OPEN

Association of Diabetes Mellitus in Pregnancy and Perinatal Depression

Richelle D. Björvang, MD, PhD, Iliana Liakea, MSc, Beatrice Carpentsier, MSc, Zoltan Kozinszky, MD, PhD, Alkistis Skalkidou, MD, PhD, and Emma Fransson, PhD

ABSTRACT

Objective: Diabetes is frequently linked with depression, and both conditions are common complications during pregnancy. However, research findings exploring the relationship between diabetes mellitus in pregnancy (DMP) and perinatal depression (PND) have been inconsistent. Thus, this study seeks to examine the association between DMP and PND in a prospective population-based cohort.

Methods: Women aged 18 to 48 years (n = 4459) were identified from the Biology, Affect, Stress, Imaging and Cognition study. The diagnosis of DMP was based on *International Classification of Diseases* code O24 from medical records and was classified as pregestational, gestational, or unspecified diabetes. PND was assessed using psychometric instruments, clinical interviews, and/or register data and categorized into antepartum or postpartum depression. Multivariable logistic regressions were used to study the associations of DMP with antepartum and postpartum depression. The association between DMP and continuous depression scores, antepartum and postpartum, was investigated with multivariable linear regressions.

Results: Of 4459 pregnancies, 949 women had antepartum depression (21.2%) and 1123 had postpartum depression (25%). DMP had a prevalence of 1.2%. Women with DMP had twofold higher odds for postpartum depression compared with women without DMP. Although no association was observed between DMP and antepartum depression, DMP was associated with higher antepartum depression scores.

Conclusions: Our study shows an association between DMP and PND, which might be considered a risk factor when screening for high-risk groups.

Key words: diabetes mellitus in pregnancy, gestational diabetes, pregestational diabetes, perinatal depression, antepartum depression, postpartum depression.

INTRODUCTION

Both diabetes and depression during the perinatal period represent significant maternal health issues, carrying substantial implications for the short- and long-term health of the mother, offspring, partners, and society as a whole (1,2). While investigations have been undertaken to explore potential shared psychophysiological mechanisms underlying these conditions, particularly outside the perinatal context (3), the body of research on these conditions during the perinatal period is comparatively limited and encumbered by several methodological limitations.

Perinatal depression (PND) is a serious psychological condition during pregnancy and in the first year after delivery that may present as loss of interest in activities, irritability, loss of energy, diminished concentration, feelings of worthlessness, and thoughts of suicide (4). This condition can be experienced by both biological and nonbiological parents. It has negative impacts on all family members, making it a major global health issue with significant societal burden. Globally, the prevalence of depression during pregnancy (antepartum depression) among women ranged from 15% to 65% (5) and depression during postpartum (postpartum depression) among women from 6% to 61% (6).

BASIC = Biology, Affect, Stress, Imaging and Cognition, **BMI** = body mass index, **CI** = confidence interval, **DMP** = diabetes mellitus in pregnancy, **EPDS** = Edinburgh Postnatal Depression Scale, **ICD** = International Classification of Diseases, **OR** = odds ratio, **PND** = perinatal depression, **RR** = relative risk

Diabetes mellitus in pregnancy (DMP) is the most common metabolic disorder in the perinatal period (7). Women with DMP could either have pregestational diabetes mellitus including type 1 and type 2 diabetes mellitus or have gestational diabetes mellitus.

SDC Supplemental Digital Content

From the Department of Women's and Children's Health (Björvang, Carpentsier, Skalkidou, Fransson), Uppsala University, Uppsala; Department of Clinical Science, Intervention and Technology (Björvang), Karolinska Institute, Stockholm, Sweden; Behavioural Science Institute (Liakea), Radboud University, Nijmegen, the Netherlands; Department of Public Health and Caring Sciences (Carpentsier), Uppsala University, Uppsala; Department of Obstetrics and Gynaecology (Kozinszky), Danderyd Hospital; and Department of Microbiology, Tumor and Cell Biology (Fransson), Karolinska Institute, Stockholm, Sweden.

Address correspondence to Iliana Liakea, MSc, Behavioural Science Institute, Radboud University, 6525 GD Nijmegen, the Netherlands. E-mail: iliana.liakea@ru.nl

R.D.B. and I.L. shared the first-authorship.

Received for publication July 20, 2023; revision received October 25, 2023.

DOI: 10.1097/PSY.0000000000001261

According to data from the International Diabetes Federation, approximately 16.7% of live births globally are impacted by DMP because the mother is afflicted with this condition (8). In Sweden, particularly in Uppsala county, the prevalence of DMP is 4.4% according to the pregnancy registry report (9). Women with DMP, regardless of type, are at a greater risk of adverse pregnancy outcomes such as high blood pressure and a higher risk of obstructed labor due to a large baby for gestational age. Also, the risk of developing type 2 diabetes mellitus after delivery is increased after gestational diabetes mellitus. Babies born to mothers with DMP have a greater lifetime risk of developing obesity and type 2 diabetes mellitus throughout the life course (8). Furthermore, DMP is characterized by impaired hormonal regulation. The significant and often rapid hormonal fluctuations in the peripartum period might expose some women at risk for depression, according to the "hormone-sensitive" postpartum depression hypothesis (10). PND may also manifest as a result of elevated hyperglycemia, potentially through two distinct routes. The first pathway is associated with increased oxidative stress, inflammation, or leptin resistance induced by hyperglycemia. The second pathway arises from heightened psychological and physical stress stemming from the management and treatment of diabetes (11).

