HHS Public Access

Author manuscript

*Paediatr Perinat Epidemiol*. Author manuscript; available in PMC 2016 July 01.

Published in final edited form as:

*Paediatr Perinat Epidemiol*. 2015 July ; 29(4): 281–289. doi:10.1111/ppe.12199.

# Pregnancy Hyperglycemia and Risk of Prenatal and Postpartum Depressive Symptoms

**Tianyi Huang**[1,2], **Sheryl L. Rifas-Shiman**[3], **Karen A. Ertel**[4], **Janet Rich-Edwards**[1,2], **Ken Kleinman**[3], **Matthew W. Gillman**[3,5], **Emily Oken**[3,5], and **Tamarra James-Todd**[1]

[1]Division of Women's Health, Department of Medicine, Connors Center for Women's Health and Gender Biology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

[2]Department of Epidemiology, Harvard School of Public Health, Boston, MA

[3]Obesity Prevention Program, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA

[4]Division of Biostatistics and Epidemiology, Department of Public Health, School of Public Health and Health Sciences, University of Massachusetts, Amherst, MA

[5]Department of Nutrition, Harvard School of Public Health, Boston, MA

## Abstract

**Background—**Glucose dysregulation in pregnancy may affect maternal depressive symptoms during the prenatal and postpartum periods via both physiologic and psychological pathways.

**Methods—**During mid-pregnancy, a combination of 50-gram 1-h non-fasting glucose challenge test (GCT) and 100-gram 3-h fasting oral glucose tolerance test (OGTT) was used to determine pregnancy glycemic status among women participating in Project Viva: normal glucose tolerance (NGT), isolated hyperglycemia (IHG), impaired glucose tolerance (IGT) and gestational diabetes mellitus (GDM). Using the Edinburgh Postnatal Depression Scale (EPDS), we assessed depressive symptoms at mid-pregnancy and again at 6 months postpartum. We used logistic regression, adjusted for sociodemographic, anthropometric and lifestyle factors, to estimate the risk of elevated prenatal and postpartum depressive symptoms (EPDS ≥ 13 on 0–30 scale) in relation to GCT glucose levels and GDM status in separate models.

**Results—**9.6% of women showed prenatal and 8.4% postpartum depressive symptoms. Women with higher GCT glucose levels were at greater odds of elevated prenatal depressive symptoms (multivariable-adjusted OR per SD increase in glucose levels (27 mg/dL): 1.25; 95%: 1.07, 1.48). Compared with NGT women, the association appeared stronger among women with IHG (OR: 1.80; 95% CI: 1.08, 3.00) than among those with GDM (OR: 1.45; 95% CI: 0.72, 2.91) or IGT (OR: 1.43; 95% CI: 0.59, 3.46). Neither glucose levels assessed from the GCT nor pregnancy glycemic status were significantly associated with elevated postpartum depressive symptoms.

**Conclusion—**Pregnancy hyperglycemia was cross-sectionally associated with higher risk of prenatal depressive symptoms, but not with postpartum depressive symptoms.

Corresponding author: Tianyi Huang, Brigham and Women's Hospital/Harvard Medical School, 1620 Tremont St., Division of Women's Health, 3rd Floor, Boston, MA 02120, Phone: 617.525.9683, Fax: 617.525.7746, tih541@mail.harvard.edu.

**Keywords**

gestational diabetes; impaired glucose tolerance; hyperglycemia; prenatal depression; postpartum depression

## Introduction

Women of reproductive age are at high risk of depression, and this vulnerability peaks during prenatal and postpartum period.[1] Approximately 8–12% of women experience at least one depressive episode during pregnancy, with a similar prevalence of about 10–12% during the first postpartum year.[1] Depression during pregnancy has been associated with adverse perinatal outcomes,[2] and is a strong predictor for postpartum depression, which can impair maternal-infant bonding, child development, marital relationship and women's long-term health.[3]

Another common pregnancy complication is gestational diabetes mellitus (GDM), which occurs in 5–10% of all pregnancies in the U.S.[4, 5] While increased insulin resistance occurs during normal pregnancy due to placental hormones, the inability to maintain glucose homeostasis poses a risk for adverse obstetric and infant outcomes.[6, 7] Through inflammatory pathways and dysregulation of the hypothalamus-pituitary-adrenal axis, hyperglycemia during pregnancy may also increase the risk of prenatal depression.[8, 9] It is also likely that concomitant behavioral and co-morbid correlates of GDM, such as obesity, physical inactivity and poor diet,[5] are involved in the pathogenesis of depression. These changes could result in altered physiology that extends to the postpartum period.

