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Gestational diabetes mellitus complicated with depression in pregnant women: a biopsychosocial analysis and intervention strategies

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Abstract

Objective To investigate the incidence and influencing factors of comorbid depression in pregnant women with gestational diabetes mellitus (GDM), analyze their interaction effects, and propose targeted intervention strategies.

Methods A retrospective analysis was conducted on clinical data from 746 pregnant women who underwent regular prenatal examinations at our hospital from March 2022 to March 2024. All participants were screened for GDM using the oral glucose tolerance test (OGTT) at 24–28 weeks of gestation. Based on GDM diagnosis, the cohort was divided into GDM and non-GDM groups, with demographic and clinical indicators compared between groups. For GDM patients, the Hamilton Depression Rating Scale-17 (HAMD-17) was used to assess depressive symptoms, categorizing them into a negative screened group (HAMD-17 score > 7) and a positive screened group (HAMD-17 score ≤ 7). Univariable analysis was performed to identify potential influencing factors, followed by multivariable logistic regression to determine independent associated factors and interaction effects.

Results Among 746 participants, 84 were diagnosed with GDM (incidence: 11.26%). Univariable analysis revealed that GDM was significantly associated with advanced maternal age (≥ 35 years), pre-pregnancy overweight/obesity (BMI ≥ 24 kg/m^2), adverse pregnancy history, family history of diabetes, polycystic ovary syndrome (PCOS), poor dietary habits, insufficient physical activity, poor sleep quality, and elevated serum estradiol (E2), progesterone (P), and cortisol (Cor) levels ($P < 0.05$). Multivariable logistic regression confirmed these factors as independent associated factors for GDM ($P < 0.05$). Among the 84 GDM patients, 27 (32.14%) had comorbid depression. Univariable analysis identified adverse pregnancy history, elevated E2/P/Cor levels, personal/family history of depression, unintended pregnancy, poor glycemic control, GDM-related complications, and low social support (SSRS score < 33) as potential associated factors for depression ($P < 0.05$). Multivariable analysis further demonstrated that adverse pregnancy history, elevated E2/P/Cor levels, prior depression history, poor glycemic control, and low social support were independent associated factors for comorbid depression ($P < 0.05$). Interaction analysis using Jvenn (https://jvenn.toulouse.inrae.fr/app/example.html) revealed that adverse pregnancy history and elevated E2/P/Cor levels were shared influencing factors for both GDM and comorbid depression.

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Conclusions (1) Advanced maternal age, pre-pregnancy overweight/obesity, adverse pregnancy history, diabetes family history, PCOS, poor lifestyle habits, and elevated E2/P/Cor levels are independent associated factors for GDM. (2) Adverse pregnancy history, elevated E2/P/Cor levels, prior depression history, poor glycemic control, and low social support are independent associated factors for comorbid depression in GDM patients. (3) Adverse pregnancy history and elevated E2/P/Cor levels represent shared interaction factors influencing both conditions.

Keywords Gestational diabetes mellitus, Depression, Associated factors, Interaction effects, Intervention strategies

Gestational diabetes mellitus (GDM), one of the most prevalent metabolic disorders during pregnancy, has shown a sustained upward trend in global incidence [1, 2]. This condition is not only strongly associated with short and long term maternal complications, such as gestational hypertension and increased cesarean delivery rates, but may also exert profound impacts on offspring health, including macrosomia, neonatal hypoglycemia, and elevated risks of metabolic syndrome in later life [3, 4].

In recent decades, there has been a growing recognition that health and disease are influenced not only by biological processes but also by psychological and social factors. This shift in perspective has led to the widespread adoption of the "biopsychosocial model" in modern medicine, which emphasizes the integration of biological, psychological, and social dimensions in understanding and treating medical conditions. Originating from the work of George L. Engel in the 1970s, the biopsychosocial model challenges the reductionist biomedical paradigm by highlighting the importance of patient context, behavior, and emotional well-being in shaping disease outcomes [5, 6]. This framework has become particularly relevant in chronic diseases, including diabetes and mental health disorders, where lifestyle, stress, and social support play central roles in pathogenesis and prognosis.

With the paradigm shift toward a "biopsychosocial" model in modern medicine, researchers have increasingly focused on the mental health of women with GDM, particularly the comorbidity of depression. Existing studies indicate that the incidence of depression in GDM patients is significantly higher than in healthy pregnant populations, and depressive states may exacerbate metabolic dysregulation and adverse pregnancy outcomes by impairing treatment adherence and aggravating insulin resistance, thereby forming a vicious cycle [7–9]. However, significant gaps remain in understanding the epidemiological characteristics, influencing factors, and interaction mechanisms between GDM and depression, posing challenges to the development of precise clinical interventions.

From a pathophysiological perspective, the development of GDM is closely linked to pregnancy-specific hormonal changes. During mid-to-late gestation, elevated levels of placental steroid hormones, such as estradiol (E2) and progesterone (P), contribute to insulin resistance by antagonizing insulin signaling and promoting lipolysis [10]. Concurrently, activation of the hypothalamic-pituitary-adrenal (HPA) axis leads to increased cortisol (Cor) secretion, which may further impair pancreatic β-cell function. Notably, these metabolic hormonal alterations overlap with neuroendocrine mechanisms underlying depression. For instance, chronic elevation of Cor—a central hormone in stress responses—may induce depressive symptoms through hippocampal neuronal damage and dysregulation of monoamine neurotransmitter metabolism [11]. Such dual roles of biomarkers suggest that GDM and depression may share common pathophysiological pathways. Nevertheless, current research predominantly focuses on isolated disease domains, with insufficient exploration of their interactions.

In clinical practice, the impact of psychosocial factors on the mental health of GDM patients has garnered growing attention. Traditional associated factors such as pre-pregnancy overweight/obesity and adverse pregnancy history are strongly associated with GDM onset, and these populations often experience psychological burdens, including body image distress and fertility-related anxiety [12]. Additionally, disease perception stress stemming from a family history of diabetes and the psychological toll of fertility treatments in women with polycystic ovary syndrome (PCOS) may act as depressive triggers. Crucially, glycemic control—the cornerstone of GDM management—depends not only on medical interventions but also on patients' psychological well-being. Studies demonstrate that depressive symptoms can undermine glycemic control by reducing adherence to dietary regimens and physical activity, while glucose fluctuations may intensify negative emotions, creating a bidirectional "metabolic-psychological" vicious cycle [13]. However, current analyses of associated factors for GDM-depression comorbidity remain largely unidimensional, lacking systematic investigation into the interactions among biomarkers, clinical features, and psychosocial determinants.

Against this background, this study aims to address the following scientific questions through a large-sample retrospective analysis: (1) The actual incidence and demographic distribution of comorbid depression in GDM patients; (2) Independent associated factors for GDM onset, particularly the interaction between hormonal fluctuations and lifestyle factors; (3) Specific predictors of depression in GDM patients, including associations

among biomarkers, clinical traits, and social support systems. By systematically addressing these questions, this research seeks to establish a theoretical foundation for constructing a mental health risk assessment model in GDM populations and to inform the development of integrated biopsychosocial intervention strategies.

Material and method

Participant inclusion

This retrospective study analyzed clinical data from 746 pregnant women who underwent regular prenatal examinations at our hospital between March 2022 and March 2024. Inclusion criteria: ① women who initiated prenatal care at our institution between 10 and 14 weeks of gestation, as confirmed by first-trimester ultrasound; ② Completion of a standard oral glucose tolerance test (OGTT) at 24–28 weeks of gestation; ③ Age 20–45 years; ④ Absence of major organ dysfunction (e.g., cardiac, hepatic, or renal failure); ⑤ No severe cognitive or communication impairments; ⑥ Ethical approval and written informed consent obtained. Exclusion criteria: ① Pre-existing diabetes (type 1, type 2, or other specific types); ② Pre-pregnancy psychiatric disorders (e.g., depression, anxiety, bipolar disorder) or current antidepressant use; ③ Neurological diseases (e.g., epilepsy, encephalitis); ④ Severe complications (e.g., gestational hypertension, preeclampsia, thyroid dysfunction); ⑤ Intellectual disability or low education level impairing questionnaire comprehension; ⑥ Malignancy, autoimmune disorders, or long-term corticosteroid use; ⑦ Missing critical data (e.g., incomplete OGTT or psychological assessments); ⑧ Infectious diseases (e.g., hepatitis B/C, syphilis, HIV); ⑨ Refusal to participate or loss to follow-up, which was operationally defined as failure to complete either the OGTT at 24–28 weeks of gestation or the depression-related questionnaires at 28–32 weeks despite at least three contact attempts via phone or WeChat.

GDM diagnostic criteria and grouping [14]

GDM was diagnosed at 24–28 weeks using OGTT with the following thresholds: fasting blood glucose (FBG) ≥ 5.1 mmol/L, 1-hour postprandial glucose ≥ 10.0 mmol/L, 2-hour postprandial glucose ≥ 8.5 mmol/L, or glycated hemoglobin (HbA1c) ≥ 6.5%. Participants meeting ≥ 1 criterion were classified into the GDM group; others comprised the non-GDM group.

Depression diagnostic criteria and grouping [15]

(1) Clinical symptoms: Core symptoms: Depressed mood, loss of interest/pleasure, fatigue/energy loss; Additional symptoms: Reduced concentration, low self-esteem, guilt/worthlessness, pessimism, suicidal ideation, sleep disturbances, appetite changes. Diagnosis required ≥ 2 core symptoms + ≥ 2 additional symptoms persisting ≥ 2 weeks.

(2) Scale assessment: The 17-item Hamilton Depression Rating Scale (HAMD-17) was used with the following thresholds: Positive: 0–7 points; Probable depression: 8–20 points; Definite depression: 21–35 points; Severe depression: 36–54 points. GDM patients with HAMD-17 > 7 were assigned to the negative screened group; others to the positive screened group.

Data collection

All data for this retrospective study were collected through electronic medical record (EMR) chart review from the hospital's obstetric database. Data extraction was performed by two trained researchers using a standardized form to ensure consistency and completeness. The following variables were obtained:

(1) Demographic characteristics: Age, marital status, education level, residence, occupation, monthly income.

(2) Clinical variables: Pre-pregnancy BMI, gravidity, parity, adverse pregnancy history (prior GDM, unexplained miscarriage, preterm birth, macrosomia, fetal anomalies), family history of diabetes, polycystic ovary syndrome (PCOS). Lifestyle-related variables were assessed through structured questionnaires at the first prenatal visit. Poor dietary habits were defined as frequent consumption of high-fat or high-sugar foods and/or irregular meal patterns, such as skipping breakfast or having fewer than two proper meals per day, occurring ≥ 3 times per week. Insufficient physical activity was defined as engaging in < 3 sessions per week of ≥ 30 min of moderate-intensity exercise (e.g., brisk walking, prenatal yoga). Poor sleep quality was defined as self-reported sleep duration < 6 h per night or the presence of insomnia symptoms (difficulty falling or staying asleep) ≥ 3 times per week. These lifestyle variables were converted into binary categorical variables (0 = good, 1 = poor) for use in the statistical models. Serum levels of estradiol (E2), progesterone (P), and cortisol (Cor) were measured during the second trimester using chemiluminescence immunoassay.

(3) Depression-specific factors: Personal/family history of depression, unintended pregnancy, glycemic control status (HbA1c ≥ 6.5% defined poor control), GDM-related complications, and low social support (Social Support Rating Scale [SSRS] score < 33) [16].

Interaction analysis

Jvenn (https://jvenn.toulouse.inrae.fr/app/example.html) was employed to analyze shared associated factors between GDM and comorbid depression. GDM cases were labeled "GDM," while GDM with depression cases were labeled "GDM&D." Input datasets for both groups were analyzed to identify overlapping factors.

Table 1 Incidence and univariable analysis of GDM

Factor	GDM group (*n*=84)	Non-GDM group(*n*=662)	*P*
Age (n)			0.003
< 35 years	67 (79.76)	599 (90.48)	-
≥ 35 years	17 (20.24)	63 (9.52)	-
Marital status (n)			0.826
Unmarried	19 (22.62)	163 (1.94)	-
Married	60 (71.43)	464 (5.52)	-
Divorced	4 (4.76)	32 (38.10)	-
Widowed	1 (1.19)	3 (3.57)	-
Education level (n)			0.540
Secondary school	21 (25.00)	165 (24.92)	-
High school	40 (47.62)	279 (42.15)	-
College or above	23 (27.38)	218 (32.93)	-
Residence (n)			0.402
Rural	16 (19.05)	153 (23.11)	-
Urban	68 (80.95)	509 (76.89)	-
Occupation (n)			0.618
Primary industry	6 (7.14)	52 (7.85)	-
Secondary industry	23 (27.38)	213 (32.18)	-
Tertiary industry	55 (65.48)	397 (59.97)	-
Monthly income (n)			0.871
< 1000 CNY	10 (11.90)	59 (8.91)	-
1000 ~ 2999 CNY	26 (30.95)	218 (32.93)	-
3000 ~ 7999 CNY	38 (45.24)	317 (47.89)	-
8000 ~ 19,999 CNY	8 (9.52)	51 (7.70)	-
≥ 20,000 CNY	2 (2.38)	17 (2.57)	-
Pre-pregnancy BMI (n)			0.001
< 24 kg/m^2	51 (60.71)	508 (76.74)	-
≥ 24 kg/m^2	33 (39.29)	154 (23.26)	-
Gravidity (n)			0.469
1 ~ 2 times	60 (71.43)	497 (75.08)	-
≥ 3 times	24 (28.57)	165 (24.92)	-
Parity (n)			0.428
0 ~ 2 times	73 (86.90)	594 (89.73)	-
≥ 3 times	11 (13.10)	68 (10.27)	-
Adverse pregnancy history (n)	12 (14.29)	39 (5.89)	0.004
Family history of diabetes (n)	26 (30.95)	123 (18.58)	0.008
PCOS history (n)	12 (14.29)	36 (5.44)	0.002
Poor dietary habits (n)	49 (58.33)	298 (45.02)	0.021
Insufficient physical activity (n)	74 (88.10)	513 (77.49)	0.025
Poor sleep quality (n)	25 (29.76)	131 (19.79)	0.034
E2 (pmol/L)	26878.41 ± 8249.98	32480.60 ± 8163.00	< 0.001
P (nmol/L)	173.56 ± 54.85	196.60 ± 47.08	< 0.001
Cor (nmol/L)	621.52 (456.29, 801.33)	525.85 (429.24, 619.24)	< 0.001

Table 2 Assignment table

Variable	assignment
Age	< 35 years = 0, ≥35 years = 1
BMI	< 24 kg/m^2 = 0, ≥ 24 kg/m^2 = 1
Adverse pregnancy history	No = 0, Yes = 1
Family history of diabetes	No = 0, Yes = 1
PCOS history	No = 0, Yes = 1
Dietary habit	Good = 0, Poor= 1
Physical activity	Good = 0, Poor= 1
Sleep quality	Good = 0, Poor= 1
E2	Continuous variable
P	Continuous variable
Cor	Continuous variable

Statistical analysis

Data were analyzed using SPSS 26.0. Categorical variables [n (%)] were compared via χ^2 tests. Normally distributed continuous variables (mean ± SD) were analyzed using independent t-tests; non-normal variables [median (P25, P75)] were assessed via Mann-Whitney U tests. Univariable analysis identified potential associated factors, followed by multivariable logistic regression to determine independent predictors. Statistical significance was set at $P < 0.05$.

Results

Incidence and univariable analysis of GDM

Among the 746 pregnant women, 84 were diagnosed with GDM, yielding an incidence rate of 11.26%. Univariable analysis revealed that GDM development was significantly associated with advanced maternal age (≥ 35 years), pre-pregnancy overweight/obesity (BMI ≥ 24 kg/m^2), adverse pregnancy history, family history of diabetes, polycystic ovary syndrome (PCOS), poor dietary habits, insufficient physical activity, poor sleep quality, and elevated serum estradiol (E2), progesterone (P), and cortisol (Cor) levels (all $P < 0.05$). In contrast, marital status, educational level, residence, occupation, monthly income, gravidity, and parity showed no significant correlations ($P > 0.05$) (Table 1).

Multivariable logistic regression analysis of GDM associated factors

Multivariable logistic regression analysis demonstrated that advanced maternal age (≥ 35 years), pre-pregnancy overweight/obesity (BMI ≥ 24 kg/m^2), adverse pregnancy history, family history of diabetes, PCOS history, poor dietary habits, insufficient physical activity, poor sleep quality, and elevated serum estradiol (E2), progesterone (P), and cortisol (Cor) levels were all independently associated with the onset of GDM ($P < 0.05$) (Tables 2 and 3).

Table 3 Multivariable logistic regression analysis of GDM incidence

Variable	β	SE	Wald	*P*	OR (95%CI)
Age (1)	0.996	0.363	7.525	0.006	2.708 (1.329, 5.517)
BMI (1)	0.870	0.288	9.117	0.003	2.387 (1.357, 4.198)
Adverse pregnancy history (1)	1.500	0.439	11.670	0.001	4.481 (1.895, 10.596)
Family history of diabetes (1)	0.801	0.304	6.951	0.008	2.228 (1.228, 4.043)
PCOS history (1)	1.141	0.441	6.688	0.010	3.129 (1.318, 7.428)
Dietary habit (1)	0.588	0.274	4.622	0.032	1.801 (1.053, 3.079)
Physical activity (1)	0.917	0.403	5.178	0.023	2.501 (1.136, 5.507)
Sleep quality (1)	0.737	0.310	5.643	0.018	2.089 (1.138, 3.836)
E2	0.000	0.000	26.803	< 0.001	1.000 (1.000, 1.000)
P	−0.011	0.003	14.361	< 0.001	0.989 (0.984, 0.995)
Cor	0.005	0.001	31.026	< 0.001	1.005 (1.003, 1.007)

Analysis of depression status and influencing factors in GDM pregnant women

The survey revealed that 27 out of 84 GDM pregnant women (32.14% incidence) exhibited comorbid depression. Univariable analysis indicated that depression in GDM patients was significantly associated with adverse pregnancy history, elevated serum E2, P, and Cor levels, history of depression, family history of depression, unplanned pregnancy, poor glycemic control, GDM complications, and low social support (SSRS score < 33) ($P < 0.05$). No statistically significant correlations were observed with age, marital status, education level, residential area, occupation, monthly income, pre-pregnancy BMI, gravidity, parity, family history of diabetes, history of PCOS, dietary habits, exercise habits, or sleep quality ($P > 0.05$) (Table 4).

Multivariable logistic regression analysis of depression in pregnant women with GDM

Multivariable Logistic regression analysis showed that adverse pregnancy history, elevated serum E2, P, Cor levels, previous depression history, poor blood glucose control, and low social support (SSRS < 33 points) were all independently associated with depression among pregnant women with GDM ($P < 0.05$). (Tables 5 and 6)

Analysis of interactive influencing factors and intervention strategies

Using the Jven tool (https://jvenn.toulouse.inrae.fr/app/example.html), we conducted an interaction analysis of influencing factors in GDM and GDM patients with comorbid depression. The analysis identified adverse pregnancy history and serum levels of E2, P, and Cor as common influencing factors in both groups (Fig. 1).

Discussion

This retrospective study analyzed clinical data from 746 pregnant women to systematically investigate the incidence, associated factors, and interactions between gestational diabetes mellitus (GDM) and comorbid depression, revealing complex associations between metabolic dysregulation and mental health issues. The discussion will elaborate on epidemiological characteristics, multifactorial interaction mechanisms, and clinical implications, proposing integrated biopsychosocial intervention strategies.

The GDM incidence in our cohort was 11.26%, consistent with recent global reports (10-15%) [17–19] but lower than the 15-20% observed in Western populations [20], potentially attributable to ethnic differences and diagnostic criteria for oral glucose tolerance tests (OGTT). Multivariable logistic regression identified traditional GDM associated factors including advanced maternal age (≥ 35 years), pre-pregnancy overweight/obesity (BMI ≥ 24 kg/m²), adverse pregnancy history, family history of diabetes, and polycystic ovary syndrome (PCOS), aligning with prior studies [21]. Notably, elevated serum estradiol (E2), progesterone (P), and cortisol (Cor) levels were independently associated with GDM, underscoring the pivotal role of endocrine homeostasis disruption in GDM pathogenesis. Physiological studies indicate that E2 and P exacerbate insulin resistance by inhibiting insulin receptor substrate-1 (IRS-1) phosphorylation and downregulating glucose transporter GLUT4 expression [22], while Cor, as a stress hormone, may aggravate hyperglycemia via activation of gluconeogenic enzymes (e.g., PEPCK) [23]. Our study found that elevated hormone levels and behavioral factors such as poor sleep quality and physical inactivity were independently associated with GDM. Their co-occurrence may suggest a cumulative impact on metabolic outcomes, warranting further investigation. The strong association between pre-pregnancy overweight/obesity (OR = 3.12) and suboptimal dietary habits (OR = 2.45) emphasizes the importance of preconception weight management and nutritional counseling.

Furthermore, the lack of significant associations between sociodemographic variables (e.g., education level, household income) and GDM in our cohort may be attributed to the unique features of China's comprehensive prenatal care system. In recent decades, China has implemented a nationwide, government-supported maternal health program that provides standardized prenatal care to nearly all pregnant women, regardless of socioeconomic status. This system includes early pregnancy registration, routine prenatal visits, standardized

Table 4 Analysis of depression and its influencing factors in pregnant women with GDM

Factor	Negative screened group (*n* = 27)	Positive screened group (*n* = 57)	*P*
Age (n)			0.755
< 35 years	21 (77.78)	46 (80.70)	-
≥ 35 years	6 (22.22)	11 (19.30)	-
Marital status (n)			0.529
Unmarried	6 (22.22)	13 (22.81)	-
Married	19 (70.37)	41 (71.93)	-
Divorced	1 (3.70)	3 (5.26)	-
Widowed	1 (3.70)	0 (0.00)	-
Education level (n)			0.179
Secondary school	7 (25.93)	14 (24.56)	-
High school	16 (59.26)	24 (42.11)	-
College or above	4 (14.81)	19 (33.33)	-
Residence (n)			0.497
Rural	4 (14.81)	12 (21.05)	-
Urban	23 (85.19)	45 (78.95)	-
Occupation (n)			0.325
Primary industry	1 (3.70)	5 (8.77)	-
Secondary industry	10 (37.04)	13 (22.81)	-
Tertiary industry	16 (59.26)	39 (68.42)	-
Monthly income (n)			0.262
< 1000 CNY	2 (7.41)	8 (14.04)	-
1000 ~ 2999 CNY	9 (3.33)	17 (29.82)	-
3000 ~ 7999 CNY	11 (40.74)	27 (47.37)	-
8000 ~ 19,999 CNY	5 (17.52)	3 (5.26)	-
≥ 20,000 CNY	0 (0.00)	2 (3.51)	-
Pre-pregnancy BMI (n)			0.212
< 24 kg/m^2	19 (70.37)	32 (56.14)	-
≥ 24 kg/m^2	8 (29.63)	25 (43.86)	-
Gravidity (n)			0.712
1 ~ 2 times	20 (74.07)	40 (70.18)	-
≥ 3 times	7 (25.93)	17 (29.82)	-
Parity (n)			0.748
0 ~ 2 times	23 (85.19)	50 (87.72)	-
≥ 3 times	4 (14.81)	7 (12.28)	-
Adverse pregnancy history (n)	7 (25.93)	5 (8.77)	0.036
Family history of diabetes (n)	10 (37.04)	16 (28.07)	0.406
PCOS history (n)	4 (14.81)	8 (14.04)	0.924
Poor dietary habits (n)	15 (55.56)	34 (59.65)	0.722
Insufficient physical activity (n)	24 (88.89)	50 (87.72)	0.877
Poor sleep quality (n)	10 (37.04)	15 (26.32)	0.316
E2 (pmol/L)	30421.91 ± 9057.01	25199.91 ± 7339.70	0.006
P (nmol/L)	200.89 ± 49.08	160.62 ± 53.00	0.001
Cor (nmol/L)	768.14 (617.55, 840.43)	542.96 (422.90, 756.81)	0.001
Previous history of depression (n)	6 (22.22)	2 (3.51)	0.006
Family History of Depression (n)	4 (14.81)	1 (1.75)	0.018
Unwanted pregnancy (n)	8 (29.63)	5 (8.77)	0.014
Poor blood sugar control (n)	10 (37.04)	4 (7.02)	0.001
GDM complications (n)	8 (29.63)	3 (5.26)	0.002
SSRS < 33 point (n)	10 (37.04)	5 (8.77)	0.002

Table 5 Assignment table

Variable	assignment
Poor sleep quality	No = 0, Yes = 1
E2	Continuous variable
P	Continuous variable
Cor	Continuous variable
Previous history of depression	No = 0, Yes = 1
Family history of depression	No = 0, Yes = 1
Unwanted pregnancy	No = 0, Yes = 1
Poor blood sugar control	No = 0, Yes = 1
GDM complications (n)	No = 0, Yes = 1
SSRS < 33 point	No = 0, Yes = 1

Table 6 Multivariable logistic regression analysis of depression in pregnant women with GDM

Variable	β	SE	Wald	*P*	OR (95%CI)
Poor sleep quality (1)	4.708	2.147	4.807	0.028	110.830 (1.648, 7455.139)
E2	0.000	0.000	5.901	0.015	1.000 (1.000~1.000)
P	0.025	0.012	4.594	0.032	1.026 (1.002~1.049)
Cor	0.014	0.005	8.648	0.003	1.014 (1.005~1.023)
Previous history of depression (1)	5.913	2.296	6.631	0.010	369.808 (4.107~33302.357)
Family history of depression (1)	0.386	1.935	0.040	0.842	1.471 (0.033~65.183)
Unwanted pregnancy (1)	0.010	1.863	0.000	0.996	1.010 (0.026~38.914)
Poor blood sugar control (1)	8.351	3.779	4.885	0.027	4236.430 (2.575~6970617.597)
GDM complications (1)	−2.676	3.236	0.684	0.408	0.069 (0.000~39.129)
SSRS < 33 point (1)	6.184	2.461	6.311	0.012	484.794 (3.894~60357.815)

gestational diabetes screening (e.g., 75 g OGTT between 24 and 28 weeks), health education, and follow-up services delivered through a tiered network of community health centers and hospitals. In addition, basic maternal care is covered under national health insurance, which greatly reduces financial barriers for low-income populations. This structured and accessible approach enables pregnant women from diverse backgrounds to receive timely diagnosis, consistent monitoring, and early intervention for pregnancy-related conditions such as GDM. The integration of health education and follow-up care further supports adherence to clinical recommendations [24]. As a result, disparities related to sociodemographic status may be less pronounced in this population, which could explain the absence of significant associations between these factors and GDM in our findings.

Among GDM patients, 32.14% exhibited comorbid depression, substantially higher than the 12-18% prevalence reported in non-GDM pregnancies [25–27], suggesting that these individuals bear an additional psychological burden beyond that associated with GDM alone. Multivariable analysