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The Association of Antenatal Depression and Cesarean Delivery Among First Time Parturients: A population based study

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Conflict of Interest: The authors declare that they have no conflict of interest.

Abstract:
Objective: Antenatal depression (AD) has been considered a risk factor for cesarean delivery (CD); however, the supporting data is inconsistent. We used a large, nationally representative dataset to evaluate whether there is an association between AD and CD among women delivering for the first time.

Study design: We utilized the 2016-2019 Multistate Pregnancy Risk Assessment Monitoring System (PRAMS) from the Centers for Disease Control. First time parturients who reported depression in the 3 months prior to or at any point during their recent pregnancy were compared to those who did not. Mode of delivery was obtained through the birth certificate. Maternal demographics, pregnancy characteristics and delivery characteristics were compared by report of AD using bivariable analyses. Population-weighted multivariable regression was performed, adjusting for maternal age, race/ethnicity, insurance, pregnancy complications, preterm birth, body mass index.

Results: Of the 61,605 people who met the inclusion criteria, 18.3% (n=11,896) reported AD, and 29.8% (n=19,892) underwent CD. Parturients with AD were younger, more likely to be non-Hispanic white, publicly insured, use tobacco in pregnancy, deliver earlier, have lower levels of education, higher BMIs and more medical comorbidities (hypertension and diabetes). After adjustment for these differences, there was no difference in risk of CD between those with AD compared with those without (aRR 1.04, 95% CI 0.97-1.13).

Conclusion: In a large, population-weighted, nationally representative sample of first time parturients, there was no association between AD and CD.

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The Association of Antenatal Depression and Cesarean Delivery Among First Time Parturients: A population based study

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Keywords
antenatal depression
perinatal depression
mode of delivery
cesarean delivery

Key points:
- Antenatal depression is increasingly common and has multiple known morbidities.
- Prior data on antenatal depression and cesarean delivery are mixed.
- We found no association between depression and cesarean delivery.

Introduction:
The incidence of perinatal depression, or depression that occurs during pregnancy or the first 12 months postpartum, has been increasing over the last two decades\(^1\). It is one of the most common pregnancy complications, which now affects up to one in seven parturients\(^2\). Perinatal depression is associated with multiple adverse maternal and neonatal outcomes including preterm birth, small for gestational age\(^3\), and poor infant bonding and attachment\(^4,5\). Likewise, severe perinatal depression can have devastating effects on women, infants, and families as maternal suicide now exceeds hemorrhage and hypertension as a cause of maternal mortality\(^6\).
Although many of the risks of perinatal depression are well-characterized, prior studies evaluating the association between AD and mode of delivery have yielded inconsistent results, with some reporting an increased risk for CD\textsuperscript{7-11} and others reporting no difference\textsuperscript{12-14}. These studies all have limitations including small sample size of depressed patients\textsuperscript{10,13}, inclusion of patients with mixed parity, where subtle differences in CD may not be detected\textsuperscript{7,8,10,12,13,15} and utilization of medical claims data\textsuperscript{9,11}. The mechanism through which AD might mediate mode of delivery also remains unclear, although proposed mechanisms include physiologic changes secondary to depression (elevated cortisol\textsuperscript{16}, abnormal placentation\textsuperscript{17}), patient factors such as patient decision-making or health behaviors\textsuperscript{18}, or implicit or explicit provider biases that impact medical decision-making\textsuperscript{19}.

Contrary to our expectations, in a recent state-wide analysis of this data, we found no difference in mode of delivery by AD status\textsuperscript{14}. Thus, we sought to evaluate the association of AD with CD in a large, nationally representative, modern obstetric cohort.

**Study Design:**

This is a secondary analysis of the multistate Pregnancy Risk Assessment Monitoring System (PRAMS). PRAMS is an ongoing, state-based surveillance project of the Centers for Disease Control and Prevention (CDC), focusing on maternal behaviors, attitudes, and experiences before, during, and shortly after pregnancy\textsuperscript{20,21}. PRAMS consists of a questionnaire with 2 components: core questions administered by all participating states/regions and a set of state-specific questions either chosen from a list of standard items developed by the CDC or by the individual sites. The questionnaire addresses major topics related to pregnancy, such as content and source of prenatal care and counseling, pregnancy-related morbidity, contraceptive use, and maternal health complications. Participating states use birth certificates to select a stratified random sample, which ranges annually from 1,000 to more than 3,400 people per state. The study invitation and survey are mailed in the first 2–4 months postpartum, then non-respondents are followed up with additional mailings and ultimately by telephone.
Completed surveys are linked to data extracted from the birth certificate and state vital statistics records, herein referred to as the birth record.

