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Elevated Risk of Adverse Obstetric Outcomes in Pregnant Women With Depression

Deborah R. KIM, M.D.[1], **Laura E. SOCKOL, M.A.**[2], **Mary SAMMEL, ScD**[3], **Caroline KELLY, M.D.**[4], **Marian MOSELEY, MSW**[4], and **C. Neill EPPERSON, M.D.**[1]

[1]Department of Psychiatry, University of Pennsylvania

[2]Department of Psychology, University of Pennsylvania

[3]Department of Biostatistics and Epidemiology, University of Pennsylvania

[4]Department of Obstetrics and Gynecology, University of Pennsylvania

Abstract

Objective—In this study, we evaluated the association between patient depression ratings at an initial obstetrics visit and adverse birth outcomes in African-American women.

Study Design—We conducted a retrospective cohort study of 261 pregnant, African American women who were screened with the Edinburgh Postnatal Depression Scale (EPDS) at their initial prenatal visit. Medical records were reviewed to assess pregnancy and neonatal outcomes, specifically pre-eclampsia, preterm birth, intrauterine growth retardation and low birth weight.

Results—Using multivariable logistic regression models, an EPDS score ≥ 10 was associated with increased risk for preeclampsia, preterm birth and low birth weight. An EPDS score ≥ 10 was associated with increased risk for intrauterine growth retardation but after controlling for behavioral risk factors this association was no longer significant.

Conclusion—A positive, patient-rated depression screening at the initial obstetrics visit depression is associated with increased risk for multiple adverse birth outcomes. Given the retrospective study design and small sample size, this finding should be confirmed in a prospective cohort study.

Keywords

depression; pregnancy; IUGR; low birth weight; preeclampsia; pregnancy; preterm birth

Introduction

Depression is a risk factor for suboptimal pregnancy outcomes (Kiely et al. 2011). With up to 30% of pregnant women experiencing significant depressive symptoms (Gavin et al. 2005; Marcus 2008; Marcus et al. 2005), research regarding the impact of depressive symptoms on obstetrical outcomes has been the focus of a number of studies. A recent meta-analysis reported that antenatal depression is independently associated with an increased risk for preterm birth (PTB) and low birth weight (LBW), but not intrauterine growth restriction (IUGR) (Grote et al. 2010). The authors likened the risk of antenatal depression on birth outcomes to smoking 10 or more cigarettes per day. Although the exact relationship between depression and adverse birth outcomes is currently unknown, it has been suggested that

Corresponding author: Deborah Kim, M.D., 3535 Market Street, 3050, Philadelphia, PA 19104, Phone: 215-573-9972, Fax: 215-573-8881, drkim@upenn.edu.

increased corticotropin-releasing hormone (CRH) in depression may lead to PTB (Straub et al. 2012, Wadwha et al. 2004). Other studies have shown an association between pre-eclampsia and depressive symptoms (Kurki et al. 2000) or a diagnosis of depression (Cripe et al. 2011, Kharaghani et al. 2011, and Qiu et al. 2009). Pre-eclampsia, characterized by hypertension, proteinuria and edema, occurs in 5-8% of births and is estimated to be responsible for 15% of pre-term births (Kanasaki and Kalluri 2009). Potentially common mechanisms linking depression and pre-eclampsia include hypothalamicpituitary axis dysfunction, impaired immune activation and activation of vasoactive hormones (Cripe et al. 2011).

Although important and necessary, diagnosing depression in a large obstetrical practice can be logistically difficult. While clinician administered diagnostic instruments are the gold standard, they are time-consuming and staff intensive to administer. Conversely, patient-rated screening instruments are easier to use but may have lower sensitivity and specificity. Because adverse obstetrical outcomes can have significant, long-term, negative health impacts, it would be useful to know how well a simple, patient-rated screening for depression at the initial obstetric visit predicts the risk of adverse pregnancy outcomes. To begin to answer this question, we examined a cohort of pregnant women in a general obstetrics clinic with the aim of determining if a depression screening performed at a patient's initial obstetric visit was associated with adverse pregnancy outcomes. The objective was to see if a known screening tool could be effectively utilized to inform obstetrical practices about the risk of depression on adverse pregnancy outcomes, such as preeclampsia, preterm birth, intrauterine growth retardation and low birth weight.

Materials and Methods

Five hundred women presenting for their initial prenatal visit from November 2008 to April 2009 were asked to complete the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al. 1996) to assess current symptoms of depression. Of this cohort, we analyzed delivery data from black, non-Hispanic women with singleton births past 20 weeks gestational age who delivered at the University of Pennsylvania, resulting in a cohort of 261 women. The EPDS is a patient-rated depression screening tool widely validated in both pregnant and postpartum women that consists of 10 questions scored from 0 – 3 with a maximum score of 30. Scores ≥ 10 are consistent with clinical depression and further evaluation is recommended (Evins et al. 2000; Jardri et al. 2006; Lee et al. 2001). The study population was derived from an urban, hospital-based clinic at the University of Pennsylvania in which the majority of patients are insured by Medicaid (95%). Prior to initiation, this study was approved by the University of Pennsylvania Institutional Review Board.

