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Impact of antidepressant treatment during pregnancy on obstetric outcomes among women previously treated for depression: an observational cohort study

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Abstract

OBJECTIVE: To examine the impact of pharmacologic treatment for depression on obstetric outcomes in women treated for depression during the 2 years prior to pregnancy.

STUDY DESIGN: Observational cohort study among 2859 women treated for depression during the 2 years prior to pregnancy. The primary exposure was any antidepressant treatment during pregnancy. Secondary analyses examined the impact of treatment by period of antidepressant exposure. Multivariable logistic regression models as well as propensity score analysis was utilized.

RESULTS: Among 2859 women, 1648 (58%) were treated with antidepressant medication during pregnancy. Women who received antidepressants had no difference in preterm and early-term deliveries, Apgar scores, and small for gestational age (SGA); they had a lower likelihood of breastfeeding (adjusted odds ratio (AOR) 0.69, (95% confidence interval (CI): 0.51 to 0.94)). In secondary analysis, women who used antidepressants all three trimesters who delivered at term were more likely to deliver early term (AOR 1.36, (95% CI: 1.09 to 1.72)). Women who were treated with antidepressants only during the first and second trimesters had a reduced likelihood of SGA (AOR: 0.51 (95% CI: 0.32 to 0.83)). Generally similar results were observed with propensity score analysis.

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CONFLICT OF INTEREST

PRH has received consultant fees or served on scientific advisory boards for Proteus Biomedical, Genomind, Healthrageous, Perfect Health, and Psy Therapeutics. The remaining authors declare no conflict of interest.

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CONCLUSION: Antidepressant exposure during pregnancy does not confer an increased risk of preterm birth nor growth restriction in women recently treated for depression, but also does not appear to markedly improve these outcomes.

INTRODUCTION

Maternal depression during pregnancy and the postpartum period is common, exceeding rates in the general female population in the second and third trimesters of pregnancy (12%).[1-4] Untreated depression during pregnancy and the postpartum period has been associated with obstetric complications, as well as with increased maternal and neonatal morbidity.[5-10] Despite data showing the deleterious consequences of maternal depression during pregnancy, there is evidence that depression is commonly undertreated during pregnancy,[6,7,11] and that many women taking antidepressants prior to pregnancy discontinue use with the onset of pregnancy.[12] This may in part be due to provider and patient concerns about the safety of treatment of depression during pregnancy due to potential negative short-term outcomes associated with fetal exposure to antidepressant medications,[13-15] although the magnitude of such risk remains debated.[16]

Recent observational reports also suggested that antidepressant medication exposure during pregnancy may be associated with preterm delivery and lower infant birth weight, regardless of whether the comparison group consisted of all unexposed mothers or only depressed mothers without antidepressant exposure.[7,15,17-21] However, these adverse delivery outcomes are also linked to untreated maternal depression.[22-25] As such, a major limitation of prior studies has been the inability to adequately address the fact that pregnant women with depression who are treated with antidepressants are inherently different than their peers with depression who are not treated (that is, confounding by indication).[26] It is therefore difficult to ascertain whether there is a causal relationship between exposure to antidepressant medications and obstetrical outcomes or whether maternal depression is itself responsible for the observed increases in infant morbidity.[10,17,27] In addition, how the impact of timing and duration of antidepressant exposure during pregnancy may influence birth outcomes remain unclear.[20,28-30]

The objective of the current study was to assess the impact of treating maternal depression with antidepressant medication during pregnancy on maternal and infant outcomes among a well-characterized cohort of women who had been treated for depression during the 2 years prior to pregnancy, while taking into account underlying psychiatric and clinical risk factors for adverse obstetric outcomes. In secondary analyses, given that clinical questions remain regarding the benefits and risks of stopping or starting antidepressants during pregnancy, associations were examined based on antidepressant use during all three trimesters, only the first and second trimesters, and only the third trimester, to assess whether the association between treatment and obstetric outcomes varied by period of exposure.

