Racial Differences in the Association Between Maternal Antenatal Depression and Preterm Birth Risk: A Prospective Cohort Study

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Abstract

Background: In the United States, racial/ethnic disparities in preterm birth (PTB) are well documented, but explanations for why the disparity persists remain to be fully explored. We examined racial/ethnic differences in the association of maternal antenatal depression with PTB (<37 completed weeks of gestation) risk.

Methods: In a prospective cohort study, participants ($n=2073$) included non-Hispanic (NH) black, NH white, Asian, and Hispanic women who received prenatal care at a university obstetric clinic January 2004–March 2010, and delivered at the university's hospital. We obtained data from self-reported questionnaires and electronic medical records. We assessed antenatal depression using the Patient Health Questionnaire-9 and self-reported antenatal antidepressant medication use. Poisson regression models were used to estimate the association between antenatal depression and PTB risk, within strata of race/ethnicity.

Results: NH black (risk ratio [RR] = 1.89; 95% confidence interval [CI]: 0.94, 3.80), NH white (RR = 1.58, 95% CI: 1.04, 2.39), and Asian (RR = 2.06; 95% CI: 0.69, 6.13) women with antenatal depression were at increased risk for delivering preterm infants, compared with women without antenatal depression, although the associations were statistically significant only among NH white women. There was no evidence of an association between antenatal depression and risk of PTB among Hispanic women (RR = 0.96; 95% CI: 0.28, 3.25); p -value for interaction = 0.81.

Conclusion: Our findings suggest race-specific associations of antenatal depression with an increased risk of delivering a preterm infant, supporting the importance of considering race/ethnicity when examining risk factors for health outcomes.

Keywords: antenatal depression, depression, maternal depression, preterm birth, racial/ethnic disparities

Introduction

MAJOR DEPRESSION IS a psychiatric disorder with major public health implications.¹ Beginning in adolescence, women are twice as likely as men to experience major depression during their lifetime.^{2,3} Three-fourths of all lifetime cases of major depression start by age 24; women between the ages of 25 and 44, relative to older or younger ages, have the highest prevalence of major depression, placing women of reproductive age at high risk of experiencing depression during pregnancy.^{4–6} In the United States, the 12-month prevalence of major depression among adult women is highest among white women (12.7%) compared with the prevalence among Asian women (5%), black women (7.6%), or Latinas

(9.9%).⁷ However, findings from studies using multivariable analysis to examine race/ethnicity as a risk factor for antenatal depression have been inconsistent,⁸ in some instances reporting higher risk among racial/ethnic minority groups.^{9,10}

In the United States, preterm birth (PTB; birth before 37 completed weeks of gestation) is the single most important predictor of infant death¹¹ and increases risk for short- and long-term morbidity among surviving infants.^{12–14} PTB rates are highest among non-Hispanic (NH) blacks (13.2%) and American Indian/Alaska Natives (10.2%), and relatively lower among Hispanics (9%), NH whites (8.9%), and Asian/Pacific Islanders (8.5%).¹⁵ Racial disparities in PTB are well documented in the United States, but explanations for the differences remain to be fully explained. Researchers have

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proposed that disparities in psychosocial factors, including maternal depression in pregnancy, may, in part, contribute to racial disparities in PTB.^{16–18}

In several meta-analyses, antenatal major depression and elevated depressive symptoms in pregnancy were associated with a 27%–39% increased risk of PTB^{19,20} while antidepressant use was associated with a 55%–69% elevated PTB risk.^{21,22} High levels of corticotropin-releasing hormone and cortisol have been linked to maternal depression, which may trigger contractions and/or the premature rupture of membranes²³ leading to premature delivery.

Grote et al. in their meta-analysis reported that race did not modify the association between maternal depression and PTB.²⁰ On the other hand, Li et al. reported an association between maternal depressive symptoms and PTB among black women that was attenuated in comparison to associations observed among white, Hispanic, and Asian/Pacific Islander women.²⁴ Studies examining the association in samples consisting of only black women have found elevated depressive symptoms associated with an increased risk of PTB.^{17,25}

Given the inconsistent findings and the small number of published studies regarding the influence of race/ethnic status on the association between antenatal depression and PTB, we conducted a prospective cohort study to examine the association between antenatal depression and the risk for PTB by racial/ethnic status. Our hypothesis was that the racial/ethnic groups with higher risk of PTB would have a stronger association between antenatal depression and PTB.