All records were de-identified prior to data extraction. Researchers blinded to EPDS scores reviewed the medical records of the subjects to determine maternal and neonatal pregnancy outcomes. Both paper and electronic charts were reviewed to collect all information. The primary outcome variables were pre-eclampsia (per the medical record as hypertension and proteinuria), preterm birth (PTB; gestational age at birth < 37 weeks gestational age), intrauterine growth retardation (IUGR; weight < 10^{th} percentile for gestational age) and low birth weight (LBW; birth weight < 2500 g at delivery). These outcomes were chosen a priori based on a review of the literature. All outcomes were coded as dichotomous variables with the unaffected group coded as the reference group.

Demographic characteristics and the prevalence of risk factors for adverse birth outcomes were calculated for the full sample. To determine risk factors associated with each specific birth outcome, *t*-tests were used to compare the groups on continuous risk factors and chi-square tests were used to compare groups on categorical risk factors (Fisher's exact test was

used when the sample size for a given risk factor resulted in expected cell values < 5). Risk factors assessed included demographic variables (age and parity), psychological risk factors (EPDS scores ≥ 10, a history of mental illness noted on the patient's problem list, known psychotropic exposure during pregnancy, medical/obstetric risk factors (chronic illness noted on the patient's problem list, history of prior preterm birth, gestational diabetes, or thyroid disease during the current pregnancy) and behavioral risk factors (known alcohol use at initial clinic visit, known recreational drug use during pregnancy, and smoking reported at initial clinic visit). A series of multivariable logistic regression models were then used to evaluate the association of potential risk factors with the risk for pre-eclampsia, PTB, IUGR and LBW. Variables were considered for the multivariable model if the risk factor was associated with the outcome at $p < 0.10$ in univariate analyses. Demographic variables (age and parity) were included in each model. Separate models were calculated for each outcome variable. For categorical variables included in the logistic regression models, the unexposed group was used as the reference group. We considered a p-value < 0.05 in the final models to be statistically significant.

Results

Characteristics of the sample screened with the EPDS have been published elsewhere (Kim et al. 2011). Briefly, 94% of the cohort agreed to respond to the EPDS and 95% were insured by Medicaid. Given that the majority of the women in our general clinic population are African American (83.3%), we a priori chose to restrict our sample to 261 African American women with a live, singleton birth, for whom delivery data was available to enhance the homogeneity of the population. It is well documented that the rates of preterm birth, pre-eclampsia, and low birth weight in the United States are higher for non-Hispanic black women than for non-Hispanic white women ((www.cdc.gov/nchs/data/databriefs/db74.htm, http://www.cdc.gov/pednss/pdfs/PNSS_2009.pdf)). Characteristics of the sample are presented in Table 1. The mean age was 24.6 years (SD = 5.4), with a range of 18 - 44 years. The mean gestational age at EPDS screening was 17.2 weeks (SD = 7.4), with a range of 6.14 - 38.86 weeks. The mean birth weight was 3152.0 g (SD = 587.9) and the mean gestational age at delivery was 39.0 weeks (SD = 2.1). For the 260 woman for whom there was parity data, just under one quarter of subjects were primiparous (23.0%, n = 60) while the majority were multiparous (76.6%, n = 200). A history of mental illness was noted in 17.2% of subjects' medical records. The most common mental illnesses were depression (n = 39), bipolar disorder (n = 7), and anxiety disorders (n = 8). Six subjects (2.3%) were known to have been exposed to psychotropic medications during pregnancy; medications included antidepressants, benzodiazepines, antipsychotics and antiepileptic medications. A history of chronic illness was noted in nearly half (49.0%) of subjects' medical records. The most common chronic illnesses were asthma (n = 56) and hypertension (n = 12). Sixty-one women (23.3%) experienced at least one adverse outcome (pre-eclampsia, LBW, PTB or IUGR). Half of these women experienced only one adverse outcome (n = 31), 20 women experienced 2 adverse outcomes, 6 women experienced 3 adverse outcomes, and 4 women experienced all 4 adverse outcomes.

Risk Factors for Preeclampsia

Of the 254 women for whom the presence or absence of pre-eclampsia during the current pregnancy was recorded, 25 (9.6%) were classified as having preeclampsia. Table 2 presents characteristics associated with pre-eclampsia in this sample. Women who received a diagnosis of pre-eclampsia had higher EPDS scores and were more likely to have EPDS scores ≥ 10. Table 3 presents the results of a multivariable logistic regression model predicting preeclampsia. Three variables were included in the model: maternal age, parity,

and EPDS scores ≥ 10. EPDS score ≥ 10 was the only significant risk factor for pre-eclampsia (OR 2.95, 95% CI 1.26-6.89).