METHODS

Study setting and participants

The current study was a longitudinal observational analysis conducted from 1 January 1998 to 5 October 2013 at Massachusetts General Hospital, MGH (Boston, MA, USA), a large tertiary-care academic medical center. All women delivered at the obstetrics unit at MGH. This study utilized data from the Partners Healthcare electronic health record (EHR) using i2b2 server software (Boston, MA, USA), which is a scalable computational framework deployed at over 100 major academic health centers internationally for managing human health data. Further details about the i2b2 platform can be found in earlier analyses by this study group.[31,32]

Among a total of 51 261 women who delivered a liveborn infant at >20 weeks during the study period, the current analysis was conducted among the cohort of 2859 unique women (5.6%) who had been prescribed an antidepressant medication within the partners system during the 2 years prior to their pregnancy. For multiparous women, data were taken from their first pregnancy during the study period. Consistent with prior studies and our study aims, we elected *a priori* to exclude non-viable gestations delivered prior to 20 weeks. A 2-year period was chosen to define a group that had any recent exposure to antidepressants, including any prescription filled, and to capture women who may have discontinued antidepressants when planning for conception. Of note, electronic prescribing was mandatory within this hospital system throughout the study period, and clinicians documented medications prescribed by outside providers using the same system. This study was approved by the Partners Healthcare Institutional Review Board with a waiver of informed consent.

Exposure and outcome ascertainment

Data on use of antidepressant medication were derived from the outpatient EHR and pharmacy record. The following socio-demographic and clinical characteristics were assessed from the EHR: age, race, household zip code, year of delivery, parity, pre-pregnancy body mass index, maternal co-morbid conditions (including diabetes, hypertension, and pre-eclampsia during the current pregnancy), tobacco use during pregnancy, and enrollment in a government insurance program. Median household income was imputed using 2013 US Census Bureau data for the patient's residential zip code.[33] The following psychiatric characteristics were assessed: past and current antidepressant use, past and current diagnosis of major depressive disorder as well as other psychiatric diagnoses, and psychotherapy and psychopharmacology visits up to 2 years prior to pregnancy.

Antidepressant exposure ascertainment.—Among women with antidepressant use 2 years prior to pregnancy, the primary exposure was continuation of antidepressant use during pregnancy, and unexposed patients were defined as those pregnant women who were not prescribed antidepressants during pregnancy. In secondary analyses, to understand whether the relative impact of antidepressant use on obstetric outcomes varied by time period of antidepressant exposure during pregnancy, the period of antidepressant use during pregnancy was further analyzed according to the following *a priori* clinically relevant categories:

(1) all three trimesters of pregnancy, (2) first and second trimesters only, and (3) third trimester only. We defined these three periods of antidepressant exposure both based upon the clinical decision making that results in these patterns (that is, desire to discontinue antidepressants prior to delivery and need for initiation of antidepressants in pregnancy due to symptomatic relapse) and based on significant socio-demographic and clinical differences between women in these groups in this study. The antidepressant medication exposure period prior to pregnancy and then during pregnancy was estimated from the days of medication provided, which was calculated from the number of pills provided and the number of refills. Consistent with prior studies,[34] we divided antidepressant exposure time based on last menstrual period (LMP) calculated from gestational age: first trimester (0 to 90 days after LMP), second trimester (91 to 180 days after LMP), and third trimester (181 days after LMP to delivery).

Obstetrical outcomes.—Primary obstetrical study outcomes included: (1) any preterm delivery < 37 weeks (including both spontaneous and medically indicated), (2) among term deliveries (that is, > 37 weeks), early-term deliveries between 37 and 39 weeks, (3) infant Apgar score of < 7 at 5 min of life, (4) infant birth weight < 2500 g, (5) infant diagnosis of small for gestational age (SGA) based on gestational age at birth and birth weight, and (7) breastfeeding at hospital discharge following delivery. SGA was defined by matching infant weights to standardized birth weights for gestational age using a recent United States national reference,[35] but not by infant sex of any other factor.

Statistical analyses

The exposed group included women who were prescribed antidepressants during pregnancy compared to the non-exposed group who included women who were not prescribed antidepressants during pregnancy. We employed logistic regression models to determine the association between antidepressant use and obstetric outcomes after controlling for the following covariates: maternal age, parity, race, imputed median household income, any tobacco use during pregnancy, year of delivery, diagnosis of major depressive disorder during pregnancy, prior diagnosis of an anxiety disorder as a single covariate (including Generalized Anxiety Disorder, Obsessive Compulsive Disorder, Panic Disorder and Post-traumatic Stress Disorder), psychotherapy visits during the 6 months prior to pregnancy, psychopharmacology visits during the 6 months prior to pregnancy and maternal medical co-morbidities as a single covariate (diabetes, hypertension or pre-eclampsia during current pregnancy). We elected to use logistic regression rather than survival analysis for ease of interpretability, to make the fewest assumptions about time-varying effects, and for comparability with prior studies. Confounding variables were selected *a priori* and based on a review of relevant studies.[7,9,19,36] Recent data suggest that women with depression have higher rates of pre-existing medical conditions in addition to other deleterious perinatal outcomes.[37] We calculated robust clustered standard errors to account for women with multiple gestations (that is, twins or higher order gestations). Allowing clustered observations takes into account not only that outcomes within a mother may be more similar than outcomes across mothers, but also that other parameters, such as age and parity, will change with each observation. We also performed an additional sensitivity analysis limited to only singleton pregnancies. We first present the multivariable analysis of obstetric

outcomes overall for all patients (Model I); and in secondary analyses, we present stratified multivariable models by period of antidepressant exposure during pregnancy, namely all three trimesters (Model II), the first and second trimesters only (Model III) and the third trimester only (Model IV), compared to no exposure. We did these analyses to understand whether the association between antidepressant exposure and obstetrical outcomes varies by period and duration of exposure during pregnancy.

To further address the issue of systematic differences in characteristics between treated vs untreated women (that is, confounding by indication), we employed propensity score analysis (PSA) showing average treatment effect in the treated group with Abadie-Imbens robust standard errors, with antidepressant exposure overall and by trimester of use.[38,39] We followed standard guidelines for such analyses.[40] Variables were selected for inclusion based on hypothesized association with outcome, or with both outcome and treatment,[41] excluding those that could be affected by treatment.[41,42] Propensity score distribution across antidepressant- exposed and -unexposed individuals was examined visually, and balance properties were tested using two-group comparisons of exposed and unexposed for the cohort as a whole and in quintiles defined by propensity score, with estimates of bias before and after matching. For base case matching, we specified a caliper width equal to 0.2SD of the logit of the propensity score with maximum of four nearest neighbors.[43] Sensitivity analyses examining a range of caliper and nearest neighbor settings yielded very similar results and are not presented here. All analyses used STATA (STATACORP, version 10.0 and 13.1, College Station, TX, USA).

RESULTS

Participant characteristics

Out of a total cohort of 51 261 pregnant women, 2859 (5.6%) women had been prescribed an antidepressant medication during the 2 years prior to pregnancy, and the current analysis is limited to these women (Supplementary Information TableA1 a). Overall, 1648 women (58%) continued to use an antidepressant medication during their pregnancy. The median age was 33 years (interquartile range, IQR, 29 to 36). Most women were white (65%) and multiparous (55%). Socio-demographic and clinical characteristics were generally similar between exposed and unexposed women (Table 1), but there were some significant differences in characteristics by trimester of antidepressant use (Supplementary Information Table A1b).

Psychiatric characteristics

Among women who continued antidepressant use during their pregnancies, 45% continued to use an antidepressant medication during all three trimesters, 16% only during the first and second trimesters, and 7% only during the third trimester (Table 2). Generally, women who continued on antidepressants all three trimesters had statistically significantly greater psychiatric morbidity compared to women who were treated only during the first and second trimesters as well as only during the third trimester (Supplementary Information Table A2). About 15% of women were diagnosed with major depressive disorder during pregnancy,

which was more common among exposed compared to unexposed women (odds ratio, OR: 4.18 (95% confidence interval (CI): 3.23 to 4.43)).

Obstetrical outcomes

17% delivered preterm before 37 weeks of gestation, and among those delivering after 37 weeks, close to half (48%) delivered early term between 37 and 39 weeks (Table 3). Over a tenth (12%) were classified as SGA at birth. Three-fourths of women were breastfeeding at hospital discharge following delivery. In unadjusted analyses, women who were treated for depression were significantly less likely to breastfeed at discharge compared to unexposed women.

Multivariable analyses

After adjusting for socio-demographic, psychiatric, and clinical covariates, overall women who were treated with antidepressants during pregnancy had similar obstetrical outcomes, namely gestational age at delivery, infant growth restriction, and infant Apgar scores, compared to women were not exposed to antidepressants (Table 4). Women who were treated were less likely to breastfeed at the time of discharge compared to unexposed women (adjusted odd ratio, AOR: 0.69 (95% CI: 0.51 to 0.94)). When the above analyses were limited to 2711 (94.8%) women with singleton pregnancies, these results were unchanged.