Among the types of DMP and PND, most studies have focused on studying the association between gestational diabetes mellitus and postpartum depression. Systematic reviews and meta-analyses have shown that gestational diabetes is a risk factor for postpartum depression (12–14), although the effect size is small and inconsistent (15). A meta-analysis including 18 studies found that gestational diabetes increases the risk of postpartum depression by 59% (relative risk [RR] = 1.59; 95% confidence interval [CI] = 1.22–2.07) (12). A national register study in Sweden including 707,701 pregnancies found an association between postpartum depression and gestational diabetes (RR = 1.70; 95% CI = 1.36–2.13) but not pregestational diabetes (RR = 1.32; 95% CI = 0.98–1.78) (16). Some studies have even investigated the association between all types of DMP and PND, but the results are contradictory. A systematic review of 48 studies did not find a clear association between DMP and PND (13). A large register study including 888,989 deliveries in Denmark found that any type of diabetes had a 28% (RR = 1.28; 95% CI = 1.02–1.60) higher risk of postpartum depression (17). However, no association was found for subtypes type 1, type 2, and other diabetes. This might partly be due to the differences in the definition of DMP and PND between the studies as well as when they were assessed (18). A systematic review of available studies pointed out significant variations in clinical cutoffs and timing of measuring DMP and PND, making findings inconsistent (18). In particular, it has elucidated inconsistencies in the evaluation of PND. Although certain studies adopted a screening approach using instruments such as the Edinburgh Postnatal Depression Scale (EPDS) (19), others opted for diagnostic methodologies based on medical records (20,21). In some instances, the presence of PND symptoms was inferred based on the prescription of antidepressant medication (19). Moreover, notable variations in the selection of cutoff scores for PND screening were discerned among these investigations. In the context of DMP, some research has relied on retrospective medical records following the *International Classification of Diseases, Ninth and Tenth Editions* (*ICD-9*, *ICD-10*) codes, whereas others have undertaken a prospective examination of DMP (19,20). Moreover, there are still limited studies exploring DMP as a whole, encompassing pregestational diabetes, gestational diabetes, and unspecified diabetes. Similarly, there are also limited studies exploring antepartum depression and postpartum depression separately, in the same cohort.

Therefore, the aim of this study was to investigate the association between DMP and its categories and symptoms of PND, while taking into account possible confounders and addressing antepartum depression and postpartum depression separately. In the context of antepartum and postpartum depression, it is noteworthy that these conditions can manifest independently, with one not necessarily preceding the other. Consequently, it becomes imperative to individually evaluate the relationship between DMP and both antepartum and postpartum depression. This detailed examination is crucial for elucidating the connections between these variables and subsequently for the development of tailored prevention and intervention programs. We hypothesized that DMP would confer an increased risk of both antepartum depression and postpartum depression.

METHODS AND MATERIALS

Study Population and Data Collection

This is a nested study within a large longitudinal population-based prospective cohort, the Biology, Affect, Stress, Imaging and Cognition (BASIC) (22). BASIC was conducted from September 2009 to November 2018 at Uppsala, Sweden, to develop further knowledge about the underlying pathophysiological processes of PND. All women undergoing routine ultrasound at gestational weeks 16 to 18 were invited to participate in the study. Exclusion criteria were as follows: a) pregnant women younger than 18 years, b) protected identity, c) difficulties in reading and understanding Swedish, d) having blood-borne infections; and e) nonviable pregnancy at ultrasound. The participation rate in BASIC was approximately 21% of the pregnant population in the community. Data for the BASIC study were collected during pregnancy at gestational weeks 16 to 18, 32, and 38, as well as postpartum at 6 weeks, 8 weeks, 6 months, and 1 year through questionnaires such as psychometric instruments and interviews. Moreover, lifestyle, medical and sociodemographic information, and information on sleeping habits, and social support were also collected through questions designed by the research team. Furthermore, medical and sociodemographic information was obtained from electronic patient records and national registers. The Swedish Medical Birth Register covers 98% of all births in Sweden (23), whereas the Pregnancy Register has a 90% coverage of all births in Sweden (24). The National Patient Register contains hospital admissions/outpatient care excluding primary care. Because of the rapid changes in hospital organization, it remains challenging to estimate dropout rate in the National Patient Register, especially in areas concerning psychiatric care (25). From the original cohort, women with singleton pregnancies, first participation during the study period, and with complete data on diabetes mellitus and PND were included in this study (n = 4459). This study has been approved by the Uppsala Regional Ethical Committee (Dnr 2009/171) and was carried out according to the Principles of the Declaration of Helsinki. All participants gave their written informed consent.