To account for the possibility that pre-eclampsia developed prior to depression, we performed a post hoc analysis restricting the sample to women who completed the EPDS at gestational ages less than 20 weeks only and for whom information regarding pre-eclampsia was available (n = 162). EPDS scores ≥ 10 remained significantly associated with an increased risk of preeclampsia (OR 5.21, 95% CI 1.69-16.03).

Risk Factors for Preterm Birth

Of the 251 women for whom gestational age at delivery was reported, 28 (11.2%) gave birth before 37 weeks gestational age. Table 2 presents characteristics associated with preterm birth (PTB) in this sample.

Mothers of preterm infants were more likely to have been diagnosed with thyroid disease during the current pregnancy and more likely to have a history of prior PTB. There was also a non-significant trend for mothers of preterm infants to have higher EPDS scores and to be more likely to have EPDS scores ≥ 10.

The multivariable logistic regression model for predicting preterm birth is presented in Table 3. Five variables were included in the model: maternal age, parity, EPDS scores ≥ 10, history of prior preterm birth, and thyroid disease during the current pregnancy. Three risk factors were significantly associated with risk for preterm birth: EPDS scores ≥ 10 (OR 2.34, 95% CI 1.03-5.36), thyroid disease during the current pregnancy (OR 7.79, 95% CI 1.52-39.99), and history of prior preterm birth (OR 3.35, 95% CI 1.29-8.73).

Risk Factors for IUGR < 10%

Of the 212 women for whom the presence or absence IUGR < 10% was recorded, 26 (10%) were classified as having IUGR during the current pregnancy. Table 2 presents characteristics associated with IUGR < 10% in this sample. Women with IUGR < 10% were more likely to have EPDS scores ≥ 10 and were more likely to have reported smoking at their initial clinic visit. There was a non-significant trend for women with IUGR < 10% to have higher EPDS scores and to be more likely to have used recreational drugs during pregnancy.

Table 3 presents the results of two multivariable logistic regression models predicting IUGR < 10%. Three variables were included in the initial model: maternal age, parity, and EPDS scores ≥ 10. EPDS scores ≥ 10 were significantly associated with IUGR < 10% (OR 2.91, 95% CI 1.26-6.72).

Two behavioral risk factors for IUGR < 10%, smoking during the current pregnancy and known recreational drug use during the current pregnancy, were not included in the initial model. As both recreational drug use during the current pregnancy and smoking reported at the initial clinic visit were associated with IUGR < 10% at $p < 0.10$ in univariate analyses, a separate logistic regression model was conducted to assess whether including these behavioral risk factors, in addition to demographic risk factors and depressive symptoms, explained further variance in IUGR < 10%. After including these additional risk factors in the model, there was a trend for EPDS scores ≥ 10 to be associated with IUGR < 10% (OR 2.32, 95% CI 0.96-5.58), but this result was no longer statistically significant ($p = 0.06$). There was also a trend for smoking reported at the initial clinic visit to be associated with IUGR < 10% (OR 2.82; 95% CI 0.91-8.79), but this result was not statistically significant ($p = 0.07$).

Risk Factors for Low Birth Weight

Of the 214 subjects for whom birth weight of the infant was reported, 22 (8.4%) were classified as low birth weight (< 2500 g). Table 2 presents characteristics associated with low birth weight in this sample. Mothers of low birth weight (LBW) infants had higher EPDS scores and were more likely to have EPDS scores ≥ 10.

The multivariable logistic regression model predicting low birth weight is presented in Table 3. Three variables were included in the model: maternal age, parity and EPDS scores ≥ 10. EPDS scores ≥ 10 were significantly associated with LBW (OR 2.90, 95% CI 1.18-7.13).

Comment

In this study population, a simple, patient-rated depression screen was significantly associated with increased risk for preeclampsia, preterm birth, and low birth weight. Approximately one third (34.9%) of our sample screened positive for depression, which is a rate similar to prior studies (Kiely et al. 2011; Marcus 2008; Scholle et al. 2003). Antenatal depression is more common in African American, single and lower socioeconomic status women (Kiely et al. 2011) and the rates have increased significantly over the past decade (Maguire et al. 2009). This group is also at increased risk for adverse birth outcomes, which may be partially explained by the increased depression risk.

Twenty-five (9.6%) women in our total sample were diagnosed with preeclampsia per the medical record. This rate is higher than expected as the baseline rate of preeclampsia in African-American women is 3% (http://www.cdc.gov/pednss/pdfs/PNSS_2009.pdf). Women with elevated levels of depressive symptoms were three times more likely to be diagnosed with preeclampsia. In another study that examined antenatal depressive symptoms and the subsequent development of preeclampsia, depression was associated with a 2.5 fold increase in preeclampsia (OR 2.5, 95% CI 1.1-5.4) (Kurki et al. 2000). This sample of nulliparous, Caucasian women was screened with a different measure of depression symptoms (Beck Depression Inventory) at a mean earlier gestational age (12 weeks). Three studies that evaluated the association between a diagnosis of depression and pre-eclampsia have found a positive association. The first study reported that women with a diagnosis of a depression during pregnancy as per the medical record had an increased risk of pre-eclampsia (OR 2.72, 95% CI 1.29-5.74) (Qui et al. 2009). Another study that used diagnosis of antenatal depression in the medical record as the main criterion had an elevated risk of pre-eclampsia close to our results (OR 3.57, 95% CI 1.83 – 6.99) (Cripe et al. 2011). Lastly, moderate to severe antenatal depression (retrospectively assessed) was associated with an increased risk of pre-eclampsia in an Iranian cohort (OR 2.52, 95% CI 1.05-6.02) (Kharaghani et al. 2012). However, other studies have not found an association between antenatal depression and pre-eclampsia (Andersson et al. 2004, Vollebregt et al. 2008). The use of antidepressants during pregnancy may also be associated with an increased risk of pre-eclampsia although the use of psychotropics may be a proxy for more severe depression (Palmsten et al. 2012, Qui et al. 2009). The association between antenatal depression and preeclampsia could be direct or indirect. Depression may directly affect vascular resistance (Kurki et al. 2000) but it is more likely that there may be characteristics or common underlying mechanisms in with both antenatal depression and pre-eclampsia such as obesity, elevated corticotropin releasing hormone (De Bonis 2012) or an impaired inflammatory response to pregnancy (Cripe 2011). While antenatal depression may exacerbate the presentation of pre-eclampsia, the genesis of pre-eclampsia occurs early in pregnancy during implantation and therefore is unlikely to be causative.

In our total sample, the preterm birth rate was 11.2%, which is lower than the national average for non-Hispanic black infants (17.5%) (http://www.cdc.gov/nchs/data/nvsr/nvsr60/

nvsr60_01.pdf). This may be due to the fact that we sampled from a group seeking prenatal care. Factors associated with PTB in our sample were depressive symptoms, thyroid disease, and a history of PTB. The results of a meta-analysis on the subject found that depression scores were significantly associated with PTB (RR 1.13, 95% CI 1.06-1.21) (Grote et al. 2010). For every 1 point increase in depression score there was an associated 3% increase in the risk of PTB. Of the 5 studies published since the meta-analysis, 3 show similar results. Van Dijk et al. (2010) screened 4044 women over 22 weeks gestational age with the Center for Epidemiologic Scale for Depression (CES-D) and found a significant association between depression and PTB (8.4% vs. 4.5%, $p<.05$). In another study, depression was associated with an increase rate of PTB (12% vs. 6.3% $p=.05$) (Field et al. 2009). Smith et al (2011) found an increase in PTB in women with depression (OR 1.82, 95% CI 1.17-2.86) in a sample of women participating in the Healthy Start initiative. Finally, in a recent study, women screened with the EPDS at 24-28 weeks gestational age had an increased risk of PTB if their EPDS score was ≥ 12 (OR 1.3, 96% CI 1.09-1.35) (Straub et al. 2012). However, Wang and Chen (2010) did not find an association, but their baseline PTB rate in their non-depressed cohort was high at 20% making it more difficult to find a difference between the groups. Goedhart et al (2010) screened 8050 pregnant women with the CES-D and did not find depression (defined as CES-D >16) to be associated with PTB. We defined low birth weight (LBW) categorically as neonates < 2500 grams. Twenty-two women (8.4%) in our sample had a LBW infant. Women with an EPDS score ≥ 10 were significantly more likely to have a LBW infant. In the meta-analysis by Grote et al (2010), the relative risk of LBW in women with antenatal depression was increased by 49% when both LBW and depression were dichotomized as categorical variables. All studies published since the Grote meta-analysis defined LBW as a continuous variable, making it difficult to compare to our study. Field et al (2009) screened 390 black women at 18-22 weeks gestational and found that women with major depressive disorder were more likely to have an infant with LBW ($p=.05$). Diego et al (2009) looked at whether another depression screening scale (CES-D) could predict which group would be more at risk for adverse birth outcomes in a prospective, case-control design. The depressed group, evaluated at 18-22 weeks GA, had higher CES-D scores, were younger, less likely to be married and of lower SES status. Women with depression were more likely to have a LBW infant (OR 4.74, 95% CI 0.94 - 23.99). Their depressed cohort had slower fetal growth across the second half of pregnancy. Wang and Chen (2010) did not find an association between high EPDS scores and LBW in a sample of 431 women. This sample was predominately middle to upper socioeconomic status which led the authors to conclude that this sample may have had good prenatal care potentially compensating for the impact of depression on birth outcomes. Twenty-six women (10%) in our sample had IUGR which was not associated with antenatal depression once smoking and recreational drug use were controlled for confirming data published in the Grote et al. meta-analysis (2010).