In exploratory analyses adjusting for the same covariates as above, we examined effects of antidepressant exposure stratified by trimester of exposure compared to no exposure. Women who were treated with antidepressants throughout all three trimesters of pregnancy and delivered at > 37 weeks were more likely to deliver early term between 37–39 weeks (AOR: 1.36 (95% CI: 1.09 to 1.72)) and to have infants with an Apgar < 7 at 5 min of life (AOR: 1.72 (95% CI: 1.01 to 2.94)). They were also less likely to breastfeed (AOR: 0.63 (95% CI: 0.42 to 0.94)) compared to unexposed women. Women who were treated with antidepressants only during the first and second trimesters were less likely to have a SGA infant at birth (AOR: 0.51 (95% CI: 0.32 to 0.83)), compared to women who were not treated for depression. Women who were treated with an antidepressant only during the third trimester were less likely to breastfeed (AOR: 0.25 (95% CI: 0.11 to 0.56)).

When utilizing propensity score analysis (PSA), results were generally concordant with the above findings (Supplementary Information Table A5).

DISCUSSION

The current study demonstrates that the treatment of depression in pregnancy with antidepressant medication is generally not associated with adverse obstetrical outcomes in a cohort of over 2800 pregnant women who had been treated with antidepressants prior to pregnancy. These results are concordant with other recent observational data;[17,18,44,45] however, a recent meta-analysis found that women who received SSRIs during pregnancy had a significantly higher risk of preterm delivery, regardless of whether the comparison group was depressed women not on SSRIs or women without depression.[21] Of note, only 3 of the 8 studies included in the meta-analysis were able to adjust for confounders, which the authors note as a potentially significant limitation. In the current study, after controlling

for psychiatric and obstetric confounders, overall, women who continued antidepressant medication did not experience significant differences in preterm delivery, infant Apgar scores, and growth restriction, compared to women who discontinued antidepressant medication prior to pregnancy.

Given that antidepressant use in many pregnancies is not a 'yes or no' phenomenon, we conducted analyses by duration and trimester of exposure, and did note some differences.[20] In particular, women who were treated for all three trimesters had a slightly higher risk of having an infant with an Apgar score < 7 at 5 min of life, as well as delivering in the early term period. These two outcomes may be related, as Apgar scores are related to gestational age. Earlier studies have generally found only a slight difference (< 1 point) in Apgar scores by treatment status and average Apgar scores in exposed infants remained high.[20,44]

In light of conflicting prior studies, our results are reassuring given some studies suggesting that exposure to antidepressants during pregnancy is associated with preterm birth and infant growth restriction.[17,18,20,21,36,44-46] The current study is unique in its design, by utilizing a carefully selected cohort of women with depression who were treated with an antidepressant prior to pregnancy; and in its analysis, by controlling for multiple confounding variables and disease severity in addition to utilizing different statistical techniques to address confounding by indication, a significant issue in the prior work regarding this topic.

The current study found that women treated with an antidepressant were less likely to breastfeed, particularly women who were treated close to the time of delivery. It is possible that women treated with an antidepressant may have been discouraged from breastfeeding by their providers, or these women may have themselves chosen not to breastfeed due to the perceived risk of antidepressant exposure to the infant. Further educational efforts may help both patients and clinicians to weigh the significant benefits of breastfeeding against the minimal neonatal risks in the setting of antidepressant use.[47]

With regards to the findings based on trimester of exposure, it has been suggested that the timing and duration of antidepressant exposure during pregnancy influences birth outcomes,[28,29] and that late rather than early exposure is more deleterious for perinatal outcomes.[30,48,49] Further research is needed to understand what, if any, implications for long term well-being short-term variation in Apgar scores, particularly related to the SSRI neonatal behavioral syndrome, may have. In terms of the gestational age at delivery, these differences were small, which is consistent with prior observational data,[17,19,50] and it is difficult to know whether they result from the clinical scenarios leading to these different patterns of exposure or from the pattern of exposure itself, as women treated for all three trimesters also had greater markers of psychiatric morbidity and socio-demographic risk factors for inferior obstetric outcomes.