Perinatal Depression

PND was assessed based on scores on the EPDS (26) (taken weeks 16–18, 32, and 38 during pregnancy, and 6 weeks, 8 weeks, and

6 months postpartum) and Depression Self-Rating Scale (27) (taken at 38 weeks of gestation and 8 weeks postpartum), the Mini International Neuropsychiatric Interview International Neuropsychiatric Interview (28) (taken at 38 weeks of gestation and 8 weeks postpartum), use of selective serotonin reuptake inhibitors, and/or a diagnosis of depression during pregnancy or after childbirth in the national registers. Psychometric properties of self-reported measurements can be found in the Supplemental Digital Content, http://links.lww.com/PSYMED/A978. The cutoff value of EPDS was 13 or higher during pregnancy, and 12 or higher during postpartum (29). For the register data, *ICD-10* F32 and F53 codes were included throughout pregnancy and until a year after delivery. PND was categorized as antepartum depression if there were symptoms of depression (EPDS scores above the cutoff during pregnancy), or a positive Depression Self-Rating Scale or Mini International Neuropsychiatric Interview, or selective serotonin reuptake inhibitor use, or a depression diagnosis in the national registers during pregnancy. The same was applied for the respective instruments/diagnoses during the postpartum period (until 1 year postpartum), classifying then the woman as having postpartum depression. The number of participants considered having antepartum or postpartum depression according to each method was provided in Table S1, Supplemental Digital Content, http://links.lww.com/PSYMED/A978.

Diabetes Mellitus in Pregnancy

Information about DMP was extracted from the electronic patient records and register data. In this study, the *ICD-10* O24 code was used to classify women as having DMP. Specific types were determined as a) pregestational diabetes mellitus, namely, type 1 diabetes mellitus (*ICD-10* O24.0) and type 2 diabetes mellitus (*ICD-10* O24.1); b) gestational diabetes mellitus (*ICD-10* O24.4); or 3) unspecified (*ICD-10* O24, O24.2, O24.3, O24.9).

Statistical Analyses

Descriptive comparisons across groups were tested by the χ^2 test or Wilcoxon rank sum test, where appropriate. Variables with more than 30% missing values and women missing more than 30% of all variables were excluded from further analyses. For the remaining data, missing values were imputed using the multivariate imputation by chained equations algorithm into 10 complete datasets (30). Logistic regression analyses were used to estimate the odds ratios (ORs) and 95% CIs of the association between DMP and antepartum depression as well as between DMP and postpartum depression. Estimates from the 10 imputed datasets were pooled together into a single estimate. Subanalyses of specific types of DMP (pregestational diabetes mellitus, gestational diabetes mellitus, and unspecified) were also performed. The models were adjusted for well-known confounders such as age, prepregnancy body mass index (BMI), parity (nulliparous versus primiparous/multiparous), and depression history or previous contact with psychiatrist/psychologist. For the postpartum depression outcome, antepartum depression (yes versus no) was added to the model. We also performed univariable analyses to identify other potential confounders such as marital status (married or cohabiting versus single), country of origin (Scandinavia versus other), education level (tertiary level versus other), employment status (working/studying versus parental leave/sick-leave/unemployed), smoking (past/present versus never), history of intimate partner violence in the current or previous relationship (yes versus no), pregnancy complications (presence of one of the following: preeclampsia, anemia, pregnancy hypertension, or placenta previa), and fear of childbirth (yes versus no). Among these covariates, only the variable pregnancy complications was added to the final model. In addition, we performed a subanalysis to examine the independent and joint effects for the risk of developing postpartum depression by having DMP and antepartum depression. We created four groups: neither DMP or antepartum depression, DMP only, antepartum depression only, and comorbidity of DMP and antepartum depression (31). This model was also adjusted for age, prepregnancy BMI, parity, pregnancy complication, and history of depression or previous contact with psychiatrist/psychologist. Another subanalysis was performed where outcomes were continuous measures of EPDS at gestational week 32 and 6 weeks postpartum. These linear regression models were adjusted for age, prepregnancy BMI, parity, pregnancy complication, and history of depression or previous contact with psychiatrist/psychologist. A sensitivity analysis was also performed by excluding individuals diagnosed with polycystic ovarian syndrome. All statistical analyses were performed using the R programming language (version 4.2.2) through RStudio (version 2022.07.01). Statistical significance was set at p value <.05.

RESULTS

Of 4459 participants, 949 had antepartum depression (21.2%) and 1123 had postpartum depression (25%). Of those with postpartum depression, half had antepartum depression. Fifty-five women (1.2%) were identified with DMP, constituting of 10 individuals with pregestational diabetes mellitus (*ICD-10* O24.0 and O24.1), 32 individuals with gestational diabetes (*ICD-10* O24.4), and 13 individuals with unspecified diabetes (*ICD-10* O24, O24.2, O24.3, O24.9). Twenty-one of 55 individuals diagnosed with DMP were treated with insulin. Table 1 shows the descriptive characteristics of women with and without DMP. Women with DMP had higher prepregnancy BMI. Moreover, history of depression or previous contact with psychiatrist/psychologist, preterm birth, and pregnancy complications (i.e., preeclampsia, anemia, pregnancy hypertension, or placenta previa) were higher in women with DMP. Among the 55 women with DMP, 16 women had antepartum depression and 27 women had postpartum depression, whereas 15 women had both antepartum depression and postpartum depression.

Association Between DMP and Its Types, and Antepartum Depression

To assess the association between DMP, its types, and antepartum depression, logistic regressions were performed. DMP was not statistically significant in the unadjusted and adjusted models (Table 2). Among the subtypes, women with unspecified diabetes had fourfold odds for antepartum depression (OR = 4.34; 95% CI = 1.45–12.9; p = .008) compared with those without diabetes mellitus. However, this did not remain significant after adjusting for covariates (OR = 2.86; 95% CI = 0.89–9.20; p = 0.08; Table 2). Similar results were found even after exclusion of individuals with polycystic ovarian syndrome.

To assess the association between DMP and its subtypes, and continuous EPDS score at gestational week 32, linear regression analyses were performed. DMP was statistically significantly associated with a higher EPDS score in both the unadjusted (β = 2.7;

TABLE 1. Descriptive Characteristics of Women With and Without DMP

	Women Without DMP (n = 4404)	Women With DMP (n = 55)	p^a
Sociodemographic data			
Maternal age, median [min–max], y	31 [18–48]	33 [20–43]	.26
Body mass index, median [min–max], kg/m^2	22.8 [15.8–50.9]	25.8 [18.9–40.2]	**<.001**
Married/cohabitant marital status, n (%)	4150 (94.2)	53 (96.4)	.70
Scandinavian origin, n (%)	4010 (91.1)	48 (87.3)	.29
Tertiary educational level, n (%)	3303 (75.0)	35 (63.6)	.076
Working/studying, n (%)	3900 (88.6)	44 (80.0)	.067
Smoking ever, n (%)	1436 (32.6)	19 (34.5)	.83
Psychosomatic characteristics			
History of violence in the past or present relationship, n (%)	503 (11.4)	6 (10.9)	.99
History of depression or previous contact with psychiatrist/psychologist, n (%)	2454 (55.7)	40 (72.7)	**.019**
Fear of childbirth, n (%)	960 (21.8)	15 (27.3)	.29
Obstetric- and pregnancy-related variables			
Nulliparous, n (%)	2373 (53.9)	22 (40)	**.027**
Polycystic ovarian syndrome, n (%)	81 (1.8)	1 (1.8)	.99
Unplanned pregnancy, n (%)	633 (14.4)	11 (20)	.32
Other pregnancy complications, n (%)[b]	389 (8.8)	17 (27.9)	**<.001**
Preterm birth, n (%)	191 (4.3)	5 (9.1)	.19
Outcome			
Antepartum depression, n (%)	933 (21.2)	16 (29.1)	.21
Postpartum depression, n (%)	1096 (24.9)	27 (49.1)	**<.001**

DMP = diabetes mellitus in pregnancy. Bold text denotes significant p value.

[a] χ^2 test or Wilcoxon rank sum test, where appropriate.

[b] Preeclampsia, anemia, pregnancy hypertension, or placenta previa.

95% CI = 1.4–4.0; $p < .001$) and adjusted models ($\beta = 1.80$; 95% CI = 0.60–3.1; $p = .003$; Table S2, Supplemental Digital Content, http://links.lww.com/PSYMED/A978). Among the subtypes, unspecified diabetes was significantly associated with a higher EPDS score (unadjusted: $\beta = 5.3$, 95% CI = 2.7–7.9, $p < .001$; adjusted: $\beta = 4.1$, 95% CI = 1.6–6.6; $p = .001$; Table S2, Supplemental Digital Content, http://links.lww.com/PSYMED/A978).

Association Between DMP Types, Comorbidity of DMP–Antepartum Depression, and Postpartum Depression

To assess the association between DMP, its types, and postpartum depression, logistic regressions were performed. In the unadjusted model, women with DMP had threefold odds for postpartum depression (OR = 2.91; 95% CI = 1.71–4.96; $p < .001$; Table 3).

TABLE 2. Association Between DMP, Subtypes, and Antepartum Depression (n = 4459)

	Antepartum Depression	No Antepartum Depression	Unadjusted OR (95% CI)	p	Adjusted[a] OR (95% CI)	p
DMP						
No DMP	933	3471	Ref		Ref	
DMP	16	39	1.53 (0.85–2.74)	.2	1.04 (0.56–1.92)	>.9
Subtypes						
No diabetes	933	3471	Ref		Ref	
Pregestational diabetes mellitus	3	7	1.59 (0.41–6.18)	.5	0.80 (0.20–3.23)	.8
Gestational diabetes mellitus	6	26	0.86 (0.35–2.09)	.7	0.66 (0.26–1.66)	.4
Unspecified	7	6	**4.34 (1.45–12.9)**	**.008**	2.86 (0.89–9.20)	.076

DMP = diabetes mellitus in pregnancy; OR = odds ratio; CI = confidence interval.

Bolded text signifies significant p value.

[a] Adjusted for age, prepregnancy body mass index, parity, depression history, and pregnancy complications.

