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# Diabetes and Depression in Pregnancy: Is There an Association?

Jodie G. Katon, Ph.C.,[1] Joan Russo, Ph.D.,[2] Amelia R. Gavin, Ph.D.,[3] Jennifer L. Melville, M.D., M.P.H.,[4] and Wayne J. Katon, M.D.[2]

## Abstract

***Background:*** Prior studies have reported inconsistent findings regarding the association of antenatal depression with pregnancy-related diabetes. This study examined the association of diabetes and antenatal depression.
***Methods:*** We conducted a cross-sectional analysis of baseline data from a prospective cohort study of pregnant women receiving prenatal care at a single University of Washington Medical Center clinic between January 2004 and January 2009. The primary exposure was diabetes in pregnancy (no diabetes, preexisting diabetes, or gestational diabetes [GDM]). Antenatal depression was defined by the Patient Health Questionnaire-9 (PHQ-9) score or current use of antidepressants. Antenatal depression was coded as (1) any depression (probable major or minor depression by PHQ-9 or current antidepressant use) and (2) major depression (probable major depression by PHQ-9 or current antidepressant use). Logistic regression was used to quantify the association between diabetes in pregnancy and antenatal depression.
***Results:*** The prevalences of preexisting diabetes, GDM, any antenatal depression, and major antenatal depression were 9%, 18%, 13.6%, and 9.8%, respectively. In the unadjusted analysis, women with preexisting diabetes had 54% higher odds of any antenatal depression compared to those without diabetes (odds ratio [OR] 1.54, 95% confidence interval [CI] 1.08-2.21). After adjusting for important covariates the association was attenuated (OR 1.16, 95% CI 0.79-1.71). Results were similar for antenatal major depression. GDM was not associated with increased odds for any antenatal depression or antenatal major depression.
***Conclusions:*** Neither preexisting diabetes nor GDM was independently associated with increased risk of antenatal depression.

## Introduction

Globally, major depressive disorder (MDD) is projected to be one of the three leading contributors to burden of disease by 2030.[1] The prevalence of major depression in women peaks during childbearing years, with recent estimates indicating that approximately 8%–12% of pregnant women may meet diagnostic criteria for major depression.[2] Antenatal major depression is associated with adverse consequences for offspring during the perinatal period and over the life course.[3] Antenatal depression is also associated with experiencing more discomfort from pregnancy-related physical symptoms,[4] increased functional impairment, and greater marital conflict.[5] Additionally, antenatal depression is a strong risk factor for postpartum depression (PPD),[5] which is associated with poor maternal-infant bonding[6] and may have adverse effects on infant development.[3] Despite these findings, depressive disorders continue to be underdetected and undertreated in pregnancy.[4]

The prevalence of diabetes in pregnancy has risen 122% in the last 20 years,[7] largely due to increased prevalence of gestational diabetes (GDM),[8] defined as glucose intolerance with first onset or recognition in pregnancy. There is evidence of a bidirectional link between depression and diabetes.[9] Depression earlier in life increases the risk for development of type 2 diabetes,[9] and diabetes-specific complications are associated with a higher risk of subsequent depression.[9,10] One study in a large Medicaid population found that diabetes that

[1]Department of Epidemiology, University of Washington School of Public Health, Seattle, Washington.
[2]Department of Psychiatry & Behavioral Sciences, University of Washington School of Medicine, Seattle, Washington.
[3]School of Social Work, University of Washington, Seattle, Washington.
[4]Department of Obstetrics and Gynecology, University of Washington School of Medicine, Seattle, Washington.

precedes pregnancy is associated with depression among pregnant women,[11] although the findings with respect to GDM are less clear.[11–14] Three earlier studies found that the mood profile of women with GDM did not differ significantly from that of women without diabetes in pregnancy.[12–14] These were relatively small studies that measured antenatal depressive symptoms rather than using diagnostic criteria for major depression. In contrast, using a large sample of pregnant women enrolled in Medicaid, Kozhimannil et al.[11] reported a 2-fold increase in odds of receiving a diagnosis of perinatal depression (defined as depression in the 6 months before delivery and in the first year postpartum) among women with prepregnancy diabetes and GDM compared to women with no diabetes. Because major depression is unlikely to remit without treatment, understanding whether or not diabetes, in particular GDM, is associated with antenatal major depression is paramount.

