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Gestational diabetes mellitus and peripartum depression: a longitudinal study of a bidirectional relationship

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Abstract

Background Gestational diabetes mellitus (GDM) and peripartum depression (PPD) are increasing global health issues with potentially long-lasting adverse outcomes. While limited studies suggest a bidirectional relationship between GDM and PPD, most research has been cross-sectional and focused on one direction of the relationship, primarily if GDM predicts postpartum depression. The interplay between antenatal depression and GDM is less explored, with a critical lack of prospective bidirectional studies. This longitudinal study aimed to investigate the bidirectional relationship between GDM and PPD in a total sample and according to different pre-pregnancy body mass index (BMI) categories. Specifically, we examined whether antenatal depression symptoms predict a subsequent GDM diagnosis and whether GDM predicts subsequent postpartum depression symptoms.

Methods A three-wave online longitudinal study included 360 women who were followed from the second trimester (20–28 weeks, T1) through the third trimester (32–42 weeks, T2), and into the postpartum period (6–20 weeks after birth, T3). Participants completed the General Data Questionnaire, one item about the diagnosis of GDM, and the Edinburgh Postnatal Depression Scale (EPDS). The sample was stratified according to pre-pregnancy BMI into normal-weight (N= 247) and overweight/obese (N= 113) subgroups. Women with type I and II diabetes, GDM at T1, and underweight BMI were excluded.

Results In the total sample, antenatal depression symptoms predicted GDM, whereas GDM did not predict postpartum depression symptoms. A bidirectional relationship was observed in normal-weight women, where antenatal depression symptoms predicted subsequent GDM diagnosis, and GDM diagnosis predicted postpartum depression symptoms. In contrast, no associations were found in either direction in the overweight/obese subgroup.

Conclusions This study provides evidence of a bidirectional relationship between GDM and PPD only in women with normal body weight before pregnancy. The results highlight the complexity of the relationship between peripartum mental and metabolic health, that is dependent on pre-pregnancy BMI. Clinicians should be aware that normal-weight women may have a unique sensitivity to the bidirectional interplay between GDM and PPD. Pregnant women should be closely monitored for both mental and metabolic health issues and targeted for prevention programs to reduce the risks and burdens associated with both conditions.

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Keywords Gestational diabetes mellitus, Peripartum depression, Pregnancy, Antenatal, Postpartum, Depression, Body mass index, Obesity, Metabolic health

Introduction

Gestational diabetes mellitus (GDM) is a pregnancyrelated metabolic disorder characterized by elevated blood glucose levels. It is thought to result from the body's inability to adapt to physiological insulin resistance, which serves to provide energy to the growing foetus and is triggered by placenta-derived factors such as TNF-alpha [1]. It is one of the most common pregnancy metabolic complications, with a prevalence of around 11% in Europe but reaching up to 32% in Eastern European countries [2]. The most significant risk factor for GDM is obesity [3, 4], which is showing an upward trend worldwide, often referred to as the 'obesity epidemic' [5]. Other factors such as advanced maternal age, sedentary lifestyle, and strict diagnostic criteria further contribute to higher GDM rates [6, 7], making diabetes (including GDM) one of the fastest-growing global health crises of the 21st century [8].

Although GDM usually resolves after childbirth, it is related to numerous adverse outcomes for mothers and infants. Women with GDM face various pregnancy risks, including higher rates of caesarean section, preterm birth, and preeclampsia [9–11], and children are at risk for macrosomia, perinatal mortality, and metabolic disorders or obesity later in life [4, 12–14]. Women themselves are at risk for developing type 2 diabetes in the future [4, 15–18], having a reduced quality of life [19], and experiencing mental health problems [20, 21], which, in, turn can affect disease management and glycaemic control [22].

One of the most common peripartum mental health problems is peripartum depression (PPD), a depressive episode with onset during pregnancy or up to a year postpartum [23, 24], affecting around 16–20% of women worldwide [25–30]. Recent studies have also identified a rise in peripartum mental health issues during the coronavirus pandemic [31, 32].

PPD is a debilitating illness associated with unwanted outcomes for mothers, children, and overall family functioning. Women with PPD tend to have lower quality of life [33], poorer health behaviours (e.g., smoking, not taking prenatal vitamins) [34], more pregnancy complications [35], more suicidal ideation or attempts [36], and difficulties in mother-infant bonding [37]. Children of mothers with PPD are at risk for developmental difficulties, behavioural problems, psychiatric issues, and attachment difficulties, which may extend beyond infancy and childhood [38, 39]. Moreover, maternal PPD correlates with PPD in fathers [40], further adversely affecting child development, health, and family relations [41, 42].