TABLE 3. Association Between DMP, Subtypes, and Comorbidity (DMP and Antepartum Depression), Respectively, and Postpartum Depression (n = 4459)

	Postpartum Depression	No Postpartum Depression	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
DMP[a]						
No DMP	1096	3308	Ref		Ref	
DMP	27	28	**2.91 (1.71–4.96)**	**<.001**	**2.37 (1.30–4.33)**	**.005**
Subtypes[a]						
No DMP	1096	3308	Ref		Ref	
Pregestational diabetes mellitus	6	4	**4.53 (1.27–16.1)**	**.020**	3.16 (0.79–12.6)	.062
Gestational diabetes mellitus	13	19	**2.07 (1.02–4.20)**	**.045**	2.12 (0.97–4.65)	.10
Unspecified	8	5	**4.83 (1.58–14.8)**	**.006**	2.50 (0.69–9.06)	.20
Comorbidity[b]						
No DMP or antepartum depression	542	2929	Ref		Ref	
DMP only	12	27	**2.40 (1.21–4.77)**	**.012**	1.84 (0.90–3.73)	.095
Antepartum depression only	554	379	**7.90 (6.73–9.27)**	**<.001**	**5.83 (4.94–6.90)**	**<.001**
DMP–antepartum depression comorbidity	15	1	**81.1 (10.7–612)**	**<.001**	**49.6 (6.49–378)**	**<.001**

DMP = diabetes mellitus in pregnancy; OR = odds ratio; CI = confidence interval.

Bolded text signifies significant p value.

[a] Adjusted for age, prepregnancy body mass index, parity, history of depression or previous contact with psychiatrist/psychologist, pregnancy complications, and antepartum depression.

[b] Adjusted for age, prepregnancy body mass index, parity, history of depression or previous contact with psychiatrist/psychologist, and pregnancy complications.

After adjusting for confounders, the association of DMP with postpartum depression remained statistically significant (OR = 2.37; 95% CI = 1.30–4.33; p = .005; Table 3). Among the types of DMP, pregestational diabetes mellitus (OR = 4.53; 95% CI = 1.27–16.1; p = .02), gestational diabetes mellitus (OR = 2.07; 95% CI = 1.02–4.20; p = .045), and unspecified diabetes (OR = 4.83; 95% CI = 1.58–14.8; p = .006) were significant in the unadjusted model (Table 3). However, the association was no longer statistically significant when confounders were accounted for. When examining the independent and joint effects of antepartum depression and DMP, DMP only (OR = 2.40; 95% CI = 1.21–4.77; p = .012), antepartum depression only (OR = 7.90; 95% CI = 6.73–9.27; p < .001), and DMP–antepartum depression comorbidity (OR = 81.1; 95% CI = 10.7–612; p < .001) were significantly associated with postpartum depression in the unadjusted model (Table 3). When adjusted for confounders, the categories antepartum depression only (OR = 5.83; 95% CI = 4.94–6.90; p < .001), and DMP–antepartum depression comorbidity (OR = 49.6; 95% CI = 6.49–378; p < .001) remained significant with an increased risk of postpartum depression. DMP followed the same trend but became only borderline significant (OR = 1.84; 95% CI = 0.90–3.73; p = 0.093; Table 3). Similar results were found even after exclusion of individuals with polycystic ovarian syndrome.

To assess the association between DMP and its subtypes, and continuous EPDS score at 6 weeks postpartum, linear regression analyses were performed. DMP was statistically significantly associated with a higher EPDS score both in the unadjusted (β = 3.0; 95% CI = 1.7–4.2; p < .001) and adjusted models (β = 2.3; 95% CI = 1.1–3.5; p < .001; Table S3, Supplemental Digital Content, http://links.lww.com/PSYMED/A978). Among the subtypes, gestational diabetes (unadjusted: β = 2.2, 95% CI = 0.56–3.8, p = 0.009; adjusted: β = 2.2, 95% CI = 0.64–3.7, p = 0.005) and unspecified diabetes (unadjusted: β = 5.0, 95% CI = 2.3–7.8, p < .001; adjusted: β = 2.9, 95% CI = 0.38–5.5; p = .024) were significantly associated with a higher EPDS score (Table S3, Supplemental Digital Content, http://links.lww.com/PSYMED/A978).

DISCUSSION

The aim of this longitudinal study was to investigate the association of DMP with antepartum depression and postpartum depression. We found a positive association between DMP and postpartum depression, even after adjusting for confounders. There were no statistically significant associations between DMP and antepartum depression, once confounders were adjusted for. Moreover, none of the specific types of DMP were significantly associated with antepartum or postpartum depression. However, individuals with DMP had higher depressive symptoms antepartum and postpartum. Among the subtypes, those with gestational diabetes had higher depressive symptoms postpartum.

Although our study's lack of association between DMP and antepartum depression was in accordance with some studies (32,33), a meta-analysis of nine studies showed that DMP was associated with a 1.43-fold increased risk (95% CI = 1.21–1.70) for antepartum depression (34). When analyzing the types of DMP in the meta-analysis, pregestational diabetes mellitus was not found to be a significant risk factor for antepartum depression, whereas gestational diabetes mellitus was (pooled RR = 1.43; 95% CI = 1.25–1.64) (34). However, another meta-analysis did not find an association between gestational diabetes mellitus and antepartum depression (14), in line with our findings. Because of the limited

sample of participants experiencing the different subtypes of DMP, the results of the current study should be interpreted with caution. It could be hypothesized that postpartum depression has an overlapping pathophysiology with diabetes, to a higher extent than that of antepartum depression. We have previously found associations between symptoms of postpartum depression and metabolic as well as proinflammatory alterations (35,36). Moreover, even though we did not observe an association between DMP and antepartum depression, those with DMP had more depressive symptoms antepartum compared with those without DMP. It is possible that there was not enough time to develop clinically meaningful depression symptoms antepartum. Hence, it is still valuable to provide extra support for those with DMP, so as to prevent progression of these symptoms.

For postpartum depression, our findings are in line with most studies. It is interesting to note that the results were not statistically significant when looking separately at types of DMP, which might be due to a power issue. Several systematic reviews and meta-analyses report that individuals with gestational diabetes mellitus have a significantly higher risk of developing postpartum depression (12,14,17,37). Similarly, Silverman et al. (16) identified pregestational diabetes mellitus had a 49% higher risk (RR = 1.49; 95% CI = 1.01–2.21) for postpartum depression among women with a history of depression. They also found that those with gestational diabetes mellitus had a 70% higher risk (RR = 1.70; 95% CI = 1.36–2.13) for postpartum depression regardless of history of depression. In the present study, the ORs ranged from twofold to threefold higher for postpartum depression, which are somewhat higher than the relative risks (RRs) reported earlier. This effect size should be interpreted with caution as ORs tend to be inflated compared with RRs, especially when outcomes approach a prevalence of 21% to 25%.

Similar to a study by Shuffrey et al. (31), we examined the independent and joint effects of DMP–antepartum depression comorbidity on postpartum depression. Our results were in line with their study; however, with a larger effect size, as women with comorbidity of gestational diabetes and antepartum depression had sevenfold odds for PPD in our study. Shuffrey et al. also found that having antepartum depression without DMP conferred fivefold odds for postpartum depression. Although our results are significant for antepartum depression only and DMP–antepartum depression comorbidity, the wide confidence interval in the latter case that denote a considerable degree of uncertainty and imprecision in estimating the true OR can be due to the small sample size. Nonetheless, our results are in accordance with Shuffrey et al. (31).

The underlying mechanisms of a possible association between DMP and PND are not fully elucidated. According to an increasing number of studies, for example, by Osborne and Monk (38), inflammatory processes in general are associated with an increased risk of PND as well as with inflammatory morbidities of pregnancy such as gestational diabetes mellitus, preeclampsia, and preterm birth. Hence, a plausible explanation is that the dysfunctional immune system is related both to the manifestation of depressive symptoms and to insulin resistance. Specifically, the hypothalamus-pituitary-adrenal axis activates the sympathetic nervous system, which in turn increases the production of inflammatory cytokines and stress hormones. Both inflammatory cytokines and stress hormones have a possible interaction with the pancreatic β cells that induce insulin resistance (37,39). We have previously shown that postpartum depression is associated with a more proinflammatory profile compared with antepartum depression, which could be one reason for stronger associations between DMP and postpartum depression versus antepartum depression (35,40), revealed in our study.

It is important to note that the diagnostic criteria of gestational diabetes in Sweden were changed in 2015 according to the World Health Organization recommendations from 2013. The early diagnostic criteria of gestational diabetes mellitus were based on stricter cutoff values. The prevalence of gestational diabetes mellitus from 2006 to 2014 in Sweden was 1% to 1.4% (41–43). The recruitment of participants for the BASIC study started in 2009 (22), and the new criteria for diagnosing gestational diabetes, according to the World Health Organization criteria, were first implemented in 2015 in Sweden (44). Hence, most of the participants were diagnosed according to the old diagnostic criteria, which gives a lower prevalence among the population than expected with the current diagnostic criteria. This low prevalence reduces the power, rendering possible associations harder to detect, and increases the misclassification of gestational diabetes mellitus cases.

This study has several strengths. Aside from the longitudinal design encompassing both antepartum and postpartum depression, antepartum depression was also used to adjust the model for postpartum depression. Our definition of DMP included pregestational diabetes mellitus, gestational diabetes mellitus, and unspecified diabetes, giving a wider perspective on DMP. Moreover, subanalyses investigating specific types of DMP were also explored. Similarly, PND was assessed with different questionnaires and interviews as well as during several time points, allowing a more inclusive characterization. By doing this, we have addressed the limited definitions of previous studies. However, this study also has limitations. As previously mentioned, the diagnostic criteria of gestational diabetes mellitus changed quite late during the study period. This resulted in a lower prevalence of DMP. Moreover, the cohort consists of relatively healthy women, many with university education and born in Sweden. This could explain the awareness of mental illnesses and increased contact with health care professionals. Moreover, this can also be attributed to the participation rate observed in the study, which indicates the presence of nonresponse bias. The inclination of women with specific characteristics, as previously outlined, to partake in the study contributes to this bias. Therefore, caution should be also exercised when interpreting results. Furthermore, the relatively low rate of participants in this present study diagnosed with DMP (1.3%) might introduce bias and lower generalizability of the study results. It is also important to note that, although studies have shown the bidirectionality of DMP and PND (18,45), this study addressed the association with DMP as an exposure and PND as the outcome.

In conclusion, our study suggests that DMP is associated with an increased risk of PND. Diabetes mellitus could constitute a risk factor to be taken into account when screening for high-risk groups for PND.

We would like to thank Meena Daivadanam and Richard White for their valuable input to this study. Special thanks to Cathrine Axfors, Emma Bränn, Hanna E. Henriksson, Charlotte Hellgren, Theodora Kunovac Kallak, Marianne Kördel, Ingegerd Clason, Lena Moby, Natasa Kollia, and Linn Wallen for the complex administration and coordination efforts while the study was being conducted. We also would like to thank all the women who participated in this study.

