Original article

Maternal psychiatric disorders and risk of preterm birth

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A B S T R A C T

Purpose: To study the effect of maternal psychiatric disorders (depression, anxiety disorder, bipolar disease, schizophrenia, unspecified psychiatric disorder, and comorbid conditions) and odds of preterm birth.
Methods: The Consortium on Safe Labor (2002–2008), an observational cohort with 12 centers from across the United States included 223,394 singleton pregnancies with clinical data obtained from electronic medical records and maternal diagnoses of psychiatric disorders from maternal discharge summaries. Length of gestation was based on the best clinical estimate and categorized as birth less than 39, less than 37, less than 34, and less than 28 weeks' gestation. The adjusted odds ratios (ORs) with 95% confidence intervals of birth were estimated by logistic regression with generalized estimating equations.
Results: Any maternal psychiatric disorder was associated with odds of birth less than 39 weeks' gestation (odds ratio [OR] = 1.32, 95% confidence interval = 1.28–1.37), less than 37 weeks' gestation (OR = 1.45, 1.38–1.52), less than 34 weeks' gestation (OR = 1.47, 1.35–1.59), and less than 28 weeks' gestation (OR = 1.57, 1.36–1.82). Specifically, odds of birth less than 37 weeks' gestation were associated with maternal depression (OR = 1.31, 1.23–1.40), anxiety disorder (OR = 1.68, 1.41–2.01), depression with anxiety disorder (OR = 2.31, 1.93–2.78), bipolar disease (OR = 1.54, 1.22–1.94), bipolar disease with depression and/or anxiety disorder (OR = 1.70, 1.30–2.22), and unspecified psychiatric disorder (OR = 1.52, 1.41–1.64).
Conclusions: Maternal psychiatric disorders, especially comorbid psychiatric conditions, were associated with increased likelihood of preterm birth.

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Introduction

Maternal psychiatric disorders are common among women of childbearing age [1–3]. During pregnancy, up to 10% and 13% have depression and anxiety disorder, respectively, whereas 3% have bipolar disorder and less than 1% have psychotic disorders [4,5].

Women with untreated psychiatric disorders are less likely to access care, including prenatal care, and may be more prone to substance abuse before and during pregnancy [6]. Treatment of maternal psychiatric disorders during pregnancy requires consideration, including the severity of the maternal condition, the medication to be used, and the potential effects of the medication on the mother and the fetus [7,8]. Although pregnancy is considered a vulnerable period for psychiatric disorders, most of the focus in the literature is on the postpartum period [5,9,10].

In 2012, 11.5% of infants in the United States were born preterm at less than 37 weeks' gestation [11]. Preterm neonates are at higher

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risk of morbidity and mortality as well as increased risk for psychiatric disorders later in life [12,13]. Pregnant women with any psychiatric disorder have a shorter gestational length [14] and are at increased risk for preterm birth [15–18]. One previous study has shown that the associations between preterm birth and maternal psychiatric morbidity seemed to be independent of familial relationships and measured covariates [19].

However, data on specific psychiatric disorders and preterm birth risk are less consistent. The risk of preterm birth has been associated with maternal depression or antidepressant use during pregnancy in some [20–24] but not all studies [25–27]. A recent study suggests that underlying psychiatric disorders might confound the association between antidepressant use and preterm birth, as women who received selective serotonin reuptake inhibitors had lower risk of preterm birth than women with psychiatric disorders without exposure to these medications [28]. Findings are somewhat less inconsistent between maternal anxiety disorders and preterm birth risk [29], whereas maternal schizophrenia and bipolar disease are more consistently associated with preterm births [30,31]. The effect of comorbid maternal psychiatric disorders is seldom studied.

In our study from a large, contemporary pregnant U.S. population, we investigated the effect of a full range of maternal psychiatric disorders, including comorbid psychiatric conditions on odds of preterm birth.

Methods

The Consortium on Safe Labor (2002–2008, with 87% of births occurring 2005–2007) was an observational nationwide U.S. cohort including 12 clinical centers with 19 hospitals, chosen due to their geographic distribution and the availability of electronic medical records [32]. The study included 228,668 women with 233,844 newborns (including multiples) [32]. We excluded 230 deliveries because of errors of identification and all multifetal pregnancies ($n = 5044$), rendering a final sample size of 203,999 women with 223,394 singleton deliveries. Most women ($n = 185,422$; 90.9%) contributed only one pregnancy. Data on maternal demographics, medical, reproductive, and prenatal history, labor, and delivery, and postpartum data were collected from the hospital delivery admission electronic medical records, supplemented with electronic maternal discharge summaries in *International Classification of Diseases, version 9* (ICD9) codes. The institutional review boards of all participating institutions approved the study. Data linkage, cleaning, recording, and validation have been previously described, with the medical chart review and the electronic data providing good agreement [32].