The consequences of comorbid diabetes and antenatal depression are still poorly understood. Among women with GDM, poor glycemic control may be associated with greater psychologic distress,[12] and poor glycemic control is, in turn, associated with increased maternal and neonatal morbidity.[15] In the nonpregnant population, comorbid depression has been shown to be associated with decreased adherence to diabetes self-care regimens (i.e., diet, exercise, cessation of smoking, and taking medication as prescribed),[16] which may explain in part the increased risk of macrovascular and microvascular complications and mortality among patients with comorbid depression and diabetes.[17] Therefore, understanding the epidemiology of depression and diabetes in pregnancy may potentially improve care of women with diabetes in pregnancy and reduce associated maternal and neonatal morbidity.

The objective of this study was to examine whether preexisting diabetes or GDM was associated with a higher prevalence of antenatal depression than is found in women without diabetes in pregnancy. To address these questions, we conducted a cross-sectional analysis of baseline data from an ongoing prospective cohort study in a large community-based sample of pregnant women receiving prenatal care at a single University of Washington Medical Center clinic between January 2004 and January 2009.

## Materials and Methods

### *Study design and population*

The participants in this study were patients receiving prenatal care at a single University of Washington Medical Center clinic from January 2004 to January 2009. Questionnaires assessing mood and psychosocial factors were introduced in January 2004 and were distributed by clinical staff as part of routine clinical care to all patients during pregnancy. All women receiving ongoing obstetrical care and completing at least one clinical questionnaire in either the second or third trimester during the study time period were eligible for inclusion in the study. Exclusion criteria included age < 15 years at the time of delivery and inability to complete the clinical questionnaire because of mental incapacitation or language difficulties (i.e., no interpreter available). Clinic staff were asked to contact and obtain consent from potentially eligible subjects for study enrollment at the time of screen completion. Among patients providing written informed consent, questionnaires were linked to automated medical records. All procedures were approved by the University of Washington's Institutional Review Board.

During the study period, 3347 women completed at least one psychosocial screening questionnaire at 4 months' gestation, during the third trimester, or postpartum (Fig. 1). Staff were present to obtain consent from 2577 (77%) for study enrollment. A total of 227 (6.8%) declined to participate in this part of the study, and 543 (16.2%) left the clinic before they could consent. Of the 2577 women who consented, 2398 (93.1%) completed the psychosocial screen before delivery.

### *Study variables and measures*

The primary exposure in our study was diabetes in pregnancy (no diabetes, preexisting diabetes, and GDM). Diagnosis of GDM was determined by a physician ICD-9 diagnosis of 648.8 in the automated medical record. GDM is clinically defined as glucose intolerance with first recognition or onset in pregnancy[18]; therefore, this diabetes category could potentially include women with previously unrecognized type 2 diabetes. Preexisting diabetes (type 1 or type 2 diabetes) was defined by a physician ICD-9 diagnosis of 250.x in the automated medical record. A subset of patients had both an ICD-9 diagnosis of preexisting diabetes and GDM, and these were reassigned as preexisting diabetes if there was a self-report on the screening questionnaire of being diagnosed with diabetes within the previous 3 years, excluding a diagnosis only in pregnancy, or if there was evidence on self-report of use of glyburide or insulin before 15 weeks of pregnancy. Otherwise, patients with both ICD-9 diagnoses were reassigned as having GDM.

Covariate information collected from the electronic medical record and the questionnaire included demographic characteristics, general health history, prior pregnancy complications, and social history. Maternal age (measured in years) was obtained from the automated medical record. Women were asked about their current marital status, which was analyzed as a categorical variable (married or living with a partner or not currently partnered). Self-reported race/ethnicity was categorized as non-Hispanic white and nonwhite. Employment status was defined as either employed (full-time or part-time) or unemployed (in school, retired, homemaker, unemployed, disabled, other).