Source of Funding and Conflicts of Interest: The authors report no biomedical financial interests or potential conflicts of interest. This work was supported by the Swedish Research Council under grant number 523-2014-2342 and 523-2014-07605.

Data Availability Statement: The data used in this study are available from the corresponding author upon reasonable request. Because of privacy and ethical considerations, the data are not publicly available.

Preregistration: This prospective cohort study was not preregistered before the initiation of the data collection that commenced in 2009.

REFERENCES

1. Howard LM, Khalifeh H. Perinatal mental health: a review of progress and challenges. World Psychiatry 2020;19:313–27.
2. Damm P, Houshmand-Oeregaard A, Kelstrup L, Lauenborg J, Mathiesen ER, Clausen TD. Gestational diabetes mellitus and long-term consequences for mother and offspring: a view from Denmark. Diabetologia 2016;59:1396–9.
3. Sartorius N. Depression and diabetes. Dialogues Clin Neurosci 2018;20:47–52.
4. Slomian J, Honvo G, Emonts P, Reginster JY, Bruyère O. Consequences of maternal postpartum depression: a systematic review of maternal and infant outcomes. Womens Health (Lond) 2019;15:1745506519844044.
5. Dadi AF, Miller ER, Bisetegn TA, Mwanri L. Global burden of antenatal depression and its association with adverse birth outcomes: an umbrella review. BMC Public Health 2020;20:173.
6. Wang Z, Liu J, Shuai H, Cai Z, Fu X, Liu Y, et al. Mapping global prevalence of depression among postpartum women. Transl Psychiatry 2021;11:543.
7. Egan AM, Dunne FP. Epidemiology of Gestational and Pregestational Diabetes Mellitus. In: Lapolla A, Metzger BE, editors. Gestational Diabetes. Freiburg, Germany: S. Karger GmbH; 2019:1–10 (Frontiers in Diabetes; vol. 28).
8. International Diabetes Federation. IDF Diabetes Atlas 2021. Available at: https://diabetesatlas.org/atlas/tenth-edition/. Accessed January 1, 2023.
9. Skogsdal Y, Connor P, Elvander C, Storck Lindholm E, Kloow M, Petersson K, Svanvik T, Granfors M. Graviditetsregistrets Årsrapport 2022 2023. Retrieved October 10, 2023, from https://www.medscinet.com/GR/uploads/hemsida/dokumentarkiv/Graviditetsregistrets%20%C3%85rsrapport%202022.pdf.
10. Yu Y, Liang H-F, Chen J, Li Z-B, Han Y-S, Chen J-X, Li J-C. Postpartum depression: current status and possible identification using biomarkers. Front Psychiatry [Internet] 2021;12:620371. Available at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.620371. Accessed November 3, 2022.
11. Lustman PJ, Clouse RE. Depression in diabetic patients: the relationship between mood and glycemic control. J Diabetes Complications 2005;19:113–22.
12. Azami M, Badfar G, Soleymani A, Rahmati S. The association between gestational diabetes and postpartum depression: a systematic review and meta-analysis. Diabetes Res Clin Pract 2019;149:147–55.
13. Ross GP, Falhammar H, Chen R, Barraclough H, Kleivenes O, Gallen I. Relationship between depression and diabetes in pregnancy: a systematic review. World J Diabetes 2016;7:554–71.
14. Wilson CA, Newham J, Rankin J, Ismail K, Simonoff E, Reynolds RM, et al. Is there an increased risk of perinatal mental disorder in women with gestational diabetes? A systematic review and meta-analysis. Diabet Med 2020;37:602–22.
15. Zhao X, Zhang Z. Risk factors for postpartum depression: an evidence-based systematic review of systematic reviews and meta-analyses. Asian J Psychiatr 2020;53:102353.
16. Silverman ME, Reichenberg A, Savitz DA, Cnattingius S, Lichtenstein P, Hultman CM, et al. The risk factors for postpartum depression: a population-based study. Depress Anxiety 2017;34:178–87.
17. Rasmussen MH, Poulsen GJ, Videbech P, Wohlfahrt J, Melbye M. Endocrine disease history and the risk of postpartum depression. Br J Psychiatry 2023;222:119–24.
18. Fischer S, Morales-Suárez-Varela M. The bidirectional relationship between gestational diabetes and depression in pregnant women: a systematic search and review. Healthcare (Basel) 2023;11:404.
19. Hinkle SN, Buck Louis GM, Rawal S, Zhu Y, Albert PS, Zhang C. A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period. Diabetologia 2016;59:2594–602.
20. Whiteman VE, Salemi JL, Mejia De Grubb MC, Ashley Cain M, Mogos MF, Zoorob RJ, et al. Additive effects of pre-pregnancy body mass index and gestational diabetes on health outcomes and costs. Obesity (Silver Spring) 2015;23:2299–308.
21. Pace R, Rahme E, De Costa D, Dasgupta K. Association between gestational diabetes mellitus and depression in parents: a retrospective cohort study. Clin Epidemiol 2018;10:1827–38.