Exposure data

Data on maternal psychiatric disorders were abstracted from the electronic medical records and supplemented with data from the maternal discharge summaries. Women were considered to have a psychiatric disorder during pregnancy if they had any of the following disorders recorded in the electronic medical record or in the discharge summary:

1. Depression ($n = 8354$), pregnancies with diagnoses of major depressive disorder (ICD9 codes 296.2 and 296.3), depressive disorder not elsewhere classified (ICD9 code 311) recorded in the maternal hospital discharge summaries ($n = 1437$; 17.2%), pregnancies with history of depression recorded in the electronic medical records ($n = 4695$; 56.2%), or pregnancies with both indications of depression ($n = 2222$; 26.6%). No other specific psychiatric disorders recorded in either database.

2. Anxiety ($n = 689$), pregnancies with diagnoses of anxiety state (ICD9 code 300.0) recorded in the maternal hospital discharge summaries. No other specific psychiatric disorders recorded in either database.
3. Bipolar disorder ($n = 515$), pregnancies with diagnoses of bipolar or manic disorder (ICD9 codes 296.0, 296.2, or 296.4 to 296.8) recorded in the maternal hospital discharge summaries. No other specific psychiatric disorders recorded in either database.
4. Depression with anxiety ($n = 885$), pregnancies with both the aforementioned diagnoses of depression and anxiety or pregnancies with diagnoses of dysthymic disorder (ICD9 code, 300.4) recorded in the maternal hospital discharge summaries.
5. Bipolar disorder with depression and/or anxiety ($n = 321$), pregnancies with the aforementioned diagnoses of bipolar disorders and with the diagnoses of depression and/or anxiety.
6. Schizophrenia ($n = 134$), women with schizophrenic disorder (ICD9 code 295) recorded in the maternal hospital discharge summaries with or without any other psychiatric disorders.
7. Unspecified psychiatric disorder ($n = 5500$), pregnancies with diagnoses of psychiatric disorders affecting the pregnancy (ICD9 code, 648.4) in the maternal hospital discharge summaries. No other specific psychiatric disorders were recorded in either database.

Women without these diagnoses were considered to be unexposed (no psychiatric disorder, $n = 206,996$, 92.7%). We also evaluated a composite category "any psychiatric disorder" ($n = 16,398$; 7.3%) to study the overall effect of psychiatric disorders on preterm birth.

Outcome data

Data on gestational age were derived from the electronic medical records and were based on the best obstetrical estimate of gestational length. We explored clinically relevant cutoffs of preterm birth: total preterm births at less than 37 weeks' gestation, early preterm births at less than 34 weeks' gestation, and very early preterm births at less than 28 weeks' gestation. We also used a cutoff of less than 39 weeks' gestation given the recent recognition that infants born at 37 and 38 weeks have increased neonatal morbidity [33,34]. We also classified the subtype of preterm delivery as spontaneous or indicated using a method previously described by our group [35]. Spontaneous preterm deliveries included women who presented in preterm labor or with premature rupture of the membranes. Indicated preterm deliveries were identified as inductions and prelabor cesareans for fetal, maternal, or obstetrical indications.

Statistics

Pregnancy was the unit of analysis in all statistical testing. The demographics of the population were tabulated using contingency tables. Missing categorical data were included in the analyses as their own category. Women with missing continuous data were excluded from the analyses.

We used logistic regression with generalized estimating equations to estimate the odds ratios (ORs) with 95% confidence intervals (CIs) of birth at certain gestational week (less than 39 vs. 39 weeks' gestation or more, less than 37 vs. 37 weeks' gestation or more, less than 34 vs. 34 weeks' gestation or more, less than 28 vs. 28 weeks' gestation or more) associated with maternal psychiatric disorders. The generalized estimating equations with autoregressive correlation matrix accounted for correlation between repeat pregnancies within a woman. The analyses were adjusted for