Due to concern for confounding by indication when treatment is the exposure (that is, antidepressant-exposed women experience greater psychopathology and treatment intensity), we employed a study design in which we only included women who had been treated with an antidepressant during the 2 years prior to pregnancy, utilized a propensity score analytic approach in sensitivity analyses, and attempted to adjust for psychiatric and clinical

disease severity in multivariable models.[6] However, there are several study limitations to note in this observational analysis utilizing a healthcare system-wide data set. We did not have data on the number of women with a prior history of a preterm delivery, nor type of preterm delivery (spontaneous vs medically indicated). It is difficult to obtain a disease-matched comparison group, and it is likely that many untreated women or women who discontinued treatment later in pregnancy may have less severe depression than women who continued treatment. We did adjust for depression severity using multiple indices (that is, psychotherapy and psychopharmacology visits before pregnancy as well as psychiatric history). The cohort size does not allow comparisons between specific antidepressants, nor does our data allow examination of dosage or adherence, limiting our ability to further assess drug- and class-specific effects. Some women who were depressed or who were treated may not have been appropriately coded and it is not possible to confirm that women actually took the medications they were prescribed, though both would likely bias results to the null. It is possible that the lack of a significant impact between treatment and perinatal outcomes in the current study may reflect the relatively small sample size of the current study. It is also possible during the course of this study that diagnostic and screening criteria, as well as awareness and management by obstetric providers, have changed, and this study did not adjust for those changes. Finally, a high proportion of women in the current study were of white race and relatively high income possibly limiting the generalizability of these findings to other populations of pregnant women.

Balancing the benefits and harms of taking antidepressants during pregnancy is challenging. Clinicians may avoid prescribing antidepressants during pregnancy and patients may be reluctant to take these medications. For some women, psychotherapy without medication may be an option, but for many women medication may be clinically warranted to treat their depression. The current study utilizing a broad set of obstetric outcome variables, adjusting for the effects of multiple potential obstetric and psychiatric confounders, and conducted among a large diverse cohort of pregnant women, can help guide patients and clinicians when considering evidence-based implications of treating depression in pregnancy on maternal and infant outcomes.[5,6,51] These findings may help to reassure clinicians and patients in deciding if and when to treat depression in pregnancy, particularly given the overall prevalence of this condition and the maternal benefits of treating depression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Socio-demographic and clinical characteristics of women overall and by antidepressant exposure in pregnancy (N = 2859)

Characteristic	Overall (N = 2859)	Antidepressant exposure (N = 1648)	No antidepressant exposure (N = 1211)	Odds ratio, OR, (95% CI) associated with antidepressant exposure
Maternal age at delivery, years				
< 25	271 (9.5)	149 (9.0)	122 (10.1)	Referent
25–⩽ 35	1720 (60.2)	991 (60.1)	729 (60.2)	1.11 (0.86-1.44)
> 35	868 (30.4)	508 (30.8)	360 (29.7)	1.15 (0.87-1.52)
Parity				
0	1265 (44.2)	717 (43.5)	548 (45.2)	Referent
1+	1594 (55.8)	931 (56.5)	663 (54.8)	1.07 (0.92–1.24)
Self-identified race/ethnicity				
White	1860 (65.1)	1100 (66.8)	760 (62.8)	Referent
Black	144 (5.0)	71 (4.3)	73 (6.0)	0.67 (0.47–0.94)[a]
Latina	419 (14.7)	244 (14.8)	175 (14.5)	0.96 (0.77–1.19)
Asian	81 (2.8)	41 (2.5)	40 (3.3)	0.70 (0.45–1.10)
Other/unknown	355 (12.4)	192 (11.7)	163 (13.5)	0.81 (0.64–1.02)
Enrolled in a government insurance program	633 (22.1)	346 (21.0)	287 (23.7)	0.85 (0.71–1.02)
Median household income, $				
1st tertile (< $51 864)	984 (34.6)	556 (33.9)	428 (35.5)	Referent
2nd tertile ($51 864–85 704)	910 (32.0)	526 (32.2)	384 (31.9)	1.05 (0.87–1.26)
3rd tertile (> $85 704)	947 (33.3)	554 (33.9)	393 (32.6)	1.08 (0.90–1.29)
Body mass index, kg m^{-2}				
< 25	1279 (46.6)	729 (46.2)	550 (47.2)	Referent
25–⩽ 30	801 (29.2)	447 (28.3)	354 (30.4)	0.95 (0.79–1.13)
> 30	661 (24.1)	401 (25.3)	260 (22.3)	1.16 (0.96–1.40)
Tobacco use during pregnancy	242 (8.5)	130 (7.9)	112 (9.3)	0.84 (0.64–1.09)
Past medical history				
Diabetes	69 (2.4)	50 (3.0)	19 (1.6)	1.96 (1.15–3.34)[a]
Hypertension	183 (6.4)	115 (7.0)	68 (5.6)	1.26 (0.92–1.71)