22. Axfors C, Bränn E, Henriksson HE, Hellgren C, Kunovac Kallak T, Fransson E, et al. Cohort profile: the Biology, Affect, Stress, Imaging and Cognition (BASIC) study on perinatal depression in a population-based Swedish cohort. BMJ Open 2019;9:e031514.
23. Cnattingius S, Källén K, Sandström A, Rydberg H, Månsson H, Stephansson O, et al. The Swedish medical birth register during five decades: documentation of the content and quality of the register. Eur J Epidemiol 2023;38:109–20.
24. Stephansson O, Petersson K, Björk C, Conner P, Wikström A-K. The Swedish Pregnancy Register—for quality of care improvement and research. Acta Obstet Gynecol Scand 2018;97:466–76.
25. National Patient Register. Socialstyrelsen. 2022. Available at: https://www.socialstyrelsen.se/en/statistics-and-data/registers/national-patient-register/. Accessed October 12, 2023.
26. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 1987;150:782–6.
27. Zung W. A Self-Rating Depression Scale. Arch Gen Psychiatry 1965;12:63–70.
28. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59(Suppl 20):22–33; quiz 34–57.
29. Rubertsson C, Börjesson K, Berglund A, Josefsson A, Sydsjö G. The Swedish validation of Edinburgh Postnatal Depression Scale (EPDS) during pregnancy. Nord J Psychiatry 2011;65:414–8.
30. van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. J Stat Softw 2011;45:1–67.
31. Shuffrey LC, Lucchini M, Morales S, Sania A, Hockett C, Barrett E, et al; program collaborators for Environmental influences on Child Health Outcomes. Gestational diabetes mellitus, prenatal maternal depression, and risk for postpartum depression: an Environmental influences on Child Health Outcomes (ECHO) Study. BMC Pregnancy Childbirth 2022;22:758.
32. Huang T, Rifas-Shiman SL, Ertel KA, Rich-Edwards J, Kleinman K, Gillman MW, et al. Pregnancy hyperglycaemia and risk of prenatal and postpartum depressive symptoms. Paediatr Perinat Epidemiol 2015;29:281–9.
33. Varela P, Spyropoulou AC, Kalogerakis Z, Vousoura E, Moraitou M, Zervas IM. Association between gestational diabetes and perinatal depressive symptoms: evidence from a Greek cohort study. Prim Health Care Res Dev 2017;18:441–7.
34. Lee KW, Ching SM, Devaraj NK, Chong SC, Lim SY, Loh HC, et al. Diabetes in pregnancy and risk of antepartum depression: a systematic review and meta-analysis of cohort studies. Int J Environ Res Public Health 2020;17:3767.
35. Bränn E, Fransson E, White RA, Papadopoulos FC, Edvinsson Å, Kamali-Moghaddam M, et al. Inflammatory markers in women with postpartum depressive symptoms. J Neurosci Res 2020;98:1309–21.
36. Bränn E, Malavaki C, Fransson E, Ioannidi M-K, Henriksson HE, Papadopoulos FC, et al. Metabolic profiling indicates diversity in the metabolic physiologies associated with maternal postpartum depressive symptoms. Front Psychiatry [Internet] 2021;12:685656. Available at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.685656. Accessed April 21, 2023.
37. Arafa A, Dong JY. Depression and risk of gestational diabetes: a meta-analysis of cohort studies. Diabetes Res Clin Pract 2019;156:107826.
38. Osborne LM, Monk C. Perinatal depression—the fourth inflammatory morbidity of pregnancy?: theory and literature review. Psychoneuroendocrinology 2013;38:1929–52.
39. Moulton CD, Pickup JC, Ismail K. The link between depression and diabetes: the search for shared mechanisms. Lancet Diabetes Endocrinol 2015;3:461–71.
40. Edvinsson Å, Bränn E, Hellgren C, Freyhult E, White R, Kamali-Moghaddam M, et al. Lower inflammatory markers in women with antenatal depression brings the M1/M2 balance into focus from a new direction. Psychoneuroendocrinology 2017;80:15–25.
41. Stokkeland K, Ludvigsson JF, Hultcrantz R, Ekbom A, Höijer J, Bottai M, et al. Increased risk of preterm birth in women with autoimmune hepatitis—a nationwide cohort study. Liver Int 2016;36:76–83.
42. Lindqvist M, Persson M, Lindkvist M, Mogren I. No consensus on gestational diabetes mellitus screening regimes in Sweden: pregnancy outcomes in relation to different screening regimes 2011 to 2012, a cross-sectional study. BMC Pregnancy Childbirth 2014;14:185.
43. Lindström L, Ageheim M, Axelsson O, Hussain-Alkhateeb L, Skalkidou A, Wikström A-K, et al. Swedish intrauterine growth reference ranges for estimated fetal weight. Sci Rep 2021;11:12464.
44. *Gränsvärden för Graviditetsdiabetes: Stöd för Beslut om Behandling*. Socialstyrelsen (The National Board of Health and Welfare). 2015. Retrieved November 15, 2023, from https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/ovrigt/2015-6-52.pdf.
45. OuYang H, Chen B, Abdulrahman A-M, Li L, Wu N. Associations between gestational diabetes and anxiety or depression: a systematic review. J Diabetes Res 2021;2021:e9959779.