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Prenatal maternal depression is associated with low birth weight through shorter gestational age in term infants in Korea

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ABSTRACT

Background: Maternal prenatal depression is associated with lower offspring birth weight, yet the impact of gestational age on this association remains inadequately understood.
Aims: We aimed to investigate the effect of prenatal depression on low birth weight, gestational age, and weight for gestational age at term.
Study design: Prospective cohort study.
Subject: Data were collected from 691 women in their third trimester of pregnancy who went on to give birth to a singleton at term without perinatal complications. One hundred and fifty-two women had a Center for Epidemiologic Studies Depression Scale-10 score ≥10 and were classed as prenatally depressed.
Outcome measures: Low birth weight (<2500 g), gestational age at birth, and birth weight percentile for gestational age.
Results: Offspring of prenatally depressed women were more likely to be low birth weight (Odds ratio [OR] 2.94, 95% confidence interval [CI] 1.14–7.58) than offspring of prenatally non-depressed women, but the association was attenuated (OR 1.66, 95% CI 0.55–5.02) when adjusted for gestational age. Offspring of prenatally depressed women had lower gestational age in weeks (OR for one week increase in gestational age: 0.66, 95% CI 0.47–0.93) than offspring of prenatally non-depressed women. There was no association between prenatal depression and birth weight percentile for gestational age.
Conclusions: Prenatal depression was not associated with low birth weight at term, but was associated with gestational age, suggesting that association between maternal depression and birth weight may be a reflection of the impact of depression on offspring gestational age.

1. Introduction

Depressive symptoms during pregnancy are common. A meta-analysis estimated that 12.0% of women in their third trimester exhibit clinically significant depressive symptoms [1], and other study reported that 18% of women exhibit depressive symptoms antenatally [2]. Recent Korean data indicate that the prevalence of prenatal depression is as high as 20.2% [3]. In addition to depression-related disabilities in the pregnant woman, prenatal depression can have numerous adverse effects on the offspring [4]. For example, the prevalence of autism spectrum disorders [5] and emotional and behavioral problems [6] was higher among infants of mothers with prenatal depression than among infants of mothers without prenatal depression.

Neonatally, prenatal depression is associated with low birth weight and intrauterine growth restriction [7], but many studies have not assessed birth weight according to gestational age, which complicates the interpretation [8,9]. The underlying determinants and etiology of

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preterm birth, typically defined as birth before 37 weeks gestation, may be different to those for term births that are low birth weight. For example, parity and gestational weight gain is a risk factor for term low birth weight but not preterm delivery [10,11]. Preterm birth was more closely associated with neurodevelopmental disorders [12], whereas low birth weight was more closely associated with endocrine disorders such as metabolic syndrome [13]. Understanding whether prenatal depression influences gestational age or birth weight is thus an important distinction.

Preterm birth increases the risk of numerous adverse outcomes; however, recent research has begun to focus on potential adverse outcomes of birth between 37 and 38 weeks gestation, namely early-term births [14]. Approximately 52% of infants are born between 37 and 39 weeks gestation [15], and these infants are at increased risk for respiratory distress syndrome [16] and autism [17], and have higher mortality [14] than infants born after 38 weeks gestation. Understanding the etiology of early-term birth is therefore an important public health priority [18].

Studies of the influence of maternal depression on gestational age and birth weight among term births are scarce, and show conflicting results [19–21]. Kelly et al. reported a two-fold increase in the odds of low birth weight in depressed women delivering at term compared to non-depressed women delivering at term [22]. Henrichs et al. and Nasreen et al. also reported a significant association between prenatal depression and low birth weight at term [20,23]. However, Evans et al. reported that, in a large sample of over 10,000 women who gave birth at term, the association between prenatal depression and low birth weight was attenuated after adjustment for health behaviors and potential confounding factors such as smoking [19], and Gawlik et al. and Lancaster et al. reported that psychosocial variables were not significant predictors of birth weight in term births [24,25]. Thus, there remains little consensus on the influence of prenatal maternal depression on birth outcomes of term births, and few investigations to date on the influence of depression on gestational age versus birth weight.

In addition, results of studies of prenatal depression and offspring health outcomes are complicated by potential confounding factors. In many samples, prenatal depression is associated with increased smoking, alcohol consumption, and other unhealthy behaviors [26]. Thus, it is unclear whether prenatal depression causally increases the risk of adverse neonatal outcomes, or whether health behaviors linked to depression are the causal agents. Causal inference from observational studies will never be absolute; however, one way to mitigate the effects of confounding is to examine the association in a diverse set of populations with a different distribution of potential risk factors for birth weight and gestational age [27].