Characteristic	***Overall*** **(N = *2859*)**	***Antidepressant exposure*** **(N = *1648*)**	***No antidepressant exposure*** **(N = *1211*)**	***Odds ratio, OR, (95% CI) associated with antidepressant exposure***
Pre-eclampsia in current pregnancy	136 (4.8)	87 (5.3)	49 (4.1)	1.32 (0.92–1.89)
Year of delivery				
1998–2003	223 (7.8)	104 (6.3)	119 (9.8)	Referent
2004–2007	874 (30.6)	491 (29.8)	383 (31.6)	1.46 (1.09–1.97)[a]
2008–2010	888 (31.1)	510 (31.0)	378 (31.2)	1.54 (1.14–2.07)[a]
2011–2013	874 (30.6)	543 (33.0)	331 (27.3)	1.87 (1.39–2.52)[a]

Abbreviation: CI, confidence interval.

[a]Findings reflect a statistically significant association, $P<0.05$.

Table 2.

Psychiatric morbidity of women overall and by antidepressant exposure in pregnancy ($N = 2859$)

Characteristic	***Overall*** **(N = *2859*)**	***Antidepressant exposure*** **(N = *1648*)**	***No antidepressant exposure*** **(N = *1211*)**	***Odds ratio, OR, (95% CI) associated with antidepressant exposure***
Period of antidepressant exposure in pregnancy				
All three trimesters	734 (25.7)	734 (44.5)	—	—
Only first and second trimesters	264 (9.2)	264 (16.02)		
Only third trimester	121 (4.2)	121 (7.3)		
Other	529 (18.5)	529 (32.1)		
> 1 antidepressant prescriptions in the 2 years prior to pregnancy	622 (21.8)	524 (31.8)	98 (8.1)	5.29 (4.20–6.67)[a]
> 1 different antidepressant prescriptions during pregnancy	1056 (36.9)	1056 (64.1)	—	—
Diagnosis of major depressive disorder during pregnancy	437 (15.3)	361 (21.9)	76 (6.3)	4.18 (3.23–4.43)[a]
Diagnosis of major depressive disorder ever	1682 (58.8)	1067 (64.8)	615 (50.8)	1.77 (1.52–2.07)[a]
Psychotherapy visit in the 2 years before pregnancy	608 (21.3)	399 (24.2)	209 (17.3)	1.53 (1.27–1.84)[a]
Psychopharmacology visit in the 2 years before pregnancy	595 (20.8)	444 (26.9)	151 (12.5)	2.58 (2.11–3.16)[a]
Past psychiatric diagnoses ever				
Bipolar disorder	203 (7.1)	125 (7.6)	78 (6.4)	1.19 (0.88–1.59)
Schizophrenia	33 (1.2)	19 (1.2)	14(1.2)	0.99 (0.49–1.99)
Substance use	597 (20.9)	347 (21.1)	250 (20.6)	1.02 (0.85–1.23)
Generalized anxiety disorder	253 (8.9)	170 (10.3)	83 (6.9)	1.53 (1.18–2.05)[a]
History of suicide attempt	85 (3.0)	39 (2.4)	46 (3.8)	0.61 (0.39–0.94)[a]
Post-traumatic stress disorder	277 (9.7)	170 (10.3)	107 (8.8)	1.18 (0.92–1.53)
Obsessive compulsive disorder	127 (4.4)	92 (5.6)	35 (2.9)	1.98 (1.33–2.95)[a]
Panic disorder	341 (11.9)	220 (13.4)	121 (10.0)	1.38 (1.09–1.75)[a]

Abbreviation: CI, confidence interval.

[a]Findings reflect a statistically significant association, $P<0.05$.

Table 3.