Overall our data shows that a positive, patient-rated depression screening at the initial obstetrics visit depression is associated with increased risk for a range of adverse birth outcomes. The ideal time to screen is not known. The biological links between depression and adverse birth outcomes are not completely understood. It is possible that depression leads to poor health behaviors, increasing the risk of adverse outcomes. Depressed women are more likely to smoke and abuse substances and are less likely to seek prenatal care (Bonari et al. 2004; Chen and Lin 2011). We found that elevated EPDS scores were no longer a significant predictor of IUGR < 10% after controlling for smoking and recreational drug use during pregnancy, while there was a trend for smoking to be associated with IUGR, which suggests that the relationship between depressive symptoms and IUGR may be mediated by negative health behaviors such as smoking. Other possible factors that could lead to an adverse obstetric outcome in depressed women include poor nutritional status (Hurley et al. 2005) and elevated pre-pregnancy BMI (Kiely et al. 2011) and the use of

psychotropic medications (Udechuku et al. 2010). It has been posited that depression causes or results from hypothalamic-pituitary-adrenal (HPA) axis dysregulation, which in leads to an abnormal uterine environment (Magiakou et al. 1997; Kammerer et al. 2006; Steiner et al. 2003). For example, stress-related increases in cortisol and/or cortisol releasing hormone (CRH) could lead to an abnormally earlier triggering of the partuition clock, leading to PTB. Or depression may be cause increased stress, which in term may in turn increase blood pressure, cause vasoconstriction, decrease uterine blood flow and fetal hypoxia, and elevate CRH and increasing the risk of adverse pregnancy outcomes (Holzman et al. 2001; Wadhwa et al. 2001). Finally, high levels of emotional distress are associated with depressed lymphocyte activity in pregnant women, increasing vulnerability to urogenital and amniotic infections, and premature rupture of membranes (Herrara et al. 1998; Newton et al. 2001). These hypotheses are yet to be definitively confirmed.

Strengths of this study include the use of a standardized depression scale that is validated for use during pregnancy. The population sample was purposely restricted to women with similar demographics to control for the effect of demographic characteristics on adverse obstetrical outcomes. The study also mimics the reality of clinical care such that women come in at different gestational ages for first appointments and screening at a single gestational age is unrealistic in most clinical settings. Limitations of this study include our inability to confirm data beyond chart review. We were unable to confirm a diagnosis of depression in this sample. Also, we could not include body mass index (BMI) as variable because maternal weight was unpredictably recorded in the medical records. BMI is a risk factor for both preterm birth and preeclampsia. Infection has also been associated with pre-eclampsia but we did not collect this information. Inclusion of BMI and infection may have decreased the association between depressive symptoms and pre-eclampsia although bacterial vaginosis did not change this association in a previous study (Kurki et al. 2000). Since pre-pregnancy BMI can be tends to be larger in depressed cohorts, its impact on the association tends to negligible (Kharaghani et al. 2011, Qiu et al. 2009). A larger, prospective study evaluating women across pregnancy would be necessary to confirm our results. In conclusion, our study joins the increasing data showing that depression during pregnancy may have a negative impact on fetal outcomes.

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References

Andersson L, Sundström-Poromaa I, Wulff M, Aström M, Bixo M. Implications of antenatal depression and anxiety for obstetric outcome. Obstet Gynecol. 2004 Sep; 104(3):467–76. [PubMed: 15339755]

Bonari L, Pinto N, Ahn E, Einarson A, Steiner M, Koren G. Perinatal risks of untreated depression during pregnancy. Can J Psychiatry. 2004; 49:726–35. [PubMed: 15633850]

Chen CH, Lin HC. Prenatal care and adverse pregnancy outcomes among women with depression: A nationwide population-based study. Can J Psychiatry. 2011; 56:273–80. [PubMed: 21586193]

Cox JL, Chapman G, Murray D, Jones P. Validation of the edinburgh postnatal depression scale (EPDS) in non-postnatal women. J Affect Disord. 1996; 39:185–9. [PubMed: 8856422]

Cripe SM, Frederick IO, Qiu C, Williams MA. Risk of preterm delivery and hypertensive disorders of pregnancy in relation to maternal co-morbid mood and migraine disorders during pregnancy. Paediatr Perinat Epidemiol. 2011 Mar; 25(2):116–23. [PubMed: 21281324]

De Bonis M, Torricelli M, Severi FM, Luisi S, De Leo V, Petraglia F. Neuroendocrine aspects of placenta and pregnancy. Gynecol Endocrinol. 2012 Mar; 28(Suppl 1):22–6. [PubMed: 22394300]