Considering the rising trend of obesity and metabolic disorders among the peripartum population [43], attention has been drawn to the role of metabolic factors such as GDM in the aetiology of PPD. Furthermore, women with comorbid PPD and GDM have more adverse pregnancy outcomes, such as preeclampsia, hypertension, and preterm delivery, than women with GDM alone [44, 45], which prompted further exploration into their interrelationship. Evidence from the general population indicates a bidirectional relationship between diabetes and depression [46], showing that people with diabetes have a higher risk of developing depression and that people with depression have a higher risk of developing diabetes. The association between the two can be attributed to shared biopsychosocial mechanisms including an activated hypothalamic-pituitary-adrenal axis, inflammation, disrupted serotonergic regulation, lifestyle, and environmental factors [47, 48].

Although several original studies did not find an association between GDM and PPD [49-54], meta-analyses indicated that GDM increases the risk for postpartum depression [47, 55, 56]. A recent umbrella review found that GDM is a risk factor for postpartum depression with intermediate evidence [57]. Similarly, studies investigating the risk for GDM among women with a history of depression or depression in early pregnancy have shown mixed results [58, 59]. Very few studies have investigated the bidirectional relationship between PPD and GDM, with some indicating a positive relationship in both directions (reviewed in [60–62]). Other studies, however, found no clear bidirectional associations between GDM and PPD [52, 63, 64], while one study revealed different results based on pre-pregnancy body mass index (BMI), with stronger effects found among non-obese women [65].

The evidence regarding the mutual impact of GDM and PPD across the peripartum period remains unclear and conflicting. A notable issue is methodological heterogeneity, including variations in the timing of depression assessment and failure to account for relevant covariates. As meta-analyses highlighted, most studies are cross-sectional, retrospective or case-control, and investigate only one direction of the relationship, predominantly if GDM predicts postpartum depression [47, 55]. The relationship between antenatal depression and GDM is less understood, with a meta-analysis identifying only four studies that assessed antenatal depression prior to a GDM diagnosis [58]. There is a lack of prospective studies testing the entire bidirectional model, thus, most studies cannot establish causality [60]. Moreover, no study performed

subgroup analyses stratified by pre-pregnancy BMI to replicate prior findings [65] and clarify if BMI moderates the hypothesised relationship [58]. Considering the high prevalence and serious consequences related to both PPD and GDM, further research into their interrelationship is essential to advance risk assessment and therapeutic strategies.

To address the knowledge gaps regarding the interplay between peripartum metabolic and mental health, this study aimed to investigate the bidirectional relationship between PPD and GDM. We hypothesised that depressive symptoms during mid-pregnancy would positively predict subsequent GDM diagnosis, and that a GDM diagnosis would positively predict subsequent postpartum depressive symptoms. Furthermore, we hypothesised that pre-pregnancy BMI might be an important moderator of these relationships. Therefore, we tested the bidirectional model in a total sample, and women with normal body weight or overweight/obesity prior to pregnancy.

Methods

Participants

A total of 584 adult women (over 18 years old and fluent in Croatian) in their second trimester of pregnancy (20–28 weeks, T1) were enrolled in the study, of whom 393 participated also in T2 and T3 (drop-off 32.7%). As the exclusion criteria were a diagnosis of type I or type II diabetes (N=3), a diagnosis of GDM before T1 (N=13), and a pre-pregnancy BMI below 18.5 (underweight; N=17), the final sample size was 360.

The average age of the participants was 31 years. They were predominantly married or cohabiting (99%), living in urban areas (79%), employed (89%), highly educated (77%), and of average socioeconomic status (57%). The majority of pregnancies were planned (65%) and singleton (98%). Most women were primiparous (57%) and had vaginal delivery (76%). Around 14% suffered from chronic diseases (e.g., asthma, thyroid issues).

Regarding pre-pregnancy BMI, 69% were normal-weight, 23% overweight, and 9% obese. At T2, 33 participants (9%) had been diagnosed with GDM, which was identified at approximately 26 weeks of pregnancy (SD = 3.23).