For this study, we utilized the Phase 8 (2016-2019) PRAMS database, focusing on parturients with no prior live births who had valid data for AD and mode of delivery and utilized the same methodology as we had employed in a prior state-based analysis on this topic. We limited our analysis to these patients because mode of delivery in multiparous people is highly correlated with their prior mode of delivery. AD was defined as an affirmative answer (‘yes’) to either the core survey questions on preconception depression (“During the 3 months before you got pregnant with your new baby, did you have any of the following health conditions? —Depression”) and/or depression during pregnancy (“During your most recent pregnancy, did you have any of the following health conditions? – Depression”). These items were combined to create a dichotomous variable for AD. The primary outcome was mode of delivery, which was categorized as CD, operative vaginal delivery (OVD, i.e., vacuum-assisted or forceps-assisted vaginal delivery) and spontaneous vaginal delivery.

Demographic variables analyzed included maternal age, race/ethnicity, education, health insurance status at delivery, marital status and tobacco use during pregnancy. Age was stratified into three categories: <20 years, 20-34 years, and ≥35 years. Self-reported race/ethnicity categories included Hispanic, non-Hispanic White, non-Hispanic Black, and non-Hispanic Other [American Indian/Alaskan Native, Native Hawaiian or Pacific Islander, Asian, Multiracial, Other], consistent with prior publications from the multistate PRAMS data. Maternal education was organized into four categories: less than high school diploma, high school diploma, some college (1-3 years) and college diploma or greater. Insurance status at delivery was stratified into private, public/governmental (Medicaid, military, Indian Health Service) and no insurance.

Pregnancy and delivery characteristics examined included gestational age at delivery by best obstetric estimate, preterm birth (<37 weeks), small for gestational age (birthweight <10th percentile), and
maternal body mass index (BMI) which we categorized into 3 categories: normal (BMI <25), overweight (BMI 25-29) and obese (BMI ≥30). Variables obtained from the core survey included Women, Infants and Children (WIC) benefit use during pregnancy, pre-gestational and gestational hypertensive disorders and diabetes mellitus.

Statistical analyses:

Analysis was performed using SAS 9.4 (SAS Institute Inc, Cary, NC). Analysis accounted for complex survey design through application of survey weights as recommended by PRAMS to obtain population level estimates. Outcomes were compared based on self-reported AD status. We first completed bivariable analyses comparing maternal demographic characteristics and potential confounders by AD status. All categorical variables were reported as numbers and weighted population proportions. Population weighted multivariable regression analysis was performed to assess for odds of CD based on self-reported AD status, adjusting for known confounders that were selected a priori based on biologic plausibility and previous literature. These included maternal age, race/ethnicity, insurance, pregnancy complications (hypertensive disorders or diabetes mellitus), preterm birth, and BMI. Lastly, in order to explore if more recent depressive symptoms were more likely to have an impact on the odds of CD, we conducted a sub-analysis of only patients with AD. Women were classified as reporting AD only prior to pregnancy (pre-conception) or reporting AD at any point during pregnancy. The population weighted multivariable regression analysis was repeated used this subset of women to assess for odds of CD delivery based on recency of depressive symptoms.

This study was determined to be exempt by our institutional review board due to use of publicly-available, de-identified data.
**Results:**

Of the 162,558 parturients included in PRAMS between 2016 and 2019, 63,056 (estimated 40.0%) had no prior live births. Of these 61,605 (97.7%) parturients had valid data for depression status and mode of delivery (Figure 1). The 11,896 (18.3%) parturients who reported antenatal depression were compared to the 49,709 (81.7%) who did not. There were significant sociodemographic differences between those reporting AD compared to those who did not: those with AD were younger, more likely to be non-Hispanic white, had lower levels of education and were less likely to be married, more likely to be publicly insured, use WIC benefits in pregnancy, and report tobacco use in pregnancy (Table 1). There were also notable differences in pregnancy and delivery characteristics between the two groups (Table 2). People with AD were more likely to have hypertension and diabetes mellitus, especially pre-gestational. They had higher rates of obesity (BMI >30) and higher rates of preterm birth. People with AD were also more likely to deliver a child that was small for gestational age.

There was no difference in the odds of having a CD when recently-delivered patients with AD were compared to those without AD (unadjusted odds 1.05; 95% CI 0.97, 1.12) (Table 3). This lack of association between AD and CD remained the same when the analysis was adjusted for maternal age, race/ethnicity, insurance status, pregnancy complications (hypertensive disorders or diabetes mellitus), preterm birth, and BMI (aOR 1.04; 95% CI 0.97, 1.13).