Tobacco use was assessed using the Smoke-Free Families Prenatal Screen, which was specifically developed to maximize disclosure of smoking status during pregnancy.[19] Women with any current smoking were classified as smokers. The T-ACE was used to assess substance use in the 12 months before pregnancy.[20] The T-ACE was developed to identify risk drinkers and has been validated in a pregnant population.[20] Women were considered to have a history of alcohol use if they met the criteria for risk drinking in the 12 months before their current pregnancy.

Women were considered to have a medical comorbidity if they reported one or more prepregnancy health conditions(excluding diabetes). Prepregnancy health conditions included asthma, hypertension, arthritis, thyroid disorders, migraines, gastrointestinal disorders, cancer, seizure disorders, heart failure, other heart disease, or a chronic physical disability (loss of limb, eyesight, or hearing). Gestational week at depression screening was calculated based on a woman's

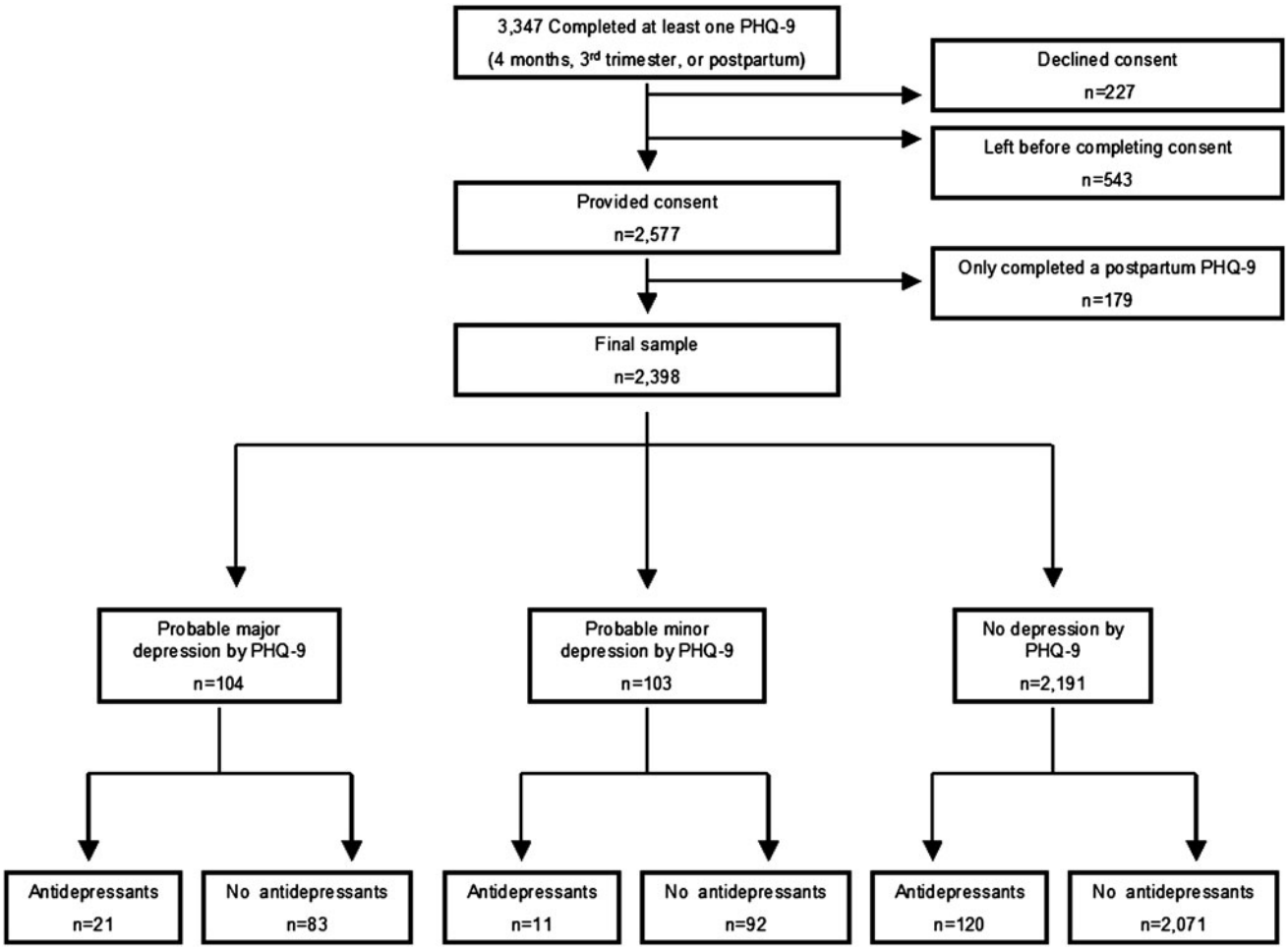


**FIG. 1.** Study population, depression status by Patient Health Questionnaire-9 (PHQ-9) and antidepressant use.

expected date of delivery and the date the depression screen was administered. A history of pregnancy complications was recorded for women self-reporting one or more significant complications in a prior pregnancy, including GDM, hypertension or preeclampsia, eclampsia, preterm labor, preterm delivery, preterm rupture of the membranes, placental abruption, oligohydramnios, or hemorrhage. Women with no prior pregnancy were categorized as having no history of pregnancy complications.

### *Study outcomes*

There were two primary study outcomes: any antenatal depression and antenatal major depression. Any antenatal depression was defined by a positive diagnosis of probable major or minor depression on the Patient Health Questionnaire-9 (PHQ-9)[21] or use of any antidepressants during the current pregnancy. Antenatal major depression was defined by a positive diagnosis of probable major depression by the PHQ-9 or use of any antidepressants during the current pregnancy. The PHQ-9 identifies major and minor depression based on *Diagnostic and Statistical Manual of Mental Disorders* IV (DSM-IV) criteria.[21] The DSM-IV criteria for major depression on the PHQ-9 require the subject to have, for at least 2 weeks, five or more depressive symptoms present for more than half of the days, with at least one of these symptoms being depressed mood or anhedonia. The criteria for minor depression require the subject to have, for at least 2 weeks, two to four depressive symptoms present for more than half of the days, with at least one of these symptoms being depressed mood or anhedonia. The PHQ-9 has been validated for diagnosis of major depression among obstetrics/gynecology patients and has a sensitivity of 73% and specificity of 98% for diagnosis of major depression based on the Structured Clinical Interview for DSM-IV (SCID).[21] Information on antidepressant usage was obtained by patient self-report. Selective serotonin reuptake inhibitors (SSRI) included sertraline, fluoxetine, fluvoxamine, paroxetine, citalopram, and escitalopram. All non-SSRI antidepressants were included in the other antidepressant category. Self-report of antidepressant use in pregnancy has reasonable agreement with pharmacy records when it is collected during pregnancy.[22] In the final analysis, SSRIs and other antidepressants were combined in the any antidepressant category. Figure 1 shows the prevalence of antenatal major and minor depression by PHQ-9 and the use of antidepressants.

### *Statistical analysis*

Characteristics of women were summarized for the total sample and by diabetes in pregnancy status. Means and 95% confidence intervals (CI) are reported for continuous variables

Table 1. Characteristics and Prevalence of Risk Factors for Antenatal Depression Among Respondents in Total Sample ($n=2398$) and by Diabetes Status