Instruments

The Edinburgh Postnatal Depression Scale (EPDS) [66] is a self-report scale measuring depressive symptoms among pregnant and postpartum women within the last week. It comprises ten items on a 4-point scale ranging from 0 to 3, where higher scores indicate higher depressive symptoms, and it has good psychometric properties [66, 67]. The EPDS was previously translated into Croatian language and showed good Cronbach α reliability of

0.86 [68]. In this study, a cut-off \geq 13 was used, which was proposed by the authors of the scale [66] and showed the highest specificity in a recent meta-analysis of individual data that also included participants from Croatia [67]. The EPDS in the current study had high reliability at all time points, with a McDonald's ω of 0.87, 0.88, and 0.89.

The General Data Questionnaire included questions on age, women's and their partner's education level and employment status, perceived income, place of residence, marital status, chronic illnesses, and anthropometric measures (pre-pregnancy weight, height, current weight). Obstetric data included questions such as gestational age, parity, and mode of birth. If, at T1, participants answered 'Yes' to the question whether they had received a diagnosis of GDM in the current pregnancy, it was an exclusion criterion, while the answer 'Yes' at T2 was the target group. In Croatia, GDM is diagnosed according to a standardized procedure based on the protocol and criteria proposed by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) [69] and implemented in a Croatian clinical setting [70].

Pre-pregnancy BMI was calculated by dividing self-reported pre-pregnancy weight in kilograms by the square of height in metres. Self-reported weight and height are widely used in research, with studies demonstrating that they greatly match the observed values and are suitable for clinical and research purposes [71–73].

Procedure

This three-wave online longitudinal study was part of a larger project conducted in the peripartum period. Ethical approval was obtained from the Ethics Committee of the Catholic University of Croatia. Participants were recruited between October 2022 and November 2023 using social media ads and Facebook groups relevant to peripartum women (e.g., pregnancy, motherhood) and a snowball sampling technique, which involved personal connections. All participants were informed about the project aims and after consenting, they completed online questionnaires using Google Forms.

The first assessment (T1) was from 20 to 28 weeks of pregnancy (mean 24 ± 3 weeks), the second assessment (T2) was from 32 to 42 weeks of pregnancy (mean 33 ± 1 week), and the third assessment (T3) was from 6 to 20 weeks postpartum (mean 9 ± 2 weeks). At T2 and T3, participants were contacted via email and/or text message to complete the online questionnaires. Participation was voluntary with the possibility to withdraw at any time. The participants had the option to enter a random draw to receive a 30 EUR voucher in a store popular among peripartum women, with two participants selected every month. Participants who reported at least occasional self-harm thoughts on item 10 of the EPDS were contacted

with additional information on psychological support and available counselling services.

Statistical analysis

Reliability was examined by the McDonald's omega (ω) coefficient. Differences between the groups were tested with an independent t-test, while the differences in the proportions were tested with a chi-square test or Fisher's exact test. To assess the correlations between the variables, Pearson's, point-biserial or Cramer's V correlation coefficients were used. These statistical analyses were performed using IBM SPSS software for Windows, version 29.0. To test the proposed model of the relationship between PPD symptoms and GDM, path analysis was performed with Mplus 8.8 software [74]. For the multigroup analysis, the sample was categorized into two subgroups based on pre-pregnancy BMI-normal-weight (BMI 18.5-24.9) and overweight/obese (BMI>25). Given that the GDM variable is binary, we used a WLSMV estimator with theta parameterization. Several fit indices were used to evaluate the model: Root Mean Square Error of Approximation (RMSEA), Comparative Fit Index (CFI), and Standardized Root Mean Square Residual (SRMR). The RMSEA below 0.06, CFI above 0.95, and SRMR below 0.08 indicated a good fit. The RMSEA below 0.08 and CFI values higher than 0.90 indicated an acceptable fit [75]. Models were adjusted for variables that were correlated with the outcomes (GDM diagnosis at T2, depression symptoms at T3), which were parity and depression symptoms from a previous time point. Utilising G*Power [76] to calculate differences between the two groups with medium effect size, at a significance level of 5% and 80% power, a minimum of 275 controls and 27 cases were required, which was surpassed. Using the same parameters for a linear regression model with one predictor (depression or GDM) and three control variables, the minimum required total sample size was 55, which was also surpassed.

Results

Differences among women with and without GDM

Women with and without GDM did not differ across most sociodemographic, obstetric, and health-related variables (Table 1). Women with GDM had significantly higher postpartum depression scores (t(358) = -2.01, p=.045).