Despite consistent prior findings of a bidirectional link between depression and type 2 diabetes in the general population,[10] the association between GDM and prenatal or postpartum depression is less clear, with null or positive findings reported from a limited number of studies.[11–15] Recent studies have reported a continuous increase in risk of certain adverse pregnancy outcomes over the range of elevated glucose levels not meeting the diagnostic criteria for GDM.[6, 7] Yet, evidence is still lacking between measured glucose levels as indicators of pregnancy hyperglycemia and perinatal depression among women with or without GDM. In addition, emerging evidence suggests that pregnancy hyperglycemia is a heterogeneous disorder, with moderate/mild hyperglycemia showing different metabolic states, predictors and risk profiles compared to GDM.[6, 7, 16, 17] However, no study to date has considered subclinical hyperglycemia separately in the evaluation of the associations with perinatal depression. Furthermore, it is unclear from existing studies whether the onset of perinatal depression could be attributed to the proposed pathophysiology linking pregnancy hyperglycemia and depression or the psychological impact of GDM diagnosis.

Therefore, we addressed the current gaps in the literature by: (1) assessing continuous blood glucose levels from a 1-hour, 50-gram non-fasting glucose challenge test at mid-pregnancy; (2) evaluating both clinical and subclinical pregnancy hyperglycemia, including categories of impaired glucose tolerance and isolated hyperglycemia. We hypothesized that

hyperglycemia during pregnancy was associated with elevated depressive symptoms during both prenatal and postpartum periods.

## Methods

### Study population

Between 1999 and 2002, women were recruited to participate in Project Viva during their first prenatal visit to Harvard Vanguard Medical Associates, a multi-specialty group practice with eight urban and suburban obstetric offices in eastern Massachusetts. Women were eligible if they were ≤ 22 gestational weeks at enrollment, able to complete questionnaires and interviews in English and had a singleton pregnancy. All participating women provided written informed consent, and the institutional review board at Harvard Pilgrim Health Care approved the study.[18]

Among 2,128 eligible women enrolled, we excluded from this analysis 16 women with preexisting type 1 or type 2 diabetes, leaving 2,112 women for the analysis of prenatal depressive symptoms. Of these, 1,686 women completed 6-month postpartum follow-up questionnaires, and were included for the analysis of postpartum depressive symptoms.

### Measurement of pregnancy hyperglycemia

Women completed a 1-hour, 50-gram non-fasting glucose challenge test (GCT) at median 28.1 weeks of gestation. If a woman's blood glucose level from her GCT was >140 mg/dL, then a 3-hour, 100-gram fasting oral glucose tolerance test (OGTT) was conducted. We defined abnormal results on the OGTT as >95 mg/dL at baseline, >180 mg/dL at 1 hour, >155 mg/dL at 2 hour, and >140 mg/dL at 3 hour, according to American Diabetes Association (ADA) criteria.[19]

For this analysis, our two primary exposures were (1) pregnancy hyperglycemia assessed using the 1-h GCT blood glucose levels for all women, and used both as a continuous measure and in categories; and (2) categories of pregnancy hyperglycemia status defined using results from both the GCT and OGTT as follows:

1. Normal glucose tolerance (NGT) — if a woman had glucose levels ≤ 140 mg/dL for the GCT;
2. Isolated hyperglycemia (IHG) — if a woman had a blood glucose level >140 mg/dL for the GCT followed by normal OGTT for all four measures as described above;
3. Impaired glucose tolerance (IGT) — if a woman had a blood glucose level >140 mg/dL for the GCT followed by an OGTT with one abnormal result as described above;
4. GDM — if a woman had a blood glucose level >140 mg/dL for the GCT followed by an OGTT with ≥ 2 abnormal results as described above.

### Measurement of depressive symptoms

Women completed the 10-item Edinburgh Postnatal Depression Scale (EPDS) during mid-pregnancy (median 27.9 weeks gestation) close to the GDM screening and again at 6 months after delivery (median 6.5 months postpartum). Each item includes 4 response options (scored 0–3), and the EPDS score overall is scaled from 0 to 30, with higher scores indicating higher levels of depressive symptoms. A cutoff score of ≥ 13 has been shown to have a sensitivity of 86% and a specificity of 78% for depression identified by clinical diagnostic interviews.[20] Since the EPDS is a validated screening tool for probable depression during the prenatal and postpartum periods, but does not necessarily correspond to a clinical diagnosis of depression, we defined a prenatal or postpartum EPDS score ≥ 13 as an indicator of prenatal or postpartum depressive symptoms, consistent with previous studies.[21, 22]

### Covariate assessment

During early pregnancy, women reported age, race/ethnicity, education, nativity, parity, marital status, household income, history of depression prior to pregnancy, smoking and physical activity via in-person interviews or self-administered questionnaires. Pre-pregnancy body mass index (BMI) was calculated as self-reported pre-pregnancy weight (kilograms) divided by height (meter squared). Women completed self-administered semi-quantitative food frequency questionnaires separately during the first and the second trimesters. Of *a priori* interest, we considered intakes of total energy, total fat, sugar-sweetened beverage, and fast food during these two periods as well as changes in these dietary factors between the first two trimesters, which may be related to both women's mood and glucose levels.