| | | Diabetes status | | |
|---|---|---|---|---|
| | *Total sample*[a] | *No diabetes* | *Preexisting* | *GDM* |
| Number | 2398 | 1747 | 226 | 425 |
| Characteristic | | | | |
| Maternal age | 30.5 (30.2-30.7) | 30.1 (29.8-30.4) | 30.7 (29.9-31.4) | 31.9 (31.3- 32.4) |
| Married or partnered, % | 87 (85.2-88.2) | 86 (84.4- 87.8) | 85 (80.2-89.6) | 90 (87.5-93.3) |
| Nonwhite race/ethnicity, % | 35 (33.2-37.1) | 33 (30.9- 35.4) | 38 (31.3-44.8) | 42 (37.3-46.9) |
| Some college, % | 79 (77.7-81.0) | 80 (77.7-81.7) | 77 (71.0-82.3) | 79 (75.3-83.3) |
| Employed, % | 55 (52.6-56.7) | 56 (53.2- 57.9) | 49 (42.1- 55.6) | 54 (49.1- 59.0) |
| Current smoker, % | 8 (6.6-8.7) | 8 (6.3-8.9) | 8 (4.4-11.7) | 8 (5.0-10.4) |
| History of alcohol use, % | 15 (13.3-16.3) | 15 (13.5-17.0) | 12 (7.8-16.8) | 14 (10.7-18.0) |
| ≥1 chronic medical condition, % | 43 (40.8-44.9) | 40 (37.3-42.1) | 65 (58.0-71.2) | 44 (39.6-49.2) |
| Prior pregnancy, % | 75 (73.3-76.8) | 72 (70.2- 74.4) | 83 (78.3-88.1) | 82 (78.1-85.5) |
| Gestational week at depression screen | 23.3 (23.0-23.7) | 23.5 (23.1-23.8) | 20.8 (19.9- 21.7) | 24.1 (23.4-24.8) |
| ≥1 Prior pregnancy complication, % | 28 (25.4-29.7) | 28 (25.4-29.7) | 51 (25.4-29.7) | 45 (40.3-49.8) |

[a]Data are mean (95% confidence interval [CI]) or percentage (95% CI) using imputed data (m=5).
GDM, gestational diabetes mellitus.

and percentages, and 95% CIs are reported for categorical variables. Means or proportions and 95% CIs of each component of our specified antenatal depression outcomes (PHQ-9 score, probable major and minor depression by PHQ-9 score, and antidepressant medication use) were also reported for the entire sample and by diabetes in pregnancy status.

The associations between diabetes and any antenatal depression and diabetes and antenatal major depression were estimated using logistic regression. Four models were fit sequentially. The first model included only the primary exposure of diabetes status (none, preexisting diabetes, GDM). The second model adjusted for demographic characteristics (maternal age at depression screen, marital status, nonwhite race/ethnicity, education, and employment). The third model adjusted for demographic characteristics and the presence of other chronic medical conditions. The fourth model adjusted for demographic characteristics, other chronic medical conditions, and pregnancy variables (prior pregnancy, gestational week at depression screening, and prior pregnancy complications). Odds ratios (OR) and 95% CIs are reported. All analysis were completed using STATA 9 (StataCorp, College Station, TX).

### *Sensitivity analyses*

As antenatal depressive symptoms may result from poor control of GDM, we ran a sensitivity analysis including only women who had a depression screen at 4 months of gestation. Antidepressants may be prescribed for conditions other than depression; therefore, we also conducted a sensitivity analysis excluding women with self-reported antidepressant use and used PHQ-9 alone to define any antenatal depression and antenatal major depression.

### *Missing data and multiple imputation*

Although data were complete for the primary outcome and exposure, there were missing data for many of the covariates; <10% of data were missing for any individual covariate. However, use of complete-case analysis would have caused the exclusion of 476 women. Additionally, when data are missing at random, use of complete-case analysis biases results and decreases efficiency.[23] Therefore, we used multiple imputation to create five complete datasets (m=5), and the regression coefficients from each dataset were combined using the rules described by Little and Rubin.[23] To impute the missing covariate values, we specified individual equations based on the selection rules recommended by van Buuren et al.[24] Among the variables considered for each imputation equation were all demographic, pregnancy, and clinical variables in addition to the outcomes of probable antenatal major, minor, or any depression; preterm delivery; very preterm delivery; low birth weight; and very low birth weight. All results presented in tables are from the multiple imputation. Results from complete-case analysis (results not shown) were similar to those from the multiple imputation.

## Results

In this study, women with preexisting diabetes compared to women without diabetes in pregnancy were older, more likely to belong to a nonwhite race/ethnicity group, and had an increased prevalence of chronic medical conditions (Table 1). Compared to women without diabetes in pregnancy, women with GDM were also older, more likely to be of nonwhite race/ethnicity, and more likely to have at least one other chronic medical condition. Among women with other chronic medical conditions, migraines (37%) and asthma (28%) were the most frequently reported. A higher percentage of women with preexisting diabetes or GDM had a history of pregnancy complications.

In our final study sample, the prevalence of preexisting diabetes was 9%, and the prevalence of GDM was 18%; 327 (13.6%) women met our criteria for any antenatal depression, and 235 (9.8%) met our criteria for antenatal major depression. The prevalence of antenatal major depression (probable major depression by PHQ-9 or antidepressant use) and any antenatal depression (probable major or minor depression by PHQ-9 or antidepressant use) was highest among women with preexisting diabetes (Table 2). Women with GDM had a

Table 2. Prevalence of Antenatal Depression, Antidepressant Use, and Use of Other Psychiatric Medications, by Diabetes Status ($n = 2398$)

| | | | Diabetes status | | |
|---|---|---|---|---|---|
| | | Total sample | No diabetes | Preexisting | GDM |
| Number | | 2398 | 1747 | 226 | 425 |
| Depression by PHQ-9 | | | | | |
| Mean PHQ-9 score | | 3.62 (3.46-3.78) | 3.5 (3.31-3.68) | 4.38 (3.79-4.96) | 3.73 (3.36-4.11) |
| Probable major depression | 104 | 4.3 (3.5-5.2) | 4.1 (3.2-5.1) | 5.8 (2.7-8.8) | 4.5 (2.5-6.4) |
| Probable minor depression | 103 | 4.3 (3.5-5.1) | 4.1 (3.2-5.1) | 6.2 (3.0-9.4) | 4.0 (2.1- 5.9) |
| Any depression | 207 | 8.6 (7.5-9.8) | 8.2 (7.0-9.5) | 12.0 (7.7-16.2) | 8.5 (5.8-11.1) |
| Medication use | | | | | |
| SSRI | 124 | 5.2 (4.3-6.1) | 5.0 (4.0-6.0) | 7.5 (4.1-11.1) | 4.7 (2.7-6.7) |
| Other antidepressant | 35 | 1.5 (1.0-1.9) | 1.5 (0.9-2.1) | 1.8 (0.05-3.5) | 1.2 (0.2-2.2) |
| Any antidepressant | 152 | 6.3 (5.4-7.3) | 6.2 (5.1-7.3) | 8.9 (5.1-12.6) | 5.7 (3.5-7.9) |
| Other psychiatric medication | 58 | 2.4 (1.8-3.0) | 2.2 (1.5-2.9) | 4.4 (1.7-7.1) | 2.1 (0.8-3.5) |
| Depression by PHQ-9 and medication use | | | | | |
| Any depression[a] | 327 | 13.6 (12.3-15.0) | 13.2 (11.6- 14.8) | 19.0 (13.9-24.2) | 12.5 (9.3-15.6) |
| Major depression[b] | 235 | 9.8 (8.6-10.9) | 9.6 (8.2-11.0) | 13.3 (8.8-17.7) | 8.7 (6.0-11.4) |

Data are mean (95% CI) or percentage (95% CI).
[a]Probable major or minor depression by Patient Health Questionnaire-9 (PHQ-9) or antenatal antidepressant use.
[b]Probable major depression by PHQ-9 or antenatal antidepressant use.
SSRI, selective serotonin reuptake inhibitors.

similar prevalence of antenatal major depression and any antenatal depression compared to women without diabetes in pregnancy. These findings were consistent for each component of our specified antenatal depression outcomes (PHQ-9 score, probable major and minor depression by PHQ-9 score, and antidepressant medication use).