Materials and Methods

Study population and setting

Women who received prenatal care at a University of Washington Medical Center obstetric clinic from January 2004 to March 2010, and delivered at the university's hospital, were the source population for this study ($n=3227$ were approached and consented to participate). Data on the proportion of the clinical population approached, along with the percentage of the approached individuals consenting to participate, are not known for the entire study period; however, from January 2004 to January 2009, 79.1% of the clinical population were approached and 91.2% of those individuals consented.²⁶

Various self-administered questionnaires (available in English and Spanish), part of routine prenatal medical care at the obstetric clinic since 2004, were used to collect data on general health history, current medication use, previous pregnancy complications, psychological factors (depression, anxiety disorders, and stress), behavioral factors (cigarette smoking, alcohol use, and drug use), physical/sexual abuse, and sociodemographic factors.

Participants were eligible for inclusion in this study if they, at least, completed questionnaires during the second (~16 weeks' gestation) trimester, and the pregnancy resulted in a live-born singleton infant. Exclusion criteria included age less than 15 years at delivery, mental incapacitation, or limited English/Spanish proficiency to complete the questionnaire. Participants with missing data on maternal race ($n=485$) or antenatal depression data for the second trimester ($n=382$) were also excluded from the analysis, as were Native American women ($n=32$) as the small sample size

was not adequate for regression analyses. The final analytic sample included 2073 participants. The University of Washington Human Subjects Institutional Review Board approved study protocols. Participants provided written informed consent.

Data collection

From the questionnaires, we extracted information on antenatal depression and antidepressant medication use during the second trimester, race/ethnicity, marital status, education, smoking, and intimate partner violence (in the past year or during the present pregnancy, up until the second trimester). Data from the electronic medical records provided information on infant birth outcomes (delivery outcome and gestational age) and maternal characteristics (age).

Outcome and exposure. The primary outcome of interest was PTB. Using the clinical estimate of gestational age based on ultrasound, we created a binary variable, term birth (birth at ≥ 37 completed weeks of gestation) versus PTB (birth before 37 completed weeks of gestation). The primary exposure was antenatal depression during the second trimester, ascertained during the second trimester visit, characterized using the Patient Health Questionnaire-9 (PHQ-9) and/or self-reported antenatal antidepressant medication use.²⁷ The PHQ-9 is a validated measure for assessing depression using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria. The tool rates the frequency of nine major depression symptomatology (not at all, several days, more than half the days, and nearly every day) in the last 2 weeks; this is factored into the score that ranges from 0 to 27.

We created a binary variable, no depression (score <10) versus probable major depression (score ≥ 10). The PHQ-9 has 88% sensitivity and 88% specificity for detecting major depression in the general population.²⁸ The PHQ-9 has also been validated in a population of pregnant women enrolled in Healthy Start, with 85% sensitivity and 84% specificity, and, in a population with 3.6% prevalence of current major depression, a positive predictive value (PPV) of 17%.²⁹ In a racially and socioeconomically diverse population of women 0–9 months postpartum, with a 9% prevalence of diagnosed major depression, the PPV of the PHQ-9 was 33%.³⁰

One of the questionnaires queried the women about current medications used. The free text was reviewed and a binary variable (yes vs. no) was created based on whether the woman reported any antidepressant medication use in the second trimester. Women were considered to have antenatal depression if they had probable major depression based on the PHQ-9 and/or used any medication classified as an antidepressant during the second trimester visit; the latter includes selective serotonin reuptake inhibitors (SSRIs), namely sertraline, fluoxetine, fluvoxamine, paroxetine, citalopram, and escitalopram, along with non-SSRI antidepressants.²⁷

Effect modifier and covariates. Due to interest in potential effect modification by race/ethnicity, we extracted self-reported mothers' race/ethnicity (Asian, Hispanic, NH black, or NH white) from the questionnaire. We also extracted information from the questionnaire on the following potential confounders: marital status (married/living with a partner vs.

single/separated/divorced), educational attainment ($\leq$ high school, some college, college graduate, or some graduate education), antenatal cigarette smoking (any vs. never), and intimate partner violence (yes vs. no). All variables were parameterized as dummy variables. Maternal age was obtained from the electronic medical record and parameterized as a linear spline with knots at 20, 25, and 35 years.