### Statistical analysis

We summarized the characteristics of the study population by prenatal or postpartum depressive symptoms, using means and standard deviations (SDs) for continuous variables and percentages for categorical variables. We used multivariable logistic regression to examine the association between pregnancy hyperglycemia and prenatal or postpartum depressive symptoms. We estimated the odds ratios (ORs) and 95% confidence intervals (95% CIs) separately for 3 indicators of hyperglycemia: (1) continuous glucose levels assessed as per SD change from the GCT; (2) 5-category glucose levels with cutoffs considering both the diagnostic threshold and the data distribution based on the GCT (55–90, 91–100, 101–120, 121–140 and 141–230 mg/dL); (3) categorized pregnancy glycemic status (i.e. NGT, IHG, IGT and GDM). We first fit age-adjusted (continuous) model (Model 1). Next, in multivariable analysis, we included covariates in the model if they were significant predictors ($p<0.05$) of either prenatal or postpartum depressive symptoms or their inclusions changed the effect estimates by >10%. We then adjusted for parity (continuous), pre-pregnancy BMI (<18.5, 18.5–24.9, 25.0–29.9, ≥30 kg/m$^2$), pre-pregnancy physical activity (hours/week, continuous), and several sociodemographic factors (Model 2), including race/ethnicity (white, black, Asian, Hispanic, other), education (high school or less, some college, college graduates, graduate degree), nativity (born in US or not), marital status (married/cohabiting, single/divorced/other) and household income (≤$40,000, $40,001-$70,000, >$70,000).

For the analysis of prenatal depressive symptoms, we further evaluated several dietary factors during pregnancy to explore potential involvement of poor diet quality during pregnancy in the association between hyperglycemia and depression, including second trimester total fat intake (quintiles), second trimester fast food intake (<1, 1, >1 servings/week) and changes in total energy intake between the first two semesters (≥500 calories reduction, 0–499 reduction, 1–500 increase, >500 increase).

Given the potentially recursive nature of the association between depression and diabetes, we stratified by history of depression in analyses, using continuous glucose levels as the exposure, to evaluate the potential difference between incident and recurrent depressive symptoms. We stratified by history of pre-pregnancy depression for prenatal analysis, and by history of depression that combined both pre-pregnancy depression and prenatal depressive symptoms for postpartum analysis. To evaluate the potential psychological impact of GDM screening on depressive symptoms, we also repeated the analyses excluding women who had prenatal depression assessment after GDM screening. We also adjusted for week gestation at GDM screening in the analysis to assess the possible influence of timing of GDM diagnosis on the estimates.

Multiple imputation (MI) was applied to impute missing data using 'chained equations' method.[23] Fifty imputed datasets were generated using exposure, outcome and covariate information from all participants. We performed sensitivity analyses restricted to women with complete information to test the robustness of the MI results. All analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC).

## Results

More than 90% of women completed GDM screening between 25 and 30 weeks' gestation. About 94% of women answered the questionnaire for prenatal depression either before or on the same day of GDM screening; these women did not likely know their GDM screening result at depression assessment. The rest of the women completed the depression assessment within the same week of their GDM screening.

Among the 2,112 women eligible for prenatal analysis, 9.6% showed prenatal depressive symptoms during mid-pregnancy. Compared with their non-depressed counterparts, women with prenatal depressive symptoms were more likely to have a higher GCT glucose level (mean: 120 versus 114 mg/dL) and an abnormal gestational glucose tolerance (25% versus 17%). Women with depressive symptoms were also more likely to be younger, non-white, born outside the US, have lower education and household income and higher pre-pregnancy BMI and less likely to be married or be partnered. Among 1,686 women with depression assessment at 6 months after delivery, 8.4% showed postpartum depressive symptoms. Among women with postpartum depressive symptoms, 35.3% also had prenatal depressive symptoms; only 7.3% had prenatal depressive symptoms among women without postpartum depressive symptoms. The population characteristics by postpartum depression were similar to those by prenatal depression, except that the difference in gestational glucose tolerance was less remarkable (Table 1).