In this study, we aimed to examine the relation between maternal prenatal depression and neonatal outcomes in a large sample of term infants in Korea. We evaluated the association between maternal depression and three main outcomes: low birth weight, gestational age, and birth weight for gestational age. We drew on the strength of a large sample of pregnancies in Korea with comprehensive data on potential confounders. Women in this sample were generally quite healthy; the rate of smoking history and drinking during pregnancy was low, and no one was undergoing treatment for psychiatric disorders. Thus, the distribution of risk factors for low birth weight in this sample is likely different from samples from other geographic areas, providing a rigorous evaluation of the association between prenatal depressive symptoms and these outcomes.

2. Methods

2.1. Study subjects

Data used were collected as part of the COhort for Childhood Origin of Asthma and allergic diseases (COCOA) study, a prospective study that aims to examine the early risk factors for childhood allergic diseases [28,29]. Women in the third trimester of pregnancy were recruited from four tertiary hospitals in Seoul, Korea between August 2007 and July 2011. For this analysis, study subjects were limited to those with depression data, who had delivery at term (later or equal to 37 weeks) and singleton births. Of 1171 women recruited, 343 women without data on prenatal depression were excluded. Women with depression data were slightly younger than those without depression data (32.2 years versus 32.8 years, $p = 0.001$) but were similar on other key demographic covariates, including educational status, occupational status, and smoking history. Additionally, 55 women with preterm delivery and 24 women who had twin births were excluded, and a further 82 women with missing data on confounders were excluded. None of the women were receiving active treatment for psychiatric disorders. Women with missing data exhibited similar demographic distribution to women without missing data. The final sample was 691 women. Written informed consent was obtained from all women, and the study was approved by the institutional review boards of Asan Medical Center (IRB No. 2008-0616), Samsung Medical Center (IRB No. 2009-02-021), Yonsei University (IRB No. 4-2008-0588), CHA Medical Center (IRB No. 2010-010), and Columbia University (IRB-AAAL4350).

2.2. Assessments

Prenatal depression was evaluated at 36th week of pregnancy using the Center for Epidemiologic Studies Depression Scale-10 (CESD-10) [30,31], a modified 10-item version of the original 20 item full-length CESD. The CESD has been validated for use during pregnancy [32]. Each item is scored in a Likert scale (0, 1, 2, 3), and the score ranges from 0 to 30, with higher scores indicating more severe depressive symptoms. Consistent with previous studies [33], a cut-off score of 10 was used to identify women with depression. The internal consistency of CESD-10 in this study indicated excellent reliability (ICC = 0.785).

Outcomes of interest were low birth weight, gestational age, and birth weight for gestational age. Birth data were obtained from hospital records. Low birth weight was defined as birth weight less than 2500 g [34]. Gestational age was recorded in number of days since the first day of the mother's last menstrual period. Pregnancies were categorized by weeks of gestation according to the lowest whole number of weeks of gestation, e.g., gestation of 37 weeks and 6 days was categorized as 37 weeks. Birth weight for gestational age was calculated as birth weight percentile for gestational age, according to the fetal weight equation proposed by Mikolajczyk et al. [35]. The standard deviation of birth weight was derived from the 2004 to 2008 WHO Global Survey on Maternal and Perinatal Health.

Data on confounding factors were collected at two time points, at baseline (36th week of pregnancy) and at delivery. At baseline, self-reported maternal age, pre-pregnancy body mass index (calculated from reported height and weight), number of existing children, smoking history (ever/never), and data on alcohol use during pregnancy (yes/no) were obtained. At delivery, data on sex of the baby and the delivery method (vaginal delivery/Cesarean section) were obtained from medical records.

2.3. Statistical analysis

Analyses were performed using SPSS 18.0 for Windows (SPSS Inc., Chicago, IL). Independent sample t tests and chi-square tests were used to compare demographic characteristics and neonatal outcomes between women with and without prenatal depression. Logistic regression was used to analyze the association between independent variables and low birth weight, in both an unadjusted model and a model adjusted for previously defined confounders. Gestational age was analyzed using a cumulative logit model with the outcome defined as 37, 38, 39, 40, and 41 weeks gestation (reference group 41 weeks). Birth weight percentile for gestational age was analyzed using a linear regression model. Models were adjusted for potential confounding variables including gestational age [for low birth weight only], pre-pregnancy BMI