Diego MA, Field T, Hernandez-Reif M, Schanberg S, Kuhn C, Gonzalez-Quintero VH. Prenatal depression restricts fetal growth. Early Hum Dev. 2009; 85:65–70. [PubMed: 18723301]

Evins GG, Theofrastous JP, Galvin SL. Postpartum depression: A comparison of screening and routine clinical evaluation. Am J Obstet Gynecol. 2000; 182:1080–2. [PubMed: 10819833]

Field T, Diego M, Hernandez-Reif M, Deeds O, Holder V, Schanberg S, et al. Depressed pregnant black women have a greater incidence of prematurity and low birthweight outcomes. Infant Behav Dev. 2009; 32:10–6. [PubMed: 19004502]

Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: A systematic review of prevalence and incidence. Obstet Gynecol. 2005; 106:1071–83. [PubMed: 16260528]

Goedhart G, Snijders AC, Hesselink AE, van Poppel MN, Bonsel GJ, Vrijkotte TG. Maternal depressive symptoms in relation to perinatal mortality and morbidity: Results from a large multiethnic cohort study. Psychosom Med. 2010; 72:769–76. [PubMed: 20668282]

Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. Arch Gen Psychiatry. 2010; 67:1012–24. [PubMed: 20921117]

Herrara JA, Alvarado JP, Martinez JE. The psychosocial environment and cellular immunity in the pregnant patient. Stress and Medicine. 1998; 4:49–56.

Holzman C, Bullen B, Fisher R, Paneth N, Reuss L. Prematurity Study Group. Pregnancy outcomes and community health: The POUCH study of preterm delivery. Paediatr Perinat Epidemiol. 2001; 15:136–58. [PubMed: 11520406]

Hurley KM, Caulfield LE, Sacco LM, Costigan KA, Dipietro JA. Psychosocial influences in dietary patterns during pregnancy. J Am Diet Assoc. 2005; 105:963–6. [PubMed: 15942549]

Jardri R, Pelta J, Maron M, Thomas P, Delion P, Codaccioni X, et al. Predictive validation study of the edinburgh postnatal depression scale in the first week after delivery and risk analysis for postnatal depression. J Affect Disord. 2006; 93:169–76. [PubMed: 16644021]

Kammerer M, Taylor A, Glover V. The HPA axis and perinatal depression: A hypothesis. Arch Womens Ment Health. 2006; 9:187–96. [PubMed: 16708167]

Kanasaki K, Kalluri R. The biology of preeclampsia. Kidney Int. 2009 Oct; 76(8):831–7. [PubMed: 19657323]

Kharaghani R, Geranmaye M, Janani L, Hantooshzade S, Arbabi M, Rahmani Bilandi R, Bagheri F. Preeclampsia and depression: a case-control study in Tehran. Arch Gynecol Obstet. 2012 Jul; 286(1):249–53. [PubMed: 22382370]

Kiely M, El-Mohandes AA, Gantz MG, Chowdhury D, Thornberry JS, El-Khorazaty MN. Understanding the association of biomedical, psychosocial and behavioral risks with adverse pregnancy outcomes among african-americans in washington, DC. Matern Child Health J. 2011; 15:S85–95. [PubMed: 21785892]

Kim DR, Sockol L, Barber JP, Moseley M, Lamprou L, Rickels K, O'Reardon JP, Epperson CN. A survey of patient acceptability of repetitive transcranial magnetic stimulation (TMS) during pregnancy. J Affect Disord. 2011 Mar; 129(1-3):385–90. [PubMed: 20864179]

Kurki T, Hiilesmaa V, Raitasalo R, Mattila H, Ylikorkala O. Depression and anxiety in early pregnancy and risk for preeclampsia. Obstet Gynecol. 2000; 95:487–9. [PubMed: 10725477]

Lee DT, Yip AS, Chiu HF, Leung TY, Chung TK. Screening for postnatal depression: Are specific instruments mandatory? J Affect Disord. 2001; 63:233–8. [PubMed: 11246101]

Magiakou MA, Mastorakos G, Webster E, Chrousos GP. The hypothalamic-pituitary-adrenal axis and the female reproductive system. Ann N Y Acad Sci. 1997; 816:42–56. [PubMed: 9238254]

Maguire J, Ferando I, Simonsen C, Mody I. Excitability changes related to GABAA receptor plasticity during pregnancy. J Neurosci. 2009; 29:9592–601. [PubMed: 19641122]

Marcus SM. Depression during pregnancy: Rates, risks and consequences--motherisk update. Can J Clin Pharmacol. 2008; 16:e15–22. [PubMed: 19164843]

Marcus SM, Flynn HA, Blow F, Barry K. A screening study of antidepressant treatment rates and mood symptoms in pregnancy. Arch Womens Ment Health. 2005; 8:25–7. [PubMed: 15868387]