### Pregnancy hyperglycemia and prenatal depressive symptoms

Compared with women with GCT glucose levels of 55–90 mg/dL, age-adjusted ORs (95% CIs) of having prenatal depressive symptoms were 1.29 (0.71, 2.35) for glucose levels of 91–100, 1.25 (0.73, 2.15) for 101–120, 1.74 (0.99, 3.06) for 121–140 and 2.41 (1.39, 4.18) for 141–230 mg/dL (p for trend=0.0005; Table 2). The multivariable-adjusted ORs were somewhat attenuated, particularly after controlling for sociodemographic and dietary factors (OR comparing glucose levels of 141–230 with 55–90 mg/dL: 2.17; 95%: 1.21, 3.88; p for trend=0.0066; Table 2). When the glucose level was used as a continuous variable, the per SD increase in the glucose level (SD=27 mg/dL) was associated with a 25% higher odds of prenatal depressive symptoms (OR: 1.25; 95% CI: 1.07, 1.48). Additional adjustment of dietary factors during pregnancy slightly attenuated the associations (OR for every SD increase in the glucose level: 1.23, 95% CI: 1.04, 1.46; data not shown). In examination of the association with pregnancy hyperglycemia categories, women with IHG had significantly higher odds of prenatal depressive symptoms (multivariable-adjusted OR: 1.80; 95% CI: 1.08, 3.00) compared to NGT women. The odds also appeared to be elevated among women with IGT (OR: 1.43; 95% CI: 0.59, 3.46) or GDM (OR: 1.45; 95% CI: 0.72, 2.91), but neither of the associations reached statistical significance.

### Pregnancy hyperglycemia and postpartum depressive symptoms

Pregnancy hyperglycemia was not associated with substantially or significantly higher odds of postpartum depressive symptoms. Women with higher glucose levels at mid-pregnancy were not at increased odds of postpartum depressive symptoms (OR comparing glucose levels of 141–230 with 55–90 mg/dL: 1.22; 95%: 0.63, 2.36; p for trend=0.34; Table 3). Compared with women with NGT, the multivariable-adjusted ORs (95% CIs) of developing postpartum depressive symptoms were 0.78 (0.36, 1.68) for IHG, 1.26 (0.45, 3.53) for IGT and 1.36 (0.64, 2.88) for GDM.

### Pregnancy hyperglycemia and perinatal depressive symptoms by subgroups

The association between pregnancy hyperglycemia and prenatal depressive symptoms did not differ substantially by history of depression (for every SD increase in the glucose level, OR among women without history of depression before pregnancy: 1.28; 95% CI: 1.02, 1.60; OR among women with pre-pregnancy depression history: 1.22; 95% CI: 0.90, 1.66). The associations for postpartum depressive symptoms were also similar within strata of depression history. The results were essentially unchanged after we excluded 135 women with GDM screening followed by prenatal depression assessment (OR for every SD increase in the glucose level: 1.25, 95% CI: 1.03, 1.50). Further adjustment for week gestation at GDM screening did not alter the results. The sensitivity analyses limited to women with complete data yielded similar results (data not shown).

## Comments

In this longitudinal cohort study, we found more than a 2-fold higher odds of prenatal depressive symptoms among pregnant women with GCT results over 140 mg/dL compared to those with a glucose level between 55–90 mg/dL. The greater risk was observed among women with GDM as well as subclinical pregnancy hyperglycemia (i.e., IHG and IGT), and

was most significant among women with IHG. In contrast, neither the GCT glucose level nor the results of 2-stage glycemic screening at mid-pregnancy was significantly associated with postpartum depressive symptoms at 6 months after delivery.

Previous studies examining the association between glucose dysregulation and prenatal depressive symptoms did not provide consistent evidence, with null or positive associations reported.[11–15] A number of factors could potentially account for the conflicting results, such as differences in the study population, timing of assessment, depression definition, and covariate adjustment. Compared to the current study, the most important difference lies in that prior studies have predominantly compared GDM with non-GDM women, which combined women with moderate/mild hyperglycemia with normoglycemic women. Our study was the first to examine the association of clinically-defined pregnancy hyperglycemia (i.e. GDM) and subclinical pregnancy hyperglycemia with perinatal depressive symptoms. We observed a positive association between pregnancy hyperglycemia and prenatal depressive symptoms, and found the most significant elevation in risk among women with IHG.

Consistent with the growing evidence relating adverse health outcomes with intermediate metabolic states between GDM and NGT, [6, 7, 16, 17] our findings suggest that any abnormal glucose homeostasis during pregnancy may pose some elevated risk of prenatal depressive symptoms. Several biological pathways have been suggested in support of this association. First, glucose dysregulation could affect the hypothalamus-pituitary-adrenal axis and lead to elevated cortisol levels,[24] which are involved in depression.[25] Second, women with GDM may have impaired thyroid function,[26] and reduced thyroid hormones are associated with increased depressive symptoms.[27] It is possible that subclinical hyperglycemia in pregnancy may also depress thyroid hormone levels and increase depressive symptoms. Third, hyperglycemia may increase the risk of depression by promoting inflammatory processes.[8] Although the observed association may be partly attributed to maternal sociodemographic and behavioral factors associated with both pregnancy hyperglycemia and prenatal depression, adjustment of these factors only modestly attenuated the associations. While diagnosis and management of pregnancy hyperglycemia could cause psychological distress and induce depressive symptoms,[28] this is unlikely to explain the observed association in this study, as most women had their prenatal depressive symptoms assessed when the GDM screening results were unknown. The exclusion of women who had prenatal depression assessment after GDM screening also resulted in similar positive associations. Furthermore, women without an official GDM diagnosis (i.e., IHG) also showed significantly increased risk of prenatal depressive symptoms.