In the sub-analysis of women with AD, there was no difference in CD between those only reporting depression pre-conceptually compared with at any point during pregnancy (aOR 1.05, 95% CI 0.90, 1.22).

**Discussion:**

In this large, nationally representative, modern sample, we found no association between reported AD and CD among recently-delivered patients in the United States. Findings from this study add to the
information from smaller, prospective studies that also found no difference in adverse perinatal outcomes, including CD, among parturients with depression during pregnancy\textsuperscript{12,13}. While these studies included cohorts of mixed parity, they still found no association between AD and CD when stratified by those with and without prior births. However, the major limitation of these studies that demonstrated no association between AD and CD is that only a small fraction of the included patients had depression. As such, the analyses may have been underpowered to detect any but the largest differences in outcomes.

The results from this study also align with our prior work, in which an analysis of PRAMS limited only to the state of Rhode Island demonstrated no difference in rates of CD among those reporting AD compared to those who did not\textsuperscript{14}. However, the RI cohort was small and only locally representative, necessitating the use of a larger and more generalizable cohort for subsequent analyses.

In contrast, some prior studies have demonstrated an increased risk for CD among patients with depression. Yedid Sion et al found that AD was associated with a more than twofold increase in CD\textsuperscript{10}. However, their population of depressed patients was only 0.1% of the study cohort, and their findings were confounded by mixed parity and differences in baseline rates of prior CD among the depressed and non-depressed group. Similarly, an association has been identified between depression in the third trimester of pregnancy and an increased rate for emergency CD\textsuperscript{7,8}, but this association is again weakened by potential confounding: both studies included a population of mixed parity and did not present data on the distribution of prior CD among the groups.

Lastly, two large medical claims based studies demonstrated increased rates of CD among patients with AD\textsuperscript{9,11}. The first, an analysis of the Nationwide Inpatient Sample (NIS)\textsuperscript{9}, demonstrated a small but significant 5% increase in CD among those with perinatal mood and anxiety disorders. However, their results are limited by their study design: only those patients whose AD was coded during the index hospitalization could be included (which leads to selection bias), CD could not be stratified into primary or repeat, and common cofounders for CD such as hypertension and maternal obesity were not
accounted for. To address these limitations, Zochowski et al.\textsuperscript{11} performed a follow-up analysis using a large, retrospective cohort of administrative claims data and found that parturients with AD had approximately 3.5% increased likelihood of CD. While they had more robust mechanisms for capturing patients with AD prior to their delivery admission and restricted their analysis to those undergoing primary CD, they only included patients with commercial/private insurance, and thus did not capture those with federal/public insurance, who are at higher risk for AD.

Our study has some important strengths: the PRAMS database provided a large, nationally-representative cohort of patients without a prior birth, in whom decreasing the cesarean rate is most likely to drive sustained reductions in cesarean-related morbidity over time. We also utilized a self-report of AD, which has been shown to have higher accuracy in identifying depression when compared to medical claims data\textsuperscript{26}. Lastly, we had minimal missing data among eligible participants (<2.5%), decreasing the likelihood of selection bias by not including eligible people in our study population who participated in PRAMS.

Nevertheless, there are some limitations to consider. First, the structure of the PRAMS database is retrospective and primarily survey-based; thus, our results are potentially limited by selection bias based on participation in PRAMS itself as well as recall bias. In particular, the experience of AD could have been incorrectly classified, with postpartum mood driving inaccuracies in antenatal mood designation, and those with the most severe forms of depression might be less likely to participate in PRAMS at all. Second, discernment of AD was based on two dichotomized variables, one for preconception depression and one for antenatal depression. While these not validated screening tools for a clinical diagnosis of depression—which might have led to capturing mild or subclinical disease and contribute to non-significant results—this is the metric currently employed by the CDC to capture AD. Third, multiple data points are derived from the birth record, which has some inherent limitations and relies on accurate documentation. While our primary outcome --mode of delivery-- has been demonstrated to be reliably
coded on the birth certificate\textsuperscript{27}, other data points may be less accurate. Furthermore, indication for CD or OVD were not available; therefore, we cannot ascertain if there is a difference in indications for CD or OVD based on AD status. Fourth, there was no assessment of depression control, nor was there information about when prior to or during pregnancy depressive symptoms may have occurred, so there was no way to stratify our analysis by these characteristics. In particular, prior studies have suggested that adverse perinatal outcome rates are higher in those who have a trajectory toward worsening depression in the third trimester of pregnancy\textsuperscript{28}, thus there may have been subtle differences among those with a worsening disease trajectory that we were unable to detect in this cohort.