Newton ER, Piper JM, Shain RN, Perdue ST, Peairs W. Predictors of the vaginal microflora. Am J Obstet Gynecol. 2001; 184:845–53. discussion 853-5. [PubMed: 11303191]

Palmsten K, Setoguchi S, Margulis AV, Patrick AR, Hernández-Díaz S. Elevated risk of preeclampsia in pregnant women with depression: depression or antidepressants? Am J Epidemiol. 2012; 175:988–97. [PubMed: 22442287]

Qiu C, Williams MA, Calderon-Margalit R, Cripe SM, Sorensen TK. Preeclampsia risk in relation to maternal mood and anxiety disorders diagnosed before or during early pregnancy. Am J Hypertens. 2009 Apr; 22(4):397–402. [PubMed: 19197246]

Scholle SH, Haskett RF, Hanusa BH, Pincus HA, Kupfer DJ. Addressing depression in obstetrics/gynecology practice. Gen Hosp Psychiatry. 2003; 25:83–90. [PubMed: 12676420]

Smith MV, Shao L, Howell H, Lin H, Yonkers KA. Perinatal depression and birth outcomes in a healthy start project. Matern Child Health J. 2011; 15:401–9. [PubMed: 20300813]

Steiner M, Dunn E, Born L. Hormones and mood: From menarche to menopause and beyond. J Affect Disord. 2003; 74:67–83. [PubMed: 12646300]

Straub H, Adams M, Kim JJ, Silver RK. Antenatal depressive symptoms increase the likelihood of preterm birth. Am J Obstet Gynecol. 2012 Oct.207(4):329. [PubMed: 22789523]

Udechuku A, Nguyen T, Hill R, Szego K. Antidepressants in pregnancy: A systematic review. Aust N Z J Psychiatry. 2010; 44:978–96. [PubMed: 21034181]

Vollebregt KC, van der Wal MF, Wolf H, Vrijkotte TG, Boer K, Bonsel GJ. Is psychosocial stress in first ongoing pregnancies associated with pre-eclampsia and gestational hypertension? BJOG. 2008 Apr; 115(5):607–15. [PubMed: 18333942]

Van Dijk AE, Van Eijsden M, Stronks K, Gemke RJ, Vrijkotte TG. Maternal depressive symptoms, serum folate status, and pregnancy outcome: Results of the amsterdam born children and their development study. Am J Obstet Gynecol. 2010; 203:563.e1–563.e7. [PubMed: 20833384]

Wadhwa PD, Culhane JF, Rauh V, Barve SS. Stress and preterm birth: Neuroendocrine, immune/inflammatory, and vascular mechanisms. Matern Child Health J. 2001; 5:119–25. [PubMed: 11573837]

Wadhwa PD, Garite TJ, Porto M, Glynn L, Chicz-DeMet A, Dunkel-Schetter C, Sandman CA. Placental corticotropin-releasing hormone (CRH), spontaneous preterm birth, and fetal growth restriction: a prospective investigation. Am J Obstet Gynecol. 2004 Oct; 191(4):1063–9. [PubMed: 15507922]

Wang SY, Chen CH. The association between prenatal depression and obstetric outcome in taiwan: A prospective study. J Womens Health (Larchmt). 2010; 19:2247–51. [PubMed: 20831438]

Table 1

Demographic Characteristics, Birth Outcomes, and Prevalence of Risk Factors for Adverse Birth Outcomes

Characteristic	Total Sample (*N* = 261)
Demographic Characteristics	
Age, *M* (*SD*), years	24.6 (5.4)
Primiparous, % (*n*)	23.0 (60)
Birth Outcomes	
Birth weight, *M (SD),* g	3146.5 (613.6)
Birth weight < 2500 g, % (*n*)	8.4 (22)
Gestational age at delivery, *M (SD),* weeks	38.9 (2.2)
Preterm birth, % (*n*)	11.2 (28)
Preeclampsia, % (*n*)	9.6 (25)
1-minute APGAR, *M (SD)*	7.9 (1.7)
IUGR < 10%, % (*n*)	10.0 (26)
Psychological Risk Factors	
EPDS, *M* (*SD*)	8.1 (6.0)
EPDS ≥ 10, % (*n*)	34.9 (91)
History of mental illness, % (*n*)	17.2 (45)
Known psychotropic exposure, % (*n*)	2.3 (6)
Medical/Obstetric Risk Factors	
Chronic illness noted on problem list % (*n*)	49.0 (128)
History of prior preterm birth % (*n*)	18.0 (47)
Gestational diabetes % (*n*)	3.1 (8)
Thyroid disease during current pregnancy	2.7 (7)
Behavioral Risk Factors	
Known alcohol use at initial visit % (*n*)	3.1 (8)
Known recreational drug use % (*n*)	6.1 (16)
Smoking reported at initial clinic visit % (*n*)	19.9 (52)

Table 2

Associations Between Demographic Characteristics, Risk Factors, and Adverse Birth Outcomes

	Preeclampsia			Low Birth Weight			Preterm Birth			IUGR < 10%		
	Yes	No	*p* value	Yes	No	*p* value	Yes	No	*p* value	Yes	No	*p* value
n	**25**	**229**		**22**	**192**		**28**	**223**		**26**	**186**	
Demographic Characteristics												
Age *M (SD)*	23.7 (5.5)	24.7 (5.5)	0.38	24.8 (6.7)	24.7 (5.5)	0.91	25.0 (6.0)	24.6 (5.4)	0.75	25.2 (6.7)	24.6 (5.4)	0.61
Primiparous % (*n*)	32.0 (8)	22.3 (51)	0.27	22.7 (5)	22.4 (43)	1.00	21.4 (6)	23.3 (52)	0.82	26.9 (7)	22.0 (41)	0.58
Psychological Risk Factors												
EPDS *M* (*SD*)	11.0 (5.3)	7.6 (5.9)	0.01	10.6 (6.8)	7.4 (5.6)	0.02	9.8 (5.8)	7.7 (6.0)	0.08	9.8 (6.4)	7.5 (5.7)	0.06
EPDS ≥ 10 % (*n*)	56.0 (14)	31.4 (72)	0.01	54.5 (12)	29.2 (56)	0.02	50.0 (14)	32.3 (72)	0.06	53.8 (14)	29.0 (54)	0.01
History of mental illness % (*n*)	8.0 (2)	17.9 (41)	0.27	13.6 (3)	15.7 (30)	1.00	14.3 (4)	17.0 (38)	1.00	15.4 (4)	15.1 (28)	1.00
Known psychotropic exposure % (*n*)	0 (0)	2.6 (6)	1.00	9.1 (2)	2.1 (4)	0.12	7.1 (2)	1.8 (4)	0.13	3.8 (1)	2.7 (5)	0.55
Medical Risk Factors												
Thyroid disease during preg. % (*n*)	0 (0)	3.1 (7)	1.00	4.5 (1)	2.1 (4)	0.42	10.7 (3)	1.8 (4)	0.03	0 (0)	2.7 (5)	1.00
Gestational diabetes % (*n*)	4.2 (1)	3.1 (7)	0.56	0 (0)	4.2 (8)	1.00	3.6 (1)	3.2 (7)	1.00	7.7 (2)	3.2 (6)	0.26
History of prior preterm birth % (*n*)	24.0 (6)	17.9 (41)	0.43	22.7 (5)	18.8 (36)	0.78	35.7 (10)	16.1 (36)	0.01	26.9 (7)	17.7 (33)	0.29
Chronic illness % (*n*)	56.0 (14)	48.5 (111)	0.48	50.0 (11)	47.1 (90)	0.80	60.7 (17)	48.0 (107)	0.20	42.3 (11)	47.8 (89)	0.60
Behavioral Risk Factors												
Known alcohol use % (*n*)	4.0 (1)	3.2 (7)	0.58	0 (0)	4.4 (8)	1.00	0 (0)	3.7 (8)	0.60	8.0 (2)	3.4 (6)	0.26
Known recreational drug use % (*n*)	4.0 (1)	6.6 (15)	1.00	9.1 (2)	6.3 (12)	0.64	3.7 (1)	6.7 (15)	1.00	15.4 (4)	4.8 (9)	0.06
Smoking reported % (*n*)	12.5 (3)	21.2 (47)	0.43	22.7 (5)	20.8 (38)	0.79	18.5 (5)	20.4 (44)	0.82	40.0 (10)	17.9 (32)	0.01

Table 3

Logistic Regressions of Risk Factors for Preeclampsia, Low Birth Weight, and Preterm Birth

	Preeclampsia			LBW			PTB			IUGR < 10%		
	β	*OR*	95% *CI*	*β*	*OR*	95% *CI*	*β*	*OR*	95% *CI*	*β*	*OR*	95% *CI*
Age	-0.03	0.97 ns	0.89-1.06	0.00	1.00 ns	0.92-1.09	0.00	1.00 ns	0.92-1.08	0.03	1.03 ns	0.95-1.11
Parity	-0.50	0.61 ns	0.23-1.62	-0.10	0.90 ns	0.29-2.83	-0.50	0.61 ns	0.20-1.86	-0.48	0.62 ns	0.22-1.73
EPDS ≥ 10	1.08	2.95 *	1.26-6.89	1.07	2.90 *	1.18-7.13	0.85	2.34 *	1.03-5.36	1.07	2.91 *	1.26-6.72
Thyroid disease during preg.							2.05	7.79 *	1.52-39.99			
History of PTB							1.21	3.35 *	1.29-8.73			
Constant	-1.65			-2.60			-2.46			-2.72		

Note. OR = odds ratio, 95% *CI* = 95% confidence interval for odds ratio

ns $p > 0.05$.

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$

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