Statistical analyses

We examined participants' characteristics across categories defined by antenatal depression status, as described above. We used Poisson regression, with robust error variance, to obtain risk ratios (RR) and 95% confidence intervals (CI) of the association between antenatal depression and PTB, within strata of race/ethnicity. In certain racial/ethnic subgroups, the baseline incidence of the outcome exceeds 10% (the rare outcome assumption). Due to noncollapsibility of odds ratios (ORs) there is an increased differential between the ORs and the RRs in the case of a common outcome. It is because of this that we used Poisson regression, with robust error variance, in lieu of logistic regression.³¹

In the adjusted models, we included potential confounding variables of maternal age, marital status, educational attainment, cigarette smoking during pregnancy, and domestic

violence. These covariates were selected a priori as factors associated with both the exposure³² and outcome,¹⁴ as well as differentially distributed among racial/ethnic groups.³³ In a subsequent adjusted model, we included an interaction term between race/ethnicity and antenatal depression, along with individual indicator variables for race/ethnicity and antenatal depression, to test multiplicative interaction. The *p*-value of the interaction term determined the statistical significance of the interaction. In all analyses, we used two-sided *p*-value <0.05 for statistical significance. We used Stata, version 13.1, software to analyze the data (Stata Corporation, College Station, TX).

Results

The participants were, on average, 31 years old, and the majority were NH white (70%), had at least an undergraduate college degree (57.35%), were married (86%), nonsmokers (92%), and reported no experiences of intimate partner violence in the past year or during the present pregnancy (97%). Participants with antenatal depression, relative to those without antenatal depression, were more likely to be Hispanic or NH black, have lower levels of educational attainment, be single/divorced/widowed, to smoke, and have experienced intimate partner violence (Table 1 and Supplementary Table S1; Supplementary Data are available online at www.liebertpub.com/jwh). Of the

TABLE 1. CHARACTERISTICS OF WOMEN WITH AND WITHOUT ANTENATAL DEPRESSION DELIVERING LIVE-BORN SINGLETON INFANTS IN SEATTLE, WASHINGTON, 2004–2010

	Overall (n=2073)		No antenatal depression (n=1799)		Antenatal depression (n=274)	
	Mean	SD	Mean	SD	Mean	SD
Maternal age	30.84	6.10	31.06	6.03	29.44	6.38
	Count	%	Count	%	Count	%
Race/ethnicity						
Asian	262	12.64	237	13.17	25	9.12
Hispanic	168	8.10	139	7.73	29	10.58
NH black	198	9.55	153	8.50	45	16.42
NH white	1445	69.71	1270	70.59	175	63.87
Education						
$\leq$ High school	400	19.98	303	17.41	97	37.02
Some college	454	22.68	372	21.38	82	31.30
College graduate	500	24.98	458	26.32	42	16.03
Some graduate education	648	32.37	607	34.89	41	15.65
Marital status						
Married/living with a partner	1731	86.33	1546	88.70	185	70.61
Single/divorced/widowed	274	13.67	197	11.30	77	29.39
Smoking						
Yes	147	7.56	98	5.81	49	18.99
No	1798	92.44	1589	94.19	209	81.01
Intimate partner violence						
Yes	65	3.17	42	2.36	23	8.55
No	1985	96.83	1739	97.64	246	91.45
PHQ-9						
Score ≥ 10	178	8.60	0		178	64.96
Score < 10	1891	91.40	1795	100.00	96	35.04
Antidepressant medication use						
Yes	123	5.93	0		123	44.89
No	1950	94.07	1799	100.00	151	55.11

Columns do not add up to 100% of the sample for each categorical variable if data were missing. NH, Non-Hispanic; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.

TABLE 2. RISK OF PRETERM BIRTH ASSOCIATED WITH ANTENATAL DEPRESSION AMONG BLACK, WHITE, ASIAN, AND HISPANIC WOMEN IN SEATTLE WASHINGTON, 2004–2010

	N	<i>Preterm birth infant</i>		<i>Unadjusted</i>		<i>Adjusted^a</i>	
		n	%	RR	CI	RR	CI
Overall ^b							
Not depressed	1799	173	9.62	1 [Reference]		1 [Reference]	
Antenatal depression	274	51	18.61	1.94	1.46, 2.57	1.56	1.11, 2.18
Black							
Not depressed	153	18	11.76	1 [Reference]		1 [Reference]	
Antenatal depression	45	10	22.22	1.89	0.94, 3.80	1.88	0.90, 3.93
White							
Not depressed	1270	112	8.82	1 [Reference]		1 [Reference]	
Antenatal depression	175	31	17.71	2.01	1.39, 2.89	1.58	1.04, 2.39
Asian							
Not depressed	237	24	10.13	1 [Reference]		1 [Reference]	
Antenatal depression	25	5	20.00	1.98	0.83, 4.73	2.06	0.69, 6.13
Hispanic							
Not depressed	139	19	13.67	1 [Reference]		1 [Reference]	
Antenatal depression	29	5	17.24	1.26	0.51, 3.11	0.96	0.28, 3.25

^aAdjusted for maternal age, marital status, educational attainment, cigarette smoking during pregnancy, and domestic violence.