Obstetric outcomes of women overall and by antidepressant exposure in pregnancy (*N* = 2859)

Outcome	*Overall* (N = *2859*)	*Antidepressant exposure* (N = *1648*)	*No antidepressant exposure* (N = *1211*)	*Odds ratio, OR, (95% CI) associated with antidepressant exposure*
Mode of delivery				
Vaginal delivery	1890 (66.1)	1073 (65.2)	817 (67.5)	Referent
Cesarean section	968 (33.9)	574 (34.9)	394 (32.5)	1.10 (0.94–1.29)
Gestational age at delivery				
⩾ 37 weeks	2357 (82.4)	1358 (82.4)	999 (82.5)	Referent
< 37 weeks	501 (17.5)	290 (17.6)	211 (17.4)	1.01 (0.83–1.22)
Among women delivering term, gestational age at delivery n = *2357*				
> 39 weeks	1226 (52.0)	681 (50.2)	545 (54.6)	Referent
37–39 weeks	1131 (48.0)	677 (49.9)	454 (45.6)	1.19 (1.01–1.40)[a]
Infant Apgar scores				
5 min Apgar ⩾ 7	2763 (96.6)	1591 (96.5)	1172 (96.8)	Referent
5 min Apgar < 7	6 (3.4)	57 (3.5)	39 (3.2)	1.07 (0.71–1.62)
Infant birth weight				
⩾ 2500 grams	2579 (90.3)	1486 (90.3)	1093 (90.3)	Referent
< 2500 grams	276 (9.7)	159 (9.7)	117 (9.7)	0.99 (0.77–1.28)
Small for gestational age, SGA, at delivery				
No	2495 (87.3)	1449 (87.9)	1046 (86.4)	Referent
Yes	364 (12.7)	199 (12.1)	165 (13.6)	0.87 (0.69–1.08)
Breastfeeding at hospital discharge, n = *1216*				
No	295 (24.3)	182 (27.0)	113 (20.8)	Referent
Yes	921 (75.7)	491 (73.0)	430 (79.2)	0.70 (0.54–0.92)[a]

Abbreviation: CI, confidence interval.

[a]Findings reflect a statistically significant association, $P<0.05$.

Table 4.

Adjusted analysis of predictors of obstetric outcomes overall and by trimester of antidepressant exposure (*N* = 2859)

	Multivariable logistic regression models overall and stratified by period of antidepressant exposure in pregnancy			
	Overall	All three trimesters	Only first and second trimesters	Only third trimester
Study outcome	Model I adjusted odds ratio, AOR (95% CI) (N = 2859)	Model II adjusted odds ratio, AOR (95% CI) (N = 1945)	Model III adjusted odds ratio, AOR (95% CI) (N = 1475)	Model IV Adjusted odds ratio, AOR (95% CI) (N = 1332)
Mode of delivery, cesarean section	1.02 (0.86 – 1.22)	1.04 (0.83 – 1.30)	1.24 (0.91 – 1.67)	1.38 (0.90 – 2.13)
Preterm delivery, < 37 weeks gestation	0.91 (0.73 – 1.15)	1.06 (0.79 – 1.43)	0.67 (0.43 – 1.04)	1.35 (0.83 – 2.18)[a]
Among women delivering term, early-term delivery 37–39 weeks	1.14 (0.95 – 1.36)	1.36 (1.09 – 1.72)[b]	0.85 (0.63 – 1.14)	1.43 (0.89 – 2.28)
Infant Apgar score < 7 at 5 min of life	1.13 (0.72 – 1.79)	1.64 (0.95 – 2.84)[a]	1.08 (0.44 – 2.63)	0.32 (0.04 – 2.59)
Low infant birth weight, < 2500 g at birth	1.00 (0.74 – 1.35)	1.08 (0.73 – 1.59)	0.64 (0.35 – 1.19)[a]	1.23 (0.65 – 2.31)
Small for gestational age, SGA, at delivery	0.93 (0.73 – 1.19)	1.00 (0.72 – 1.37)	1.34 (0.78 – 2.31)	0.51 (0.32 – 0.83)[a,b]
Breastfeeding at hospital discharge	0.69 (0.51 – 0.94)[a,b]	0.63 (0.42 – 0.94)[a,b]	0.90 (0.54 – 1.52)	0.25 (0.11 – 0.56)[a,b]

Abbreviation: CI, confidence interval. Models adjusted for age, race, parity, imputed household income, prior diagnosis of an anxiety disorder, psychotherapy visit 6 months prior to pregnancy, psychopharmacology visit six months prior to pregnancy, tobacco use during pregnancy, year of delivery, and maternal co-morbidities (diabetes, hypertension, or pre-eclampsia during current pregnancy)

[a]Findings reflect a statistically significant association, $P<0.05$, when using propensity score analysis (PSA).

[b]Findings reflect a statistically significant association, $P<0.05$.