The prevalence of PPD among women with GDM was 21% in both the second and the third trimesters, which

 Table 1
 Descriptive characteristics and differences between women with and without GDM

Characteristics	With GDM	Without GDM (n = 327)	Difference	p
	(n=33)			
	M (SD) / n (%)	M (SD) / n (%)	$t(df) / \chi^2(df)$	
Sociodemographic variables				
Maternal age ^a	31.03 (4.21)	30.65 (4.45)	-0.47(358)	0.637
Married or cohabiting ^b	33 (100%)	322 (98.5%)	-	1.00
College/university degree or higher ^c	25 (75.8%)	252 (77.1%)	0.29(1)	0.865
Employment status, woman ^{1c}	29 (87.9%)	291 (89%)	0.04(1)	0.774
Employment status, partner ^{1c}	32 (97%)	321 (98.2%)	0.23(1)	0.493
Urban residence ^c	30 (90.9%)	255 (78%)	3.04(1)	0.113
Obstetric variables				
Gestational age at T1 ^a	24.58 (2.55)	24.22 (2.66)	-0.74(358)	0.463
Gestational age at T2 ^a	33.42 (1.25)	33.32 (1.34)	-0.43(358)	0.671
Planned pregnancy ^c	23 (69.7%)	211 (64.5%)	0.35(1)	0.553
Primiparity ^c	15 (45.5%)	189 (57.8%)	186(1)	0.173
Caesarean section ^{2 c}	7 (21.2%)	72 (22%)	0.01(1)	0.915
Anthropometric variables				
Pre-pregnancy BMI (kg/m²) ^a	23.73 (3.68)	23.74 (4.24)	0.13(358)	0.990
Gestational weight gain at mid-pregnancy ^a	9.74 (4.77)	11.04 (4.67)	1.47(348)	0.142
Gestational weight gain at the end of pregnancy ^a	12.15 (5.96)	14.57 (6.03)	2.20(356)	0.029*
Medical history				
Chronic illness ^b	4 (12.1%)	48 (14.7%)	-	1.00
Mental health				
EPDS score T1 ^a	9.09 (5.52)	7.68 (4.76)	-1.60(358)	0.111
EPDS score T2 ^a	9.03 (4.92)	7.34 (4.69)	-1.97(358)	0.050
EPDS score T3 ^a	10.09 (5.83)	8.17 (5.16)	-2.01(358)	0.045*

Note. *p<.05. ¹ Employment status, woman/partner: 0=unemployed, 1=employed or partially employed; ² Caesarean section: 0=vaginal/instrumental vaginal birth, 1=planned or emergency caesarean section; a Student t-test; b Fisher's exact test; c x² test; GDM – gestational diabetes mellitus; BMI – body mass index; EPDS – Edinburgh Postnatal Depression Scale

did not significantly differ from the 15% in the second trimester ($\chi^2(1)$ =0.79, p=.374) and 14% in the third trimester ($\chi^2(1)$ =1.22, p=.270) among women without GDM. However, the postpartum depression prevalence of 39% in women with GDM was significantly higher than the prevalence of 20% in women without GDM ($\chi^2(1)$ =7.01, p=.008).

Correlation analyses

Total sample

The correlation analyses (Table 2) showed that GDM was not associated with depression symptoms during pregnancy at T1 but had a positive correlation with depression symptoms during pregnancy at T2 and postpartum depression symptoms at T3. GDM was also correlated with lower gestational weight gain at the end of the pregnancy. At T1, only having a chronic illness was positively correlated with depressive symptoms.

Pre-pregnancy normal-weight and overweight/obese subgroups

Correlation analyses stratified by pre-pregnancy BMI showed different patterns between the normal-weight and overweight/obese subgroups. In the normal-weight group, GDM was significantly associated with depression symptoms during pregnancy (T1 and T2) and postpartum (T3), while these associations were not found among overweight/obese women. Furthermore, in the normal-weight group, parity was negatively correlated with postpartum depression symptoms. In the overweight/obese group, none of the sociodemographic, medical or obstetric variables were correlated with GDM or depression symptoms.

Path models of the relationship between PPD and GDM *Total sample*

We tested a path model where depression symptoms at T1 predicted GDM at T2, and GDM at T2 predicted depression symptoms at T3. The model was adjusted for depression symptoms from previous time points. The fit of the model was good ($\chi^2(2)=6.62$, $\chi^2/df=3.31$; RMSEA=0.08, SRMR=0.04, CFI=0.97). Autoregressive coefficients for depression symptoms were significant ($\beta_{T1-T2}=0.66$, p<.001; $\beta_{T1-T2}=0.57$, p<.001). Depression symptoms at T1 predicted GDM at T2 (β =0.18, p=.039), while GDM at T2 did not predict postpartum depression symptoms at T3 (β =0.12, p=.142).