^bAdjusted for maternal race/ethnicity, age, marital status, educational attainment, cigarette smoking during pregnancy, and domestic violence.

CI, confidence interval; RR, risk ratio.

women classified as having antenatal depression, 65% had PHQ-9 score greater than or equal to 10, 45% were on antidepressant medications, and 10% had both a PHQ-9 score of at least 10 and reported taking medication classified as an antidepressant.

In adjusted analyses, overall antenatal depression was associated with 1.56 times (95% CI: 1.11, 2.18) the risk of delivering a preterm infant. NH black (RR=1.88; 95% CI: 0.90, 3.93), NH white (RR=1.58, 95% CI: 1.04, 2.39), and Asian (RR=2.06; 95% CI: 0.69, 6.13) women with antenatal depression were at increased risk for delivering preterm infants, compared with their counterparts who did not have antenatal depression, although this association was statistically significant only among NH white women. There was no evidence of an association between antenatal depression and risk of PTB among Hispanic women (RR=0.96; 95% CI: 0.28, 3.25) (Table 2). The interaction term of race and antenatal depression was not statistically significant ($p=0.81$).

Discussion

In this study, we examined whether there were racial differences in the association between antenatal depression and the risk for PTB. In general, among NH black, NH white, and Asian study participants, women experiencing antenatal depression tended to have an increased risk for delivering preterm infants. Among Hispanic women, a similar association was not observed, although we did not find evidence for statistically significant interaction on the multiplicative scale.

Few peer-reviewed studies have assessed potential race-specific risk of PTB associated with antenatal depression and the findings are inconsistent. In a meta-analysis, Grote et al. reported no race/ethnicity-specific difference in the association between depression and PTB, but did not report these estimates.²⁰ Liu et al. conducted a population-based prospective cohort study ($n=791$) in northern California among

women enrolled in a large managed care organization. They ascertained depressive symptoms using the Center for Epidemiological Study Depression Scale (CES-D). After adjusting for various potential confounders, white (Hazard Ratio=2.7; 95% CI: 0.9, 7.9), Hispanic (HR=2.0; 95% CI: 0.5, 8.6), and Asian/Pacific Islander (HR=1.9; 95% CI: 0.5, 6.9) mothers were at an increased risk for delivering a preterm infant if they had moderate/major depressive symptoms (CES-D ≥ 16), compared with mothers with low depressive symptoms (CES-D < 16). The estimate was attenuated among African American women (HR=1.2; 95% CI: 0.3, 5.2). However, these estimates did not reach statistical significance; and, without data on antidepressant use, the comparison group would include those with managed depression.²⁴

Dole et al. conducted a prospective cohort study ($n=1898$) recruiting primarily low-income women from two prenatal care sites in North Carolina. After adjusting for potential confounders, they reported that African American (RR=1.1; 95% CI: 0.7, 1.7) and white (RR=1.1; 95% CI: 0.8, 1.7) mothers were not at increased risk of delivering a preterm infant if they had elevated depressive symptoms (CES-D > 24), compared to mothers with low depressive symptoms.¹⁸ Orr et al. conducted a prospective cohort study of primarily low-income African American women ($n=1399$) receiving prenatal care at four clinics in Maryland and reported an increased risk of spontaneous PTB (OR=1.96; 95% CI: 1.04, 3.72) associated with elevated depressive symptoms (CES-D ≥ 16).¹⁷ The inconsistent findings are likely due, in part, to differences in study methodology and design, including the use of various thresholds and assessment tools to determine probable major depression, timing of depression screening in pregnancy, and differences in sample characteristics.³⁴

In this study, we found no increased PTB risk associated with antenatal depression among Hispanics. Social support at the familial and community level may be a protective factor against the potentially harmful effects of socioeconomic and

psychosocial factors on the health of Hispanic populations; however, we did not formally test this in our study. The historical and current environments/experiences of racial groups in and across the United States are varied. We posit that the cumulative impact of the social, economic, and physical environment affects racial/ethnic disparities in health.³⁵ Since the current and historical environment of any one population is unique, it is reasonable to assume that the identification of such disparities would also vary depending on the context of the population from which the study sample is drawn.