Further research should focus on diagnosis of AD utilizing a validated diagnostic instrument, and the association of depression trajectory with mode of delivery. If differences are detected, it will be essential to elucidate whether these appear to be secondary to physiologic or behavioral/decisional differences between birthing people with and without depression, and if there is a provider component that might be mediated by implicit or explicit biases. Since cesarean delivery is associated with higher short and long term morbidity\textsuperscript{29}, determining intervenable opportunities to prevent unnecessary cesarean deliveries is paramount.\textsuperscript{22}

In conclusion, while depression has been considered a risk factor for cesarean delivery, findings from this study did not support an association between AD and CD among recently-delivered parturients in the United States. This finding can provide important reassurance for pregnant patients with AD, many of whom are concerned about the potential implications of AD and its treatment on pregnancy-related health for them and their offspring.

\textbf{Disclosure of financial support for the study}
None

\textbf{Conflicts of interest}
None
Acknowledgements
None

References:


Figure 1: Study flow diagram

Table 1: Demographic characteristics of recently-delivered parturients with and without antenatal depression, PRAMS 2016-19.

<table>
<thead>
<tr>
<th>Demographic characteristic</th>
<th>Antenatal Depression</th>
<th>No antenatal depression</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>11,896 (18.3)</td>
<td>49,709 (81.7)</td>
<td></td>
</tr>
<tr>
<td>Maternal age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>1,990 (15.8)</td>
<td>4,385 (8.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>20-34</td>
<td>8,804 (75.7)</td>
<td>39,476 (80.3)</td>
<td></td>
</tr>
<tr>
<td>≥35</td>
<td>1,101 (8.5)</td>
<td>5,846 (11.6)</td>
<td></td>
</tr>
<tr>
<td>Maternal race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1,634 (11.8)</td>
<td>8,729 (15.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>6,208 (66.8)</td>
<td>23,298 (59.3)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>1,962 (14.0)</td>
<td>8,058 (14.0)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1,742 (7.4)</td>
<td>8,233 (10.9)</td>
<td></td>
</tr>
<tr>
<td>Demographic characteristic</td>
<td>Antenatal Depression</td>
<td>No antenatal depression</td>
<td>P-Value</td>
</tr>
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<td>---------</td>
</tr>
<tr>
<td>Population</td>
<td>11,896 (18.3)</td>
<td>49,709 (81.7)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-gestational</td>
<td>1,746 (14.5)</td>
<td>1,575 (2.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gestational</td>
<td>2,340 (17.9)</td>
<td>7,269 (12.7)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-gestational</td>
<td>1,262 (11.2)</td>
<td>711 (1.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gestational</td>
<td>1,083 (8.5)</td>
<td>3,756 (7.0)</td>
<td></td>
</tr>
<tr>
<td>Body Mass Index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>6,023 (53.1)</td>
<td>29,001 (61.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>25-29</td>
<td>1,515 (13.2)</td>
<td>6,617 (13.9)</td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td>3,980 (33.7)</td>
<td>12,222 (24.9)</td>
<td></td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;34 weeks</td>
<td>1,020 (3.2)</td>
<td>3,464 (2.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>34-36 weeks</td>
<td>1,529 (7.4)</td>
<td>5,255 (6.0)</td>
<td></td>
</tr>
<tr>
<td>≥37 weeks</td>
<td>9,339 (89.4)</td>
<td>40,955 (91.5)</td>
<td></td>
</tr>
<tr>
<td>Preterm birth</td>
<td>2,549 (10.6)</td>
<td>8,719 (8.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>2,292 (13.5)</td>
<td>8,613 (12.4)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

* Columns are unweighted N and weighted %

**Table 2:** Pregnancy and delivery characteristics of recently-delivered parturients with and without antenatal depression, PRAMS 2016-19.

<table>
<thead>
<tr>
<th>Antenatal depression* N=11,896</th>
<th>No antenatal depression* N=49,709 (81.7)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
</table>

* Columns are unweighted N and weighted %

**Table 3:** Prevalence, unadjusted and adjusted odds ratio of cesarean delivery among recently-delivered parturients with and without antenatal depression, PRAMS 2016-19.
<table>
<thead>
<tr>
<th></th>
<th>(18.3)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean delivery</td>
<td>3,979</td>
<td>15,913</td>
<td>1.05 (0.97-1.12)</td>
<td>1.04 (0.97-1.13)</td>
</tr>
<tr>
<td>Operative vaginal delivery</td>
<td>634</td>
<td>2,672</td>
<td>1.07 (0.93-1.24)</td>
<td>1.13 (0.97-1.31)</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>7,283</td>
<td>31,124</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* Columns are unweighted N and weighted %

** Adjusted for: maternal age, race/ethnicity, insurance, pregnancy complications (HTN or DM), preterm birth, body mass index.