In the unadjusted analysis, women with preexisting diabetes, compared to those with no diabetes, had 54% higher odds (OR 1.54, 95% CI 1.08-2.21) for any antenatal depression (probable minor or major depression by PHQ-9 or antidepressant use) and 44% higher odds (OR 1.44, 95% CI 0.95-2.18) for antenatal major depression (probable major depression by PHQ-9 or antidepressant use) (Table 3). Adjustment for demographic characteristics had little effect on these findings. After adjusting for demographic and chronic medical conditions, the associations between preexisting diabetes and any antenatal depression (OR 1.26, 95% CI 0.86-1.84) and antenatal major depression (OR 1.18, 95% CI 0.76-1.82) were attenuated and no longer statistically significant. Controlling for demographic characteristics, chronic medical conditions, and pregnancy variables further attenuated the association of antenatal depression with preexisting diabetes. GDM was not associated with increased odds of any antenatal depression or antenatal major depression in either the unadjusted or adjusted analysis. The results remained unchanged when only women who were screened for depression by 4 months of gestation were included in the analysis or when women with self-reported antidepressant use were excluded.

## Discussion

In this study of 2398 women, there was an increased risk of any antenatal depression associated with preexisting diabetes in the unadjusted analysis; however, this association was

Table 3. Odds Ratio (95% Confidence Interval) for Any Antenatal Depression and Major Antenatal Depression Among Pregnant Women After Multiple Imputation ($m = 5$)

| | Any antenatal depression[a] | | Major antenatal depression[b] | |
|---|---|---|---|---|
| *Covariate adjustment* | *Preexisting diabetes* | *GDM* | *Preexisting diabetes* | *GDM* |
| Unadjusted | 1.54 (1.08-2.21) | 0.94 (0.68-1.29) | 1.44 (0.95-2.18) | 0.90 (0.62-1.30) |
| Adjusted for Demographic characteristics[c] | 1.50 (1.04-2.18) | 0.98 (0.71-1.37) | 1.39 (0.91-2.13) | 0.92 (0.63-1.35) |
| Demographic characteristics[c] and chronic medical conditions[d] | 1.26 (0.86-1.84) | 0.95 (0.68-1.32) | 1.18 (0.76-1.82) | 0.89 (0.60-1.30) |
| Demographic characteristics,[c] chronic medical conditions,[d] and pregnancy variables[e] | 1.16 (0.79-1.71) | 0.95 (0.68-1.33) | 1.12 (0.72-1.74) | 0.90 (0.61-1.32) |

Odds ratios for antenatal depression compare those with preexisting diabetes or GDM to those without any diabetes.
[a]Probable major depression or minor depression by PHQ-9, or antidepressant use vs. no depression.
[b]Probable major depression by PHQ-9 or antidepressant use vs. no depression or probable minor depression by PHQ-9.
[c]Demographic characteristics: maternal age at depression screen (years), marital status (married or partnered, single), nonwhite race/ethnicity, education (some college, high school or less), employment (yes, no).
[d]One or more other chronic medical condition (yes, no).
[e]Pregnancy variables: prior pregnancy (yes, no), gestational week at depression screen (weeks), ≥1 prior pregnancy complication (yes, no).

attenuated and no longer statistically significant after adjusting for demographic, clinical, and pregnancy characteristics. There was no independent association between GDM and either measure of antenatal depression in the unadjusted or adjusted analyses.

Our findings differ from some of those reported in prior studies. Kozhimannil et al.,[11] in a study of 11,024 pregnant women on Medicaid, found a 2-fold increased odds of an ICD-9 code for perinatal depression (depression 6 months before 1 year after delivery) or a prescription for antidepressants among women with preexisting diabetes and women with GDM. Although in the unadjusted analysis, we found a similar association of preexisting diabetes and any antenatal depression, this association was largely accounted for by the greater percentage of women with preexisting diabetes who also had other chronic medical conditions. Type 2 diabetes is often associated with comorbid illnesses, such as hypertension. Thus, the burden of chronic illness, and not diabetes alone, may be more likely to be associated with depression. The study by Kozhimannil et al.[11] did not adjust for the presence of other chronic medical conditions. Additionally, this study used a Medicaid sample and given the higher prevalence of risk factors for diabetes among low-income women,[25] it is possible that a greater proportion of women diagnosed with GDM in this study had previously unrecognized type 2 diabetes, which manifested as more severe GDM.