It is unclear why the risk estimates were somewhat higher for women with IHG compared to women with IGT or GDM, since the IHG group likely represented those with the mildest form of glucose abnormality. This could be a result of more accurate estimate in the IHG group, as there were more women with IHG than women with IGT or GDM. Also, the bidirectional nature of the association between glucose dysregulation and depression may provide a plausible explanation. For example, women with depressive symptoms may tend to consume a larger amount of food with greater frequency. If true, these women may have

been more likely to have eaten a large quantity of food with a higher glycemic load prior to the GCT, which could lead to being identified as having IHG on the non-fasting GCT.

Contrary to our hypothesis, we did not note an association of pregnancy hyperglycemia with postpartum depressive symptoms. This is different from one prior study, which reported 69% increased odds of incident postpartum depression among women with GDM or preexisting diabetes.[11] Given that GDM or pregnancy hyperglycemia in most women would spontaneously remit after delivery, our data suggest that pregnancy hyperglycemia may not have a prolonged effect on postpartum depression. While prenatal depression is strongly correlated with postpartum depression, women may develop postpartum depression independent of any depressive symptoms before or during pregnancy.[29] In our study, 44% of women with postpartum depressive symptoms had no previous history of depression, the onset of which may have greater relevance to emerging factors post-pregnancy, such as newly diagnosed postpartum hyperglycemia. Therefore, future studies may need to focus on sustained postpartum glucose dysregulation after pregnancy hyperglycemia and newly diagnosed postpartum hyperglycemia to explore their associations with postpartum depression.

The study has several limitations. Although we attempted to focus on incident pregnancy hyperglycemia (including GDM) and incident prenatal depressive symptoms,[30] it is difficult to establish the temporality for these two dynamic conditions that we assessed almost concurrently within a short period. Therefore, the association between pregnancy hyperglycemia and prenatal depressive symptoms was essentially cross-sectional, and could be explained by either direction of the association, or both. In addition, the number of IGT or GDM women was relatively small, and may limit our power to detect a modest association. Our definition of prenatal and postpartum depression using EPDS may introduce misclassification, in contrast to using clinical diagnosis or treatment. However, given that perinatal depression is generally under-diagnosed and under-treated,[31] EPDS may be a more consistent measure to identify women with depressive symptoms. Furthermore, although the data were collected approximately 15 years ago, our cohort appeared comparable to more recent ones, given the distribution of age, BMI and other sociodemographic factors.

Another potential limitation of this study is that we used the non-fasting GCT to categorize women with pregnancy hyperglycemia. Given that the glycemic response to GCT may be potentially complicated by several factors, including fasting status and diet choices prior to GCT,[32] our findings should be interpreted with caution and replicated in future studies However, a previous study found fasting GCT and 1-h postprandial GCT to be similar in pregnant women with diabetes.[33] Thus, regardless of prior meal intake, an abnormally high GCT (i.e., ≥140 mg/dL) should reliably reflect a woman's hyperglycemia status. Also, the non-fasting GCT is a clinically-relevant tool used to diagnose GDM, with more than 90% of women in the present study undergoing the GCT near the end of the second trimester. Further, other studies have suggested that false-positive GCT (i.e., IHG) may independently predict postpartum metabolic dysfunction as well as several adverse perinatal outcomes.[34, 35]

In conclusion, our study provides evidence that pregnancy hyperglycemia is associated with prenatal, but not postpartum depressive symptoms. Our results lend support to the pathophysiology linking hyperglycemia to depressive symptoms during pregnancy that warrants further investigations. If confirmed by future research, these findings could assist in identifying a high-risk group for interventions to prevent prenatal depression, with implications for improving pregnancy outcomes.

## Acknowledgments

This research was funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (K12HD051959, R01HD034568, K24HD069408) and the National Institutes of Health (P30DK092924).