Our findings suggest the importance of considering race/ethnicity in similar investigations as it captures biological, social, economic, and environmental factors, many of which are unknown or unmeasured in most public health and clinical research studies. Future studies should examine the synergistic effects of these factors on PTB among the various racial/ethnic groups.

The main strength of this study is the diversity of the population. This study has some limitations. The estimates for the non-white women were not statistically significant and may be less precise due to smaller stratum-specific sample sizes. A number of participants ($n = 485$) were excluded due to missing data on maternal race, which likely contributed to the precision of the estimates. However, participants with missing race did not differ substantially from the rest of the sample on selected characteristics. Use of antidepressant medications and assessment of antenatal depression were determined at ~16 weeks' gestation, but not available for over 45% of the women in the third trimester. Women diagnosed in the third trimester may be included in the "unexposed" category, thus attenuating the association between antenatal depression and PTB. Non-white women are less likely than white women to receive treatment for depression.³⁶ To our knowledge, no study has assessed the validity of the PHQ-9 among various racial groups. As a result, there could be misclassification of antenatal depression status among the non-white groups.

The use of antidepressants may confound the association between antenatal depression and PTB (confounding by indication) because women using antidepressants may not currently experience symptoms of depression. As a result, we combined women with major/minor depression with those self-reporting to take antidepressants. Due to the dynamic nature of depression, we included in the exposed group those with minor depression along with those with probable major depression. However, it is possible that these subgroups of depression affect the offspring in different ways or to different degrees.

Non-SSRI antidepressant medications may be taken to treat conditions other than depression. Including these individuals in the exposed group could bias the results. We conducted a sensitivity analysis wherein we excluded, from the exposed group, individuals taking non-SSRI medications. The race/ethnicity-specific risk estimates did not differ substantially and the conclusions made from these findings are comparable to those previously reported. Estimates were closer to the null among NH black and white women, larger among Asian women, and smaller (further from the null) among Hispanics. Of note, the association of interest was no longer statistically significant among NH whites. Given the wide CIs of the estimates (as reported in the Results) we cannot rule out the possibility that this study had insufficient power, within the various race/ethnic subgroups.

Some SSRIs treat multiple conditions, such as both depression and anxiety. Conditions comorbid with depression, such as anxiety³⁷ and stress,³⁸ are known to be associated with PTB and could partly account for the observed associations. However, we chose not to adjust for these due to collinearity. A limitation of this study is the likely inclusion of individuals in the exposed group who are on SSRIs for comorbid conditions, which could bias our results. Congenital anomalies in the current birth³⁹ and a history of preterm delivery and low birthweight are factors associated with PTB in the current pregnancy.

A limitation of this study is that we were not able to exclude births complicated by congenital anomalies and women with a history of low birthweight offspring as these data were not provided to the study team as part of the deidentified medical record data. This limited the sensitivity of our study to detect the association of interest. However, we performed a sensitivity analysis including only parous women without a history of preterm delivery.⁴⁰ The risk estimates for NH black and white women were attenuated (closer to the null), while that of Asian women were larger, and that of Hispanic women smaller (further from the null). Of note, the association was statistically significant among Hispanics. As mentioned above, given the wide CIs, our study likely has limited power to detect a statistically significant association within the racial/ethnic groups were it present.

The number of eligible women approached to participate in the study and the percentage of those approached that consented to participate are unknown. Due to Health Insurance Portability and Accountability Act regulations, the characteristics of individuals who declined to participate were not available. The women who did not enroll are likely different from those enrolled in the study on some characteristics associated with their pregnancy outcomes. However, the consent rate was high during an earlier part of the study period (January 2004–January 2009), as presented in the Materials and Methods section. As we would expect the consent rate to remain comparable for the entirety of the study period, we have few concerns about selection bias.

There is potential for residual confounding due to crude adjustment for some of the confounding variables, as well as not including in the statistical analyses other variables that confound the relationship between antenatal depression and PTB, but were not collected as part of the study, such as social support and pregnancy intention. Last, this sample included a relatively low-risk population; therefore, the findings may not be generalizable to other populations.

Conclusion

We found suggestive evidence for racial differences in antenatal depression and PTB associations in a prospective cohort study of relatively low-risk women receiving prenatal care at a university hospital. These findings support the importance of considering race/ethnicity when examining risk factors for health outcomes.

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Author Disclosure Statement

The authors report no conflict of interests.

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