, mothers reported depression during pregnancy on the NYS birth certificate, with reports ranging from not depressed to depressed requiring help. We categorized mothers as having antenatal depressive symptoms if their answers included “moderately depressed,” “very depressed,” or “very depressed and had to get help” (i.e., “Self-reported antenatal depressive symptoms: Birth certificate”).

Combining clinical and self-reported depression measures would be useful to address comprehensive assessment of depression status because each depression measure may capture a unique aspect that may not be captured by other measures (24). Therefore, we constructed a combined antenatal depression or depressive measure from self-reported depressive symptoms on birth certificates and depression records in SPARCS. Similarly, a combined postnatal depression or depressive symptoms measure was constructed by aggregating EPDS and SPARCS data. In addition, the combined effects of both antenatal and postnatal depression on child growth in any four measures were evaluated. We reported combined depression measures, defining depression as present if either a diagnosis was present or the participant reported a high level of symptoms. In subsequent analyses, we investigated their independent associations, as different measures also correspond to different time points of exposure.

Children’s growth was assessed longitudinally from mothers. Mothers completed health journals designed to capture children’s height, weight, and head circumference that were measured by health care personnel during well baby and child visits at 4, 8, 12, 18, 24, 30, and 36 months. These data were then used with the World Health Organization child growth standards to calculate sex- and age-specific weight, height, BMI, and weight-for-height z scores (25).

Statistical analyses

Descriptive statistics for the study population were summarized and compared by the timing of maternal depression, with significance
Maternal Depression and Child Growth

TABLE 1 Descriptive characteristics of the study population by maternal depressive symptoms, the Upstate KIDS Study

| Maternal characteristics                  | Antenatal depression<sup>a</sup> | Postnatal depressive symptoms<sup>b</sup> |
|-------------------------------------------|----------------------------------|-----------------------------------------|
| Total                                     | Total (100.0)                    | Postnatal depression symptoms (100.0)  |
| Maternal age at delivery, y, mean (SD)    | 30.8 (6.0)                       | 31.0 (5.9)                              |
| Maternal race (white), n (%)              | 3,619 (82.4)                     | 3,298 (83.1)                            |
| Maternal education, n (%)                 |                                  |                                        |
| High school or less                       | 693 (15.8)                       | 555 (14.0)                              |
| High school to some college               | 1,329 (30.2)                     | 1,183 (29.8)                            |
| Marital status (married), n (%)           | 3,805 (86.6)                     | 3,483 (87.7)                            |
| Breastfeeding at hospital discharge, n (%)| 3,477 (79.1)                     | 3,193 (80.4)                            |
| Prepregnancy BMI, n (%)                   |                                  |                                        |
| Underweight/normal weight                 | 2,145 (48.8)                     | 1,967 (49.6)                            |
| Overweight                                | 1,102 (25.1)                     | 1,006 (25.3)                            |
| Smoking during pregnancy, n (%)           | 556 (12.7)                       | 450 (11.3)                              |
| Drinking during pregnancy, n (%)          | 558 (12.7)                       | 505 (12.7)                              |
| Infertility treatment, n (%)              | 1,374 (31.3)                     | 1,266 (31.9)                            |
| Gestational diabetes, n (%)               | 450 (10.2)                       | 399 (10.1)                              |
| Private insurance, n (%)                  | 3,413 (77.7)                     | 3,165 (79.7)                            |
| Child characteristics                     |                                  |                                        |
| Infant sex, n (%)                         |                                  |                                        |
| Boy                                       | 2,268 (51.6)                     | 2,033 (51.2)                            |
| Girl                                      | 2,126 (48.4)                     | 1,937 (48.8)                            |
| Birth weight, g, mean (SD)                | 3,189 (685.1)                    | 3,198 (681.2)                           |
| Gestational age, wk, mean (SD)            | 38.1 (2.4)                       | 38.1 (2.4)                              |
| Plurality, n (%)                          |                                  |                                        |
| Singleton                                 | 3,440 (78.3)                     | 3,107 (78.3)                            |
| Twin                                      | 954 (21.7)                       | 863 (21.7)                              |
| Weight for age, z score, mean (SD)<sup>c</sup> | 0.2 (1.1)                      | 0.2 (1.1)                               |
| Length or height for age, z score, mean (SD)<sup>c</sup> | -0.2 (1.7)                    | -0.2 (1.7)                              |
| BMI for age, z score, mean (SD)<sup>c</sup> | 0.4 (1.6)                       | 0.4 (1.6)                               |
| Weight for length/height, z score, mean (SD)<sup>c</sup> | 0.4 (1.6)                   | 0.4 (1.6)                               |
| Mo at the last assessment, mean (SD)      | 20.7 (12.6)                      | 20.9 (12.6)                             |