Another key difference between the two studies is that we relied on antenatal diagnostic screening for depression that was applied to the entire study population independent of diabetes status. Kozhimannil et al.[11] defined depression based on ICD-9 codes and use of antidepressants in the 6 months before and 1 year after delivery, thus focusing on women with recognized depression and including PPD in their study outcome. Only 20%–50% of women meeting the criteria for major depression in pregnancy are accurately diagnosed, and physicians are likely to recognize women with more severe and persistent symptoms of depression.[2,4] Moreover, if women with preexisting diabetes or GDM are more likely to be diagnosed with perinatal depression because of a greater number of healthcare visits, this might explain the observed increased odds of depression among women with preexisting diabetes and GDM in the study by Kozhimannil et al.[11]

With respect to the lack of association between GDM and antenatal depression, our findings were similar to those of three prior smaller studies.[12–14] However, evidence from the Australian Carbohydrate Intolerance Study in Pregnant Women, a randomized trial of treatment of hyperglycemia in pregnancy, suggests that treatment of hyperglycemia in pregnancy may improve mood profile,[26] and if women with GDM in our study were screened for depression after beginning treatment for GDM, this could explain our null findings. Therefore, we conducted a sensitivity analysis excluding women screened for depression after 4 months of gestation. The results (not shown) did not differ from the results of our primary analysis.

The current study has several important strengths. We identified antenatal depression using a diagnostic instrument (PHQ-9) that was administered independent of a woman's diabetes status; therefore, we were able to identify clinically relevant depression in an unbiased manner. Further, use of the PHQ-9 also enabled us to distinguish between probable minor and major depression to further refine our outcome definition and analysis. We were also able to collect information about current use of antidepressants in addition to detailed demographic, pregnancy, and clinical information. Finally, this study included a large and diverse population, making our findings more generalizable to the broader population of pregnant women than previous studies, which had small sample sizes or studied a Medicaid population.

There are also several limitations to consider. Despite the diversity of the study population, our study was from a single large obstetrics clinic in one geographic region of the United States, thus limiting the generalizability of our findings. This study examined prevalent antenatal depression and did not distinguish between preexisting and incident depression or include information on past history of depression. Depression is thought to have a bidirectional effect on chronic diseases, such as diabetes,[9] and thus is both a risk factor for and a consequence of diabetes. Therefore, by focusing on prevalent antenatal depression, this study could not determine the direction of causality. Depression status was determined by the PHQ-9, not a structured psychiatric interview. Thus, we used the term "probable" major and minor depression, as clinical interviews were not done to confirm questionnaire diagnosis. Although we were able to adjust for a large number of confounders, information on prepregnancy BMI was not available. However, two prior studies that examined the association of depression and diabetes found that adjusting for BMI did not appreciably change the measured association.[27,28] Additionally, prepregnancy BMI may have been a consequence of preexisting depression or management of preexisting diabetes through weight loss, and, therefore, adjustment for prepregnancy BMI would have been inappropriate. Finally, a portion of data on important covariates was missing. Therefore, we used multiple imputation, a technique shown to decrease bias and increase efficiency when data are missing at random.[23] Results using complete-case analysis were similar to the multiple imputation results.

## Conclusions

In this study of 2398 women screened for depression, there was no detectable independent association of diabetes and antenatal depression in pregnancy after accounting for the presence of other chronic medical conditions. Although diabetes may not independently increase the risk of antenatal depression, the presence of one or more chronic medical conditions significantly increased a woman's risk of antenatal depression, highlighting the importance of depression screening among pregnant women with chronic medical conditions. Future research needs to replicate these findings and should also focus on the potential impact of antenatal depression in patients with diabetes in pregnancy on glycemic control, birth outcomes, and infant health.

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## Disclosure Statement

No competing financial interests exist for any of the authors.

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Address correspondence to:
*Jodie G. Katon, Ph.C.*
*Department of Epidemiology, Box 357236*
*University of Washington*
*Seattle, WA 98195*

*E-mail:* jkaton@u.washington.edu