## References

1. 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; 106:1071–1083. [PubMed: 16260528]
2. 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; 67:1012–1024. [PubMed: 20921117]
3. O'Hara MW, McCabe JE. Postpartum depression: current status and future directions. Annu Rev Clin Psychol. 2013; 9:379–407. [PubMed: 23394227]
4. Lawrence JM, Contreras R, Chen W, Sacks DA. Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999–2005. Diabetes Care. 2008; 31:899–904. [PubMed: 18223030]
5. Ben-Haroush A, Yogev Y, Hod M. Epidemiology of gestational diabetes mellitus and its association with Type 2 diabetes. Diabet Med. 2004; 21:103–113. [PubMed: 14984444]
6. Carr DB, Newton KM, Utzschneider KM, Tong J, Gerchman F, Kahn SE, et al. Modestly elevated glucose levels during pregnancy are associated with a higher risk of future diabetes among women without gestational diabetes mellitus. Diabetes Care. 2008; 31:1037–1039. [PubMed: 18223032]
7. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008; 358:1991–2002. [PubMed: 18463375]
8. Osborne LM, Monk C. Perinatal depression--the fourth inflammatory morbidity of pregnancy?: Theory and literature review. Psychoneuroendocrinology. 2013; 38:1929–1952. [PubMed: 23608136]
9. Kammerer M, Taylor A, Glover V. The HPA axis and perinatal depression: a hypothesis. Arch Womens Ment Health. 2006; 9:187–196. [PubMed: 16708167]
10. Mezuk B, Eaton WW, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: a meta-analysis. Diabetes Care. 2008; 31:2383–2390. [PubMed: 19033418]
11. Kozhimannil KB, Pereira MA, Harlow BL. Association between diabetes and perinatal depression among low-income mothers. JAMA. 2009; 301:842–847. [PubMed: 19244191]
12. Ertel KA, Silveira M, Pekow P, Braun B, Manson JE, Solomon CG, et al. Prenatal depressive symptoms and abnormalities of glucose tolerance during pregnancy among Hispanic women. Arch Womens Ment Health. 2014; 17:65–72. [PubMed: 24057869]
13. Katon JG, Russo J, Gavin AR, Melville JL, Katon WJ. Diabetes and depression in pregnancy: is there an association? J Womens Health (Larchmt). 2011; 20:983–989. [PubMed: 21668382]
14. Kim C, Brawarsky P, Jackson RA, Fuentes-Afflick E, Haas JS. Changes in health status experienced by women with gestational diabetes and pregnancy-induced hypertensive disorders. J Womens Health (Larchmt). 2005; 14:729–736. [PubMed: 16232105]
15. Langer N, Langer O. Comparison of pregnancy mood profiles in gestational diabetes and preexisting diabetes. Diabetes Educ. 2000; 26:667–672. [PubMed: 11140075]

16. Hillier TA, Pedula KL, Schmidt MM, Mullen JA, Charles MA, Pettitt DJ. Childhood obesity and metabolic imprinting: the ongoing effects of maternal hyperglycemia. Diabetes Care. 2007; 30:2287–2292. [PubMed: 17519427]
17. Stuebe AM, Mantzoros C, Kleinman K, Gillman MW, Rifas-Shiman S, Seely EW, et al. Gestational glucose tolerance and maternal metabolic profile at 3 years postpartum. Obstet Gynecol. 2011; 118:1065–1073. [PubMed: 22015874]
18. Oken E, Baccarelli AA, Gold DR, Kleinman KP, Litonjua AA, De Meo D, et al. Cohort Profile: Project Viva. Int J Epidemiol. 2014
19. Standards of medical care in diabetes--2008. Diabetes Care. 2008; 31 (Suppl 1):S12–54. [PubMed: 18165335]
20. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987; 150:782–786. [PubMed: 3651732]
21. Rich-Edwards JW, Kleinman K, Abrams A, Harlow BL, McLaughlin TJ, Joffe H, et al. Sociodemographic predictors of antenatal and postpartum depressive symptoms among women in a medical group practice. J Epidemiol Community Health. 2006; 60:221–227. [PubMed: 16476752]
22. Rich-Edwards JW, Mohllajee AP, Kleinman K, Hacker MR, Majzoub J, Wright RJ, et al. Elevated midpregnancy corticotropin-releasing hormone is associated with prenatal, but not postpartum, maternal depression. J Clin Endocrinol Metab. 2008; 93:1946–1951. [PubMed: 18303075]
23. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. Stat Med. 2011; 30:377–399. [PubMed: 21225900]
24. Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE. Depression and poor glycemic control: a meta-analytic review of the literature. Diabetes Care. 2000; 23:934–942. [PubMed: 10895843]
25. Belmaker RH, Agam G. Major depressive disorder. N Engl J Med. 2008; 358:55–68. [PubMed: 18172175]
26. Olivieri A, Valensise H, Magnani F, Medda E, De Angelis S, D'Archivio M, et al. High frequency of antithyroid autoantibodies in pregnant women at increased risk of gestational diabetes mellitus. Eur J Endocrinol. 2000; 143:741–747. [PubMed: 11124856]
27. Hage MP, Azar ST. The Link between Thyroid Function and Depression. J Thyroid Res. 2012; 2012:590648. [PubMed: 22220285]
28. Seguin L, Potvin L, St-Denis M, Loiselle J. Chronic stressors, social support, and depression during pregnancy. Obstet Gynecol. 1995; 85:583–589. [PubMed: 7898838]
29. Wisner KL, Sit DK, McShea MC, Rizzo DM, Zoretich RA, Hughes CL, et al. Onset timing, thoughts of self-harm, and diagnoses in postpartum women with screen-positive depression findings. JAMA Psychiatry. 2013; 70:490–498. [PubMed: 23487258]
30. Rasmussen-Torvik LJ, Harlow BL. The association between depression and diabetes in the perinatal period. Curr Diab Rep. 2010; 10:217–223. [PubMed: 20425585]
31. Vesga-Lopez O, Blanco C, Keyes K, Olfson M, Grant BF, Hasin DS. Psychiatric disorders in pregnant and postpartum women in the United States. Arch Gen Psychiatry. 2008; 65:805–815. [PubMed: 18606953]
32. Sermer M, Naylor CD, Gare DJ, Kenshole AB, Ritchie JW, Farine D, et al. Impact of time since last meal on the gestational glucose challenge test. The Toronto Tri-Hospital Gestational Diabetes Project. Am J Obstet Gynecol. 1994; 171:607–616. [PubMed: 8092205]
33. Lewis GF, McNally C, Blackman JD, Polonsky KS, Barron WM. Prior feeding alters the response to the 50-g glucose challenge test in pregnancy. The Staub-Traugott effect revisited. Diabetes Care. 1993; 16:1551–1556. [PubMed: 8299450]
34. Retnakaran R, Qi Y, Sermer M, Connelly PW, Hanley AJ, Zinman B. An abnormal screening glucose challenge test in pregnancy predicts postpartum metabolic dysfunction, even when the antepartum oral glucose tolerance test is normal. Clin Endocrinol (Oxf). 2009; 71:208–214. [PubMed: 19178531]
35. Stamilio DM, Olsen T, Ratcliffe S, Sehdev HM, Macones GA. False-positive 1-hour glucose challenge test and adverse perinatal outcomes. Obstet Gynecol. 2004; 103:148–156. [PubMed: 14704259]