Information was missing for postnatal maternal depressive symptoms (i.e., EPDS (n = 190), self-reported antenatal depressive symptoms (n = 508), breastfeeding at hospital discharge (n = 46), marital status (n = 155), prepregnancy BMI (n = 8), and private insurance (n = 3).

<sup>a</sup>Antenatal depression derived from SPARCS for mothers with any in- or outpatient discharge records due to depression before date of child delivery.
<sup>b</sup>Postnatal depressive symptoms were measured with abridged EPDS at 4, 12, 24, and 36 months after delivery by using five items assessing emotional experiences over the past 7 days. Postnatal depressive symptoms ever were used for summary purposes only in this table, as they were time-variant measures.
<sup*c</sup>Values at last assessment were used to calculate means and SDs.

(P < 0.05) formally tested by using either the χ² and Student t tests for categorical and continuous variables, respectively. Linear mixed effects models with random intercepts for age and robust standard errors (25) were used to estimate mean differences of four growth outcomes from birth through 3 years of age between children of mothers with depression and those without. Nested infant-level random effects accounted for correlations between repeated growth measures. Models were analyzed for all study participants and then estimated separately for singletons, singleton boys and girls, and twins. Unadjusted models assessed the relations between antenatal depression and child growth (results not shown) and were then adjusted for a priori selected potential confounders from previous research (26), informed by the study’s directed acyclic graph. These included maternal age at delivery (years, continuous), race (white, nonwhite), education (high school or less, some college or an associate’s degree, bachelor’s degree or higher), marital status (married or living with partner, single), infertility treatment for index birth (yes, no), health insurance (yes, no), and prepregnancy BMI (underweight/normal weight, overweight, obesity). Similarly, unadjusted models for the associations between longitudinal postnatal depression and child growth (results not shown) and were then adjusted for a priori selected potential confounders from previous research (26), informed by the study’s directed acyclic graph. These included maternal age at delivery (years, continuous), race (white, nonwhite), education (high school or less, some college or an associate’s degree, bachelor’s degree or higher), marital status (married or living with partner, single), infertility treatment for index birth (yes, no), health insurance (yes, no), and prepregnancy BMI (underweight/normal weight, overweight, obesity). Similarly, unadjusted models for the associations between longitudinal postnatal depression and child growth (results not shown) and were then adjusted for a priori selected potential confounders from previous research (26), informed by the study’s directed acyclic graph. These included maternal age at delivery (years, continuous), race (white, nonwhite), education (high school or less, some college or an associate’s degree, bachelor’s degree or higher), marital status (married or living with partner, single), infertility treatment for index birth (yes, no), health insurance (yes, no), and prepregnancy BMI (underweight/normal weight, overweight, obesity). Similarly, unadjusted models for the associations between longitudinal postnatal
depressive symptoms and child growth (results not shown) were followed by adjusted models of postnatal depressive symptoms on child growth. We additionally adjusted for antenatal depression (27) (yes, no), cigarette smoking during pregnancy (yes, no), alcohol usage during pregnancy (yes, no), gestational diabetes (28) (yes, no), gestational hypertension (yes, no), and breastfeeding at hospital discharge (29) (yes, no), as well as for the confounders listed above. All models were adjusted for the children's age at last assessment of child growth. We additionally adjusted for antenatal depression (27) (yes, no), cigarette smoking during pregnancy (yes, no), alcohol consumption (yes, no), prepregnancy BMI, history of smoking, history of alcohol consumption, prepregnancy or gestational diabetes, gestational hypertension, breastfeeding status at hospital discharge, and antenatal depression.

Table 2 summarizes the associations of antenatal and postnatal depressive symptoms and child growth between those whose mothers had depression and those whose mothers did not.

### Results

Sociodemographic characteristics and behavioral factors were associated with maternal depression (Table 1). As compared with mothers without any depression, those with either antenatal depression or postnatal depressive symptoms were younger, had lower educational attainment, and were more likely to be unmarried, to develop obesity before pregnancy, to have smoked during pregnancy, and to lack private health insurance; they were less likely to be breastfeeding at hospital discharge or to have received infertility treatment. In addition, mothers with postnatal depressive symptoms were more likely to be nonwhite as compared with mothers without postnatal depressive symptoms. Children of mothers with antenatal depression were shorter than their counterparts but similar on all other growth measures. Children of mothers reporting postnatal depressive symptoms were born earlier and weighed less than children whose mothers did not report such symptoms.

Table 2 summarizes the associations of antenatal and postnatal depression with early child growth. Regression coefficients indicate the differences of z scores for children’s growth between those whose mothers had depression and those whose mothers did not.

| TABLE 2 Associations between maternal depression and children's growth through 3 y, the Upstate KIDS Study |
|-------------------------------------------------------------|
| | All participants | Singletons | Singleton boys | Singleton girls | Twins |
| | b | 95% CI | b | 95% CI | b | 95% CI | b | 95% CI | b | 95% CI |
| Antenatal depression (from both SPARCS and self-reported depressive symptoms)a | | | | | | | | | | |
| Weight for age | -0.13, -0.27 | 0.00 | -0.13, -0.28 | 0.01 | -0.24, -0.43 | -0.05 | -0.02 | -0.22 | 0.18 | -0.23 | -0.58 | 0.08 |
| Height for age | -0.12, -0.29 | 0.04 | -0.12, -0.29 | 0.05 | -0.26, -0.51 | -0.02 | 0.03 | -0.21 | 0.26 | -0.30 | -0.66 | 0.07 |
| Weight for height | -0.05, -0.21 | 0.12 | -0.05, -0.21 | 0.12 | -0.05, -0.27 | 0.17 | -0.04 | -0.28 | 0.20 | -0.15 | -0.47 | 0.17 |
| BMI for age | -0.07, -0.22 | 0.09 | -0.07, -0.23 | 0.09 | -0.12, -0.33 | 0.09 | -0.01 | -0.24 | 0.22 | -0.14 | -0.44 | 0.16 |
| Postnatal depression (from both SPARCS and EPDS)b | | | | | | | | | | |
| Weight for age | 0.04, -0.06 | 0.15 | 0.04, -0.06 | 0.15 | -0.02, -0.17 | 0.13 | 0.11 | -0.04 | 0.27 | 0.00 | -0.20 | 0.21 |
| Height for age | -0.07, -0.22 | 0.09 | -0.07, -0.23 | 0.09 | -0.16, -0.37 | 0.06 | 0.00 | -0.23 | 0.23 | -0.04 | -0.31 | 0.23 |
| Weight for height | 0.13, 0.00 | 0.26 | 0.13, 0.00 | 0.26 | 0.08, -0.10 | 0.26 | 0.21 | 0.01 | 0.42 | 0.07 | -0.18 | 0.31 |
| BMI for age | 0.13, 0.00 | 0.26 | 0.13, -0.01 | 0.27 | 0.10, -0.08 | 0.28 | 0.19 | -0.02 | 0.40 | 0.03 | -0.22 | 0.29 |

Both antenatal and postnatal depression (Self-reported depressive symptoms, SPARCS, and EPDS)c | | | | | | | | | |
| Weight for age | -0.06, -0.22 | 0.10 | -0.06, -0.22 | 0.11 | -0.26, -0.47 | -0.05 | 0.14 | -0.11 | 0.39 | -0.33 | -0.65 | -0.02 |
| Height for age | -0.16, -0.35 | 0.03 | -0.16, -0.35 | 0.03 | -0.43, -0.70 | -0.16 | 0.09 | -0.17 | 0.36 | -0.30 | -0.77 | 0.17 |
| Weight for height | 0.10, -0.10 | 0.29 | 0.10, -0.10 | 0.30 | 0.05, -0.22 | 0.31 | 0.16 | -0.13 | 0.45 | -0.26 | -0.72 | 0.20 |
| BMI for age | 0.07, -0.12 | 0.26 | 0.07, -0.12 | 0.27 | -0.02, -0.27 | 0.24 | 0.18 | -0.11 | 0.46 | -0.23 | -0.61 | 0.16 |

Regression coefficients indicate differences of z scores for children’s growth between those whose mothers had depression and those whose mothers did not.

aCombined antenatal measure consisted of mothers with self-reported antenatal depressive symptoms and SPARCS data. Antenatal models adjusted for a priori selected confounders, such as maternal age, race, education, marital status, infertility treatment, health insurance status, and prepregnancy BMI.

bCombined postnatal measure consisted of SPARCS and EPDS. Postnatal models adjusted for a priori selected confounders, such as maternal age, race, education, marital status, infertility treatment, health insurance status, prepregnancy BMI, history of smoking, history of alcohol consumption, prepregnancy or gestational diabetes, gestational hypertension, breastfeeding status at hospital discharge, and antenatal depression.

cWe denoted depression as present if either diagnosis was present or participant reported high level of symptoms.

EPDS, Edinburgh Postnatal Depression Scale.

SPARCS, Statewide Planning and Research Cooperative System.
TABLE 3 Associations between antenatal depression and children’s growth through 3 y, the Upstate KIDS Study

|                          | All participants | Singletons | Singleton boys | Singleton girls | Twins |
|--------------------------|------------------|------------|----------------|----------------|-------|
|                          | b                | 95% CI     | b              | 95% CI         | b     | 95% CI |
| Self-reported antenatal depressive symptoms: birth certificate |                  |            |                |                |       |
| Weight for age           | −0.15            | −0.36, 0.06| −0.15          | −0.36, 0.07    | −0.16 | −0.47, 0.15|
| Height for age           | −0.05            | −0.28, 0.19| −0.04          | −0.28, 0.20    | −0.06 | −0.43, 0.31|
| Weight for height        | −0.20            | −0.44, 0.04| −0.21          | −0.45, 0.04    | −0.16 | −0.50, 0.18|
| BMI for age              | −0.20            | −0.43, 0.04| −0.20          | −0.44, 0.05    | −0.19 | −0.52, 0.14|
| Antenatal depression: SPARCS |                  |            |                |                |       |
| Weight for age           | −0.09            | −0.25, 0.07| −0.09          | −0.26, 0.07    | −0.27 | −0.48, −0.06|
| Height for age           | −0.16            | −0.30, 0.08| −0.16          | −0.31, 0.04    | −0.42 | −0.69, −0.14|
| Weight for height        | 0.06             | −0.13, 0.25| 0.06           | −0.13, 0.25    | 0.03  | −0.23, 0.28 |
| BMI for age              | 0.03             | −0.16, 0.21| 0.03           | −0.16, 0.22    | −0.06 | −0.31, 0.19 |

Regression coefficients indicate differences of z scores for children’s growth between children whose mothers had antenatal depression and children whose mothers did not. Models adjusted for a priori selected confounders, such as maternal age, race, education, marital status, infertility treatment, health insurance status, and prepregnancy BMI.

 Mothers with self-reported antenatal depressive symptoms categorized as those whose answer included “moderately depressed,” “very depressed,” and “very depressed and had to get help” from self-reported maternal depression during pregnancy on the NYS birth certificate.

Antenatal depression derived from SPARCS for mothers with any in- or outpatient discharge records due to depression before date of child delivery.

SPARCS, Statewide Planning and Research Cooperative System.

whose mothers had antenatal depression weighed less ($b = −0.27; 95% CI: −0.48, −0.06$) and were shorter ($b = −0.42; 95% CI: −0.69, −0.14$) than boys whose mothers did not have antenatal depression, after adjusting for covariates. Self-reported antenatal depressive symptoms from birth certificate data were not associated with growth measures.

Table 4 captures postnatal associations. Again, associations were made stratified by source of data to provide indications of severity. In general, we found some indications that postnatal depressive symptoms were associated with increased growth among singletons but differed by severity and infant sex. For girls, depressive symptoms were associated with increased weight for height ($b = 0.27; 95% CI: 0.1, 0.54$) and BMI ($b = 0.21; 95% CI: −0.07, 0.49$; not significant). For boys, maternal depression requiring hospitalization rather than depressive symptoms alone tended to be associated with increased weight for height ($b = 0.24; 95% CI: −0.01, 0.49$; not significant) and BMI ($b = 0.26; 95% CI: −0.03, 0.55$; not significant).

TABLE 4 Associations between postnatal depression and children’s growth through 3 y, the Upstate KIDS Study

|                          | All participants | Singletons | Singleton boys | Singleton girls | Twins |
|--------------------------|------------------|------------|----------------|----------------|-------|
|                          | b                | 95% CI     | b              | 95% CI         | b     | 95% CI |
| Severe postnatal depressive symptoms: EPDS\textsuperscript{a} |                  |            |                |                |       |
| Weight for age           | −0.03            | −0.16, 0.10| −0.04          | −0.17, 0.10    | −0.08 | −0.25, 0.10|
| Height for age           | −0.11            | −0.30, 0.08| −0.11          | −0.31, 0.08    | −0.03 | −0.28, 0.22|
| Weight for height        | 0.06             | −0.11, 0.23| 0.06           | −0.11, 0.23    | −0.11 | −0.32, 0.11|
| BMI for age              | 0.04             | −0.13, 0.20| 0.04           | −0.13, 0.21    | −0.10 | −0.30, 0.11|
| Postnatal depression: SPARCS\textsuperscript{b} |                  |            |                |                |       |
| Weight for age           | 0.08             | −0.07, 0.23| 0.08           | −0.07, 0.24    | 0.05  | −0.16, 0.27|
| Height for age           | −0.04            | −0.25, 0.17| −0.04          | −0.25, 0.17    | −0.22 | −0.52, 0.08|
| Weight for height        | 0.14             | −0.04, 0.32| 0.14           | −0.04, 0.32    | 0.24  | −0.01, 0.49|
| BMI for age              | 0.16             | −0.03, 0.35| 0.16           | −0.03, 0.35    | 0.26  | −0.03, 0.55|

Regression coefficients indicate differences of z scores for children’s growth between those whose mothers had postnatal depression and those whose mothers did not. Models adjusted for a priori selected confounders, such as maternal age, race, education, marital status, history of smoking, history of alcohol consumption, infertility treatment, health insurance status, prepregnancy BMI, prepregnancy or gestational diabetes, gestational hypertension, breastfeeding status at hospital discharge, and antenatal depression.

\textsuperscript{a}Severe postnatal depressive symptoms measured with abridged EPDS at 4, 12, 24, and 36 months after delivery by using five items assessing emotional experiences over the past 7 days.

\textsuperscript{b}Postnatal depression derived from SPARCS for mothers with any in- or outpatient discharge records due to depression after date of child delivery.

EPDS, Edinburgh Postnatal Depression Scale.

SPARCS, Statewide Planning and Research Cooperative System.
Again, these associations may have been driven by the persisting maternal depressive episodes, and findings were only marginally significant.

We conducted sensitivity analyses to assess missingness, including the complete case analyses for exposures and outcomes and multiple imputation, and our findings remained robust (data not shown).

Discussion

We observed no consistent associations between various maternal depression measures and children’s growth through 3 years of age. Overall, maternal depression or depressive symptomatology during both antenatal and postnatal periods was associated with decreased weight and height only for singleton boys. We also found sex-specific associations between the timing of maternal depression and children’s growth among singletons. Antenatal depression or depressive symptomatology was associated with decreased weight and height for age among singleton boys, whereas postnatal depression or depressive symptomatology was associated with decreased height for age. When examining individual measures, antenatal depression from SPARCS records was associated with decreased height for age only for singleton boys, whereas severe postnatal depressive symptoms from EPDS were associated with increased weight for height only for singleton girls. Exact mechanisms remain unknown, but several explanations can be suggested to better understand our findings on how depression would be associated with child growth. Antenatal depression may increase cortisol and ovarian hormone levels, which are associated with a dysregulation of the maternal HPA axis (12). These changes may reprogram fetal HPA regulation and increase an infant’s cortisol stress responses, potentially resulting in infant adiposity or impaired mother-child interaction or attachment (12). As compared to mothers without depression, mothers with depression were less sensitive to children’s signs of interest (30), less likely to support or be attached to their children (31), and less likely to complete well child visits (32).

Different responsiveness and vulnerability to maternal depression by infant sex may determine sexually dimorphic growth patterns in utero and ex utero (19,33). Previous studies have suggested that males may be more vulnerable to adverse conditions in utero, whereas females may be more vulnerable ex utero (19,33,34). Relatively higher fetal and neonatal mortality and morbidity among males than females, despite their larger size, could be due to different survival strategies between male and female fetuses (33). Meanwhile, relatively higher adaptability in utero among female fetuses may be related to higher variabilities in growth ex utero, resulting in higher susceptibility and vulnerability to behavioral or environmental conditions (34). Although the mechanisms are not fully understood yet, sex-specific growth patterns in utero and ex utero may be due to the differential responses in the placenta by sex. Female placenta is known to be more responsive to maternal glucocorticoid concentration (34). Studies have also documented sex-specific differences in placental cytokine expression or insulin-like growth factor pathways, as well as in fetal growth, survival, and obstetric outcomes (33). For example, differing caloric densities in breast milk by infant sex demonstrate potential sexually dimorphic programming in utero that subsequently affects child growth ex utero (35). Cheng and colleagues documented that the caloric density in breast milk differed by infant sex; on average, the density was 63 to 64 kcal/100 mL for girls and 68 to 78 kcal/100 mL for boys. Formula-fed girls grew faster than formula-fed boys because the caloric density in formula (67 kcal/100 mL) is greater than in breast milk for girls but similar to breast milk for boys (35). It is also possible that sex-specific growth is the result of differential child care practices that vary by infant sex. Differential child care practices by infant sex among humans have not been investigated yet, but animal studies have documented that maternal child care practices may vary by infant sex (36). However, it is unclear whether the observed sex-specific maternal child care practices are embedded behaviors of mothers or if they are a reflection of sex differences of newborns (36).

Our study is one of few studies indicating potential sex-specific associations between the timing of maternal depression and child growth (5,16,18). This study advances the research in this area by examining both antenatal and postnatal depression via medical records, self-reported antenatal depression status, and longitudinal assessment of postnatal depressive symptoms. Therefore, given the number of sources of data used along with the timing of depression, this remains one of the most comprehensive population-based cohort studies on the topic of maternal depression on child growth.

Despite notable strengths, including our population-based cohort with longitudinal measurement of children’s growth in relation to a set of maternal depression measures at various critical windows, our findings need to be cautiously interpreted in the context of important limitations. Our self-reported measure for antenatal depression or depressive symptoms is likely to be subject to underreporting (37). Hospital discharge data from SPARCS may have high specificity but low sensitivity for depression, as SPARCS data do not include subclinical depression or claims from state psychiatric centers or private psychiatric hospitals and only covered 61% of inpatient bed capacity in NY as of 2016 (38). Although our measure for postnatal depressive symptoms, the abridged EPDS, was found to have psychometric properties for research purposes in postnatal women (23) that were as sound as those from the full EPDS, it may not be directly comparable to clinically diagnosed depression measures. Given the number of comparisons using different definitions and measures of maternal depression, we cannot rule out chance findings that resulted in only a couple of associations attaining conventional 5% levels of significance.

Conclusion

In this study, we found some evidence that maternal depression is differentially associated with children’s growth, depending upon its timing. Specifically, antenatal depression was associated with lower weight and smaller height among boys but not girls, whereas postnatal depression was associated with higher weight for height among girls. These findings underscore the importance of both the timing of maternal depression and the sex of children for child growth, although underlying mechanisms remain unknown. O

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