Pre-pregnancy normal-weight and overweight/obese subgroups

We conducted a multigroup path analysis on normal-weight (n=247) and overweight/obese (n=113) subgroups, testing the same model as in the total sample and adjusting for depression scores from a previous time

Table 2 Correlation analysis for the total sample (N = 360) and subgroups stratified by pre-pregnancy BMI as normal pre-pregnancy BMI subgroup (N = 247; below the diagonal) and overweight/obese subgroup (N = 113; above the diagonal]

	Total sample	mple								Subgro	nps basec	Subgroups based on pre-pregnancy BMI	regnanc	y BMI					
	-	2.	3.	4.	5.	9	7.	8	6	1.	2.	3.	4.	5.	9.	7.	8	6.	10.
1. EPDS score T1										,	0.64	0.48	- 0.04	-0.11	-0.02	0.07	0.03	0.17	- 0.01
2. EPDS score T2	**09.0	1								0.59	1	0.61	-0.03	-0.05	-0.04	0.02	-0.10	0.15	-0.07
3. EPDS score T3	0.46	0.53**	1							0.45	0.49	1	-0.04	-0.03	-0.17	-0.03	-0.02	60.0	-0.08
4. GDM ¹	0.08	0.10*	0.11*	1						0.14*	0.17**	0.18**	1	0.05	0.03	-0.10	-0.16	0.18	0.14
5. Maternal age	-0.04	-0.02	- 0.09	0.03	1					-0.01	-0.00	-0.11	0.02	1	0.30	-0.03	-0.09	0.38	- 0.08
6. Education ²	-0.03	-0.02	-0.02	-0.01	0.23	1				-0.06	0.01	-0.11	-0.03	0.20	,	0.00	0.02	80.0	-0.08
7. GWGT2	0.04	-0.00	-0.01	- 0.08	-0.02	-0.06	1			-0.03	0.02	0.04	-0.07	0.03	-0.10	,	0.88 **	-0.14	-0.03
8. GWGT3	0.01	-0.04	-0.01	-0.12*	-0.06	-0.13*	*88.0	1		0.00	-0.00	0.02	-0.10	-0.05	-10	0.82**	,	-0.25**	-0.07
9. Parity ³	0.04	0.07	-0.07	0.07	0.32**	0.00	-0.06	-0.13*	,	-0.02	0.04	-0.14*	0.02	0.30	-0.06	-0.06	-0.06	1	0.07
10. Chronic illness ¹ 0.12*	0.12*	0.02	0.02	0.02 -0.02	0.10	-0.02	-0.07	-0.06	60.0	0.18**	90:0	0.07	- 0.09	0.17**	0.01	-0.05	0.10	0.10	1
														6					

Note. *P < .05; **P < .01; '4DM/Chronic illness. 0=No, 1 = Yes, 'Education: 0=elementary school and high school; 1 = college or university degree or higher; ³Parity: 0=primipara, 1=multipara; EPDS – Edinburgh Postnatal Depression Scale; BMI – body mass index; GDM – gestational diabetes mellitus; GWG – gestational weight gain

point. The model had a good fit ($\chi^2(4)$ =7.03, χ^2/df =1.76, RMSEA=0.07, SRMR=0.04, CFI=0.98). Different results were obtained for the two subgroups (Fig. 1).

In the group of women with a normal pre-pregnancy BMI, depression symptoms at T1 predicted GDM at T2 (β =0.27, p=.005) and GDM at T2 predicted post-partum depression symptoms at T3 (β =0.22, p=.023). In the overweight/obese subgroup, neither antenatal depression symptoms at T1 predicted GDM at T2 (β = -0.07, p=.683) nor did GDM at T2 predict postpartum depression symptoms at T3 (β = -0.03, p=.837). After we adjusted the models for parity, since it was correlated with depression scores at T3, the results remained the same.