## Table 1

Population characteristics by prenatal or postpartum depression status

| | Prenatal depression | | Postpartum depression | |
|---|---|---|---|---|
| | Yes (n=203, 9.6%) | No (n=1909, 90.4%) | Yes (n=141, 8.4%) | No (n=1545, |
| | Mean (SD) | | | |
| Age at enrollment (yrs) | 30.1 (6.5) | 32.0 (5.1) | 31.0 (5.7) | 32.4 (4.9) |
| GCT glucose (mg/dL) | 120 (32) | 114 (27) | 116 (27) | 114 (27) |
| Pre-pregnancy BMI (kg/m$^2$) | 25.5 (6.6) | 24.8 (5.5) | 26.5 (6.8) | 24.6 (5.1) |
| Physical activity (hours/week) | 11.3 (12.1) | 9.8 (9.1) | 9.5 (8.1) | 9.7 (7.5) |
| Change in caloric intake (kcal)[1] | 117 (814) | 80 (651) | -- | -- |
| Total fat intake (g/day)[2] | 66.5 (13.7) | 65.6 (13.6) | -- | -- |
| Fast food intake (servings/week)[2] | 1.1 (1.2) | 0.9 (0.9) | -- | -- |
| | Percent | | | |
| Glucose homeostasis | | | | |
| Normal glucose tolerance | 76 | 83 | 82 | 83 |
| Isolated hyperglycemia | 13 | 8 | 7 | 8 |
| Impaired glucose tolerance | 4 | 3 | 4 | 3 |
| Gestational diabetes | 8 | 6 | 7 | 5 |
| Age categories | | | | |
| < 20 years | 6 | 3 | 6 | 2 |
| 20–<25 years | 14 | 6 | 12 | 5 |
| 25–<30 years | 21 | 22 | 16 | 20 |
| 30–<35 years | 38 | 42 | 43 | 43 |
| 35–<40 years | 18 | 24 | 21 | 25 |
| ≥40 years | 2 | 4 | 3 | 5 |
| Pre-pregnancy BMI categories | | | | |
| Underweight (<18.5 kg/m$^2$) | 6 | 4 | 5 | 3 |
| Normal (18.5–<25 kg/m$^2$) | 50 | 60 | 50 | 61 |
| Overweight (25–<30 kg/m$^2$) | 26 | 21 | 20 | 22 |
| Obese (≥30 kg/m$^2$) | 19 | 15 | 25 | 14 |
| Race/Ethnicity | | | | |
| White | 50 | 68 | 57 | 72 |
| Black | 24 | 16 | 19 | 13 |
| Hispanic | 14 | 7 | 12 | 6 |
| Asian | 7 | 6 | 4 | 5 |
| Other | 6 | 4 | 7 | 3 |
| Education | | | | |
| High school or less | 22 | 11 | 16 | 8 |
| Some college | 27 | 23 | 27 | 21 |
| College graduate | 27 | 36 | 29 | 39 |
| Graduate degree | 23 | 30 | 28 | 32 |

| | Prenatal depression | | Postpartum depression | |
|---|---|---|---|---|
| | Yes (n=203, 9.6%) | No (n=1909, 90.4%) | Yes (n=141, 8.4%) | No (n=1545, |
| Born in US | 73 | 80 | 83 | 81 |
| Prenatal parity | | | | |
| Nulliparous | 46 | 48 | 50 | 48 |
| 1 child | 36 | 36 | 32 | 36 |
| 2 children | 12 | 12 | 14 | 12 |
| 3 children or more | 6 | 4 | 5 | 4 |
| Married or cohabiting | 78 | 93 | 85 | 94 |
| Annual household income | | | | |
| $5,001–40,000 | 37 | 17 | 31 | 14 |
| $40,001–70,000 | 24 | 23 | 25 | 22 |
| >$70,000 | 39 | 60 | 44 | 65 |
| History of depression[3] | 45 | 16 | 56 | 21 |

[1] Total caloric intake in the second trimester compared to the first trimester

[2] Dietary intakes during the second trimester

[3] Count prenatal depression as history of depression for postpartum depression

**Table 2**

Odds ratios and 95% confidence intervals for the association between hyperglycemia during pregnancy and prenatal depression

| Glucose assessment | % with depressive symptoms / number of women | Model 1[1] | Model 2[2] |
|---|---|---|---|
| Continuous[4] | | | |
| Per SD changes (SD=27 mg/dL) | 9.6 / 2112 | 1.31 (1.12, 1.52) | 1.25 (1.07, 1.48) |
| Glucose categories (mg/dL)[3] | | | |
| 55–90 | 7.4 / 385 | 1.00 (Reference) | 1.00 (Reference) |
| 91–100 | 9.1 / 316 | 1.29 (0.71, 2.35) | 1.30 (0.70, 2.41) |
| 101–120 | 8.4 / 649 | 1.25 (0.73, 2.15) | 1.21 (0.69, 2.12) |
| 121–140 | 10.8 / 388 | 1.74 (0.99, 3.06) | 1.68 (0.93, 3.02) |
| 141–230 | 13.5 / 374 | 2.41 (1.39, 4.18) | 2.17 (1.21, 3.88) |
| p for trend[4] | | 0.0005 | 0.0066 |
| GDM status | | | |
| Normal | 8.8 / 1738 | 1.00 (Reference) | 1.00 (Reference) |
| IHG | 14.4 / 179 | 2.02 (1.25, 3.29) | 1.86 (1.12, 3.09) |
| IGT | 11.5 / 65 | 1.45 (0.61, 3.45) | 1.44 (0.60, 3.46) |
| GDM | 12.7 /130 | 1.69 (0.88, 3.23) | 1.47 (0.74, 2.93) |

[1] Adjusted for age

[2] Model 1 plus race/ethnicity, education, nativity, parity, marital status, household income, pre-pregnancy BMI and pre-pregnancy physical activity

[3] Based on glucose levels from glucose challenge test

[4] p for trend was calculated using continuous glucose levels as a linear term

*Paediatr Perinat Epidemiol*. Author manuscript; available in PMC 2016 July 01.

**Table 3**

Odds ratios and 95% confidence intervals for the association between hyperglycemia during pregnancy and postpartum depression

| Glucose assessment | % of depressive women / number of women | Model 1[1] | Model 2[2] |
|---|---|---|---|
| Continuous[3] | | | |
| Per SD changes | 8.3 / 1686 | 1.14 (0.96, 1.37) | 1.10 (0.91, 1.33) |
| Glucose categories (mg/dL)[3] | | | |
| 55–90 | 7.6 / 312 | 1.00 (Reference) | 1.00 (Reference) |
| 91–100 | 7.7 / 254 | 1.01 (0.52, 1.98) | 1.00 (0.50, 1.98) |
| 101–120 | 7.1 / 523 | 0.96 (0.54, 1.68) | 0.91 (0.51, 1.62) |
| 121–140 | 11.0 / 309 | 1.63 (0.92, 2.90) | 1.50 (0.83, 2.73) |
| 141–230 | 9.2 / 288 | 1.38 (0.74, 2.57) | 1.22 (0.63, 2.36) |
| p for trend[4] | | 0.14 | 0.34 |
| GDM status | | | |
| Normal | 8.3 / 1398 | 1.00 (Reference) | 1.00 (Reference) |
| IHG | 7.1 / 133 | 0.91 (0.44, 1.91) | 0.78 (0.36, 1.68) |
| IGT | 9.7 / 52 | 1.25 (0.46, 3.40) | 1.26 (0.45, 3.53) |
| GDM | 11.0 / 103 | 1.45 (0.71, 2.99) | 1.36 (0.64, 2.88) |

[1] Adjusted for age

[2] Model 1 plus race/ethnicity, education, nativity, parity, marital status, household income, pre-pregnancy BMI and pre-pregnancy physical activity

[3] Based on glucose levels from glucose challenge test

[4] p for trend was calculated using continuous glucose levels as a linear term

*Paediatr Perinat Epidemiol*. Author manuscript; available in PMC 2016 July 01.