Discussion

A bidirectional relationship between diabetes and depression is well-documented in the general population [46], but findings in the peripartum population remain limited. Therefore, the aim of this study was to examine the bidirectional relationship between GDM and PPD. Our study demonstrated a positive bidirectional relationship between GDM and PPD in women with a normal pre-pregnancy BMI. Among these women, higher mid-pregnancy depression symptoms predicted subsequent GDM diagnosis, and GDM predicted postpartum depression symptoms. In the total sample, antenatal depression symptoms predicted GDM, whereas GDM did not predict postpartum depression symptoms. In contrast, no significant associations were found among women who were overweight/obese prior to pregnancy. These findings suggest that pre-pregnancy body weight has a moderating role in the bidirectional relationship between GDM and PPD, with this association evident only in normal-weight women, who may be particularly sensitive to the interplay between peripartum metabolic and mental health issues.

The prevalence of PPD in women with GDM was 21% in the second and third trimesters and 39% in the post-partum. Depression rates were similar among women with and without GDM, except for the higher prevalence of postpartum depression among women with GDM. The observed PPD rates are similar to other studies on women with GDM, which found a PPD prevalence of around 30% [49, 77]. These rates are somewhat higher than the usually reported PPD prevalence in general [25–30] or Croatian peripartum population [78, 79], but in line with a recent umbrella review that reported a prevalence around 26% [80]. Moreover, higher prevalence rates might reflect the negative impact of the coronavirus pandemic on maternal mental health, as described in many studies [31, 32, 81].

The key finding in this study is evidence of a bidirectional relationship, in which antenatal depression symptoms at mid-pregnancy predicted subsequent GDM diagnosis, and GDM diagnosis predicted postpartum depression symptoms among normal-weight women only, but not in women with overweight/obesity. These findings remained significant after adjusting for empirically relevant covariates (i.e., parity and depression from a previous time point).

Regarding antenatal depression raising the risk for GDM, our findings show a positive relationship in the normal-weight subsample. Conversely, without BMI stratification, some studies found no such association [49, 64, 82, 83], but others indicated a positive relationship [58, 59]. Other studies found that pregnancy hypergly-caemia or uncontrolled glycaemic status were associated with antenatal depressive symptoms [84–86]. One explanation may be that emotional eating, often associated with depressive symptoms [87], may potentially alter gut microbiota and contribute to inflammation, insulin resistance and the risk for GDM [88].

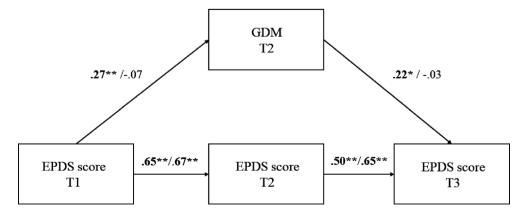


Fig. 1 Path model of the relationship between GDM and depression symptoms during the peripartum period in normal-weight (N=247) and overweight/obese (N=113) subgroups. *Note*. *p < .05; **p < .01; the results (β) for the normal-weight subgroup are on the left, and for the overweight/obese subgroup on the right (separated by a slash); EPDS – Edinburgh Postnatal Depression Scale; GDM – gestational diabetes mellitus

Regarding GDM raising the risk for postpartum depression, similar to our null findings in the total sample, some studies without stratifying by pre-pregnancy BMI status found that GDM was not associated with postpartum depression [49–51, 53, 54]. A prospective study with four measures across the peripartum period found that neither GDM or blood glucose levels were associated with PPD in the second and third trimester or postpartum, nor with any depression trajectory [52]. In contrast, a large population-based study on over 700,000 Swedish women found that GDM was a risk factor for clinical depression up to a year postpartum [89].

A randomised control trial provided further evidence showing that GDM treatment (dietary advice, glucose monitoring, insulin) decreased the incidence of postpartum depression symptoms in the intervention group [90]. However, they did not disclose the GDM diagnosis to the control group, excluded severe GDM cases, and updated their exclusion criteria during the study. Another study found that only when comorbid with antenatal depression, GDM predicted postpartum depression [91]. Notably, others showed that both insulin resistance and mental health fluctuate during the peripartum period, with small associations among them [92]. A large-scale umbrella review and two meta-analyses involving a combined population of over 7,500,000 participants, found that GDM significantly increased the risk of postpartum depression symptoms [47, 55, 57], yet methodological issues, such as high heterogeneity, limited conclusions. As normal body weight is the most common pre-pregnancy BMI category [93-95], those results might be a reflection of the relationship occurring among normal-BMI women, which might be at least partially driving the overall effect, as found in our study when stratified by BMI status. Therefore, BMI stratification might yield different results and should be incorporated in sensitivity and subgroup analyses in future meta-analyses.

Regarding the bidirectional relationship found in our study, some studies similarly indicated a positive relationship [65], which was supported by a recent review paper [61]. On the other hand, one review reported no consensus [63], suggesting high variability across studies. A study utilising BMI stratification [65], similar to our results, found different effects among different BMI categories. The latter study found effects between antenatal depression and GDM in the non-obese (combined normal-weight and overweight) group only and not in the obese group [65]. However, grouping overweight and obese categories, as done in our study, seems more theoretically appropriate due to shared excess body weight, metabolic similarities, and other characteristics among the two groups [96–98]. Nevertheless, pre-pregnancy BMI appears to have an important role in the complex interplay between GDM and mental health during the peripartum period, which warrants further clarification.

Although mechanisms linking PPD and GDM are unclear, our findings could suggest distinct pathways and increased sensitivity to the biopsychosocial changes arising from impaired mental and metabolic health among the normal-weight subgroup. Conversely, the absence of an association among overweight/obese subgroup implies different underlying mechanisms that may be specific to higher adiposity or excess weight. For example, both PPD and GDM are related to elevated insulin resistance and inflammation [99-101]. Furthermore, women with normal weight typically have lower baseline inflammation and greater insulin sensitivity than obese women, who have chronic upregulation of inflammation and insulin resistance due to higher adiposity [102, 103]. Therefore, women who are overweight/obese may already have pre-existing altered metabolic or inflammatory markers and higher baseline risks for GDM and PPD [3, 4, 104], which might obscure effects of antenatal depression on GDM, and GDM on postpartum depression. On the other hand, women with normal weight may experience different than usual metabolic and inflammatory disruptions associated with antenatal PPD, thus elevating the risk for GDM, and could be more vulnerable to the depressogenic effects of GDM in the postpartum period.

Psychosocially, some physiological features of PPD, such as appetite changes, sleep disturbances, and diminished energy, may indirectly contribute to GDM risk and could represent more pronounced differences in behaviour among women with normal weight, who usually maintain better eating practices and physical activity than women with overweight and obesity [105]. Also, the diagnosis of GDM may be more unexpected and changes to their lifestyle in terms of managing the disease with diet, exercise or medication, more unfamiliar to women of normal-weight. Women who are overweight and obese may receive earlier antenatal or even preconception counselling regarding dieting and nutrition [106] compared to normal-weight women who may receive it only upon GDM diagnosis, usually at mid-pregnancy. One study pointed out that underweight and normal-weight women received stricter medical advice on gestational weight gain (GWG), which was below the global GWG recommendations and, in turn, had the highest proportion of inadequate GWG, whereas women with overweight BMI received weight gain advice ending above the global recommendations and had more excessive GWG [107]. Therefore, women with normal weight might have more stringent GWG expectations. However, if women experience elevated blood glucose levels despite dieting, they might feel stressed over losing control over GDM [108], which can also contribute to higher fasting

glucose levels [109]. Additionally, depression and stress are related to emotional eating [87] and poorer glycaemic control [22], which can enhance the fear regarding their own and the baby's health [108], potentially creating a vicious cycle of adverse effects.

Conversely, obese women might already have prior experience with GDM [110] and dieting throughout life [111]. Also, misconceptions that GDM affects only overweight people may increase stigma or negative emotions regarding the diagnosis in normal-weight women. Moreover, clinical features of depression may differ across BMI categories, whereas obese participants were shown to have more atypical depression [112], characterised by low mood, decreased interest, low energy, feelings of inadequacy, higher inflammation, and obesity-related diseases [113]. It is hypothesised that atypical depression raises the risk for GDM through more indirect behaviours (e.g., increased appetite), which may be less apparent among obese women [65]. Nevertheless, there are no studies investigating psychosocial differences related to a GDM diagnosis among women with different BMIs to provide evidence-based explanations.

Strengths and limitations

The main strength of this study is its prospective three-wave design across the peripartum period, which enabled temporal causal inferences. In a field of predominantly cross-sectional studies, this is one of the few studies that longitudinally and bidirectionally investigated the relationship between PPD and GDM. Moreover, we stratified models by pre-pregnancy BMI, as shown important in a previous study [65], and we controlled for empirically relevant covariates.

However, some limitations should be addressed. First, continuous measures of fasting blood glucose levels or access to medical records with glucose tolerance test results would provide more accurate measures of metabolic functioning disturbances. Such finer measures could give an approximate critical level of the metabolic dysfunction at which the relationship with PPD is more prominent. Furthermore, online recruitment may have underrepresented certain groups and possibly reflected those of higher socioeconomic status. Also, due to a small proportion of women with underweight pre-pregnancy BMI, they were excluded. A lack of a clinical interview to diagnose PPD is another limitation, as some studies found a more robust relationship with GDM when clinical assessments of PPD were included [57]. When it is not feasible to administer the clinical interview, a new diagnostic tool for PPD can also be useful [114]. Additionally, we did not examine overt diabetes, which is pre-existing diabetes detected in pregnancy or a more severe form of hyperglycaemia that is associated with worse outcomes [115], nor did we measure new-onset PPD by excluding women with a history of depression, which might jointly obscure the true relationship between GDM and PPD. However, we did control for antenatal depression symptoms in the path analyses.

Given the increasing prevalence of GDM and PPD, along with the far-reaching adverse effects of both conditions, more longitudinal research is needed to clarify their complex relationship. As PPD fluctuates throughout the peripartum period [116], it should be assessed multiple times across the entire postpartum year to uncover the long-term duration of the observed impact of GDM on postpartum mental health. Investigating the dynamics between mental and metabolic health in larger samples and more disadvantaged populations at risk for both conditions is another research opportunity. This could foster the understanding of how some social determinants of health, such as access to healthy foods, housing, and financial security, may impact the relationships we have observed. Also, including a measure of perceived control over GDM management [117] could be an important mediator for mental health. Furthermore, potential covariates of both conditions, such as physical exercise, could be investigated in future studies. Weight classification other than BMI should also be explored, as metabolically obese but normal-weight BMI individuals have previously been identified [118]. Unravelling PPD phenotypes that are more strongly related to hyperglycaemia during pregnancy and identifying critical time points of increased sensitivity could also provide valuable insights. Understanding the biopsychosocial mechanisms and determining how risk factors interact [119], holds the potential for new therapeutic and preventative avenues for both conditions.

Conclusion

This study demonstrated a bidirectional relationship in which antenatal depression symptoms predicted subsequent GDM diagnosis, and GDM diagnosis predicted postpartum depression symptoms among pre-pregnancy normal-weight women only, and not in overweight or obese women. These results highlight the complex and multifaceted nature of the dynamics between GDM and PPD, which appears to be dependent on pre-pregnancy BMI.

Our findings, alongside the limited literature, suggest that normal-weight women may be particularly sensitive to the biological, psychological, and social disturbances associated with antenatal depression, which may increase their risk of GDM. In turn, GDM diagnosis in normal-weight women may exacerbate metabolic and psychological strain, thereby increasing the risk of postpartum depressive symptoms, even months after the GDM diagnosis.

Clinical application

These findings underscore the necessity of considering pre-pregnancy BMI both in clinical practice and future research on the interrelation between GDM and PPD. Given that the majority of peripartum women are of normal weight and a considerable portion experience PPD and GDM, further investigation of this relationship is warranted to advance risk assessments and therapeutic strategies.

Integrating both physical and mental health aspects into antenatal interventions seems crucial for delivering high-quality care. Also, recognising normal-weight women as an at-risk group for the interplay between mental and metabolic health can facilitate early identification and targeted prevention. Healthcare providers should closely monitor the mental health of women early in pregnancy, provide education and support in maintaining good metabolic health (e.g., promoting daily exercise and avoiding high-carbohydrate diets), and take timely preventative actions, ultimately reducing the risks and burden of both conditions.

Abbreviations

BMI Body mass index
CFI Comparative Fit Index
GDM Gestational diabetes mellitus
EPDS Edinburgh Postnatal Depression Scale

IADPSG International Association of the Diabetes in Pregnancy Study

Group

PPD Peripartum depression

RMSEA Root Mean Square Error of Approximation SRMR Standardized Root Mean Square Residual

GWG Gestational Weight Gain

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Author contributions

Conceptualisation: MŽ, SNR; Data curation: MM; Formal analysis: MM, MŽ; Funding acquisition: SNR; Investigation: SNR, MŽ, MM, JŠ, MB; Methodology: SNR, MŽ, MM, JŠ, MB; Project administration: SNR; Writing original draft: MŽ, MM; Writing review & editing: JŠ, MB, SNR. All authors approved final version.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Catholic University of Croatia (Class: 641-03/21 – 03/21; No: 498 – 16/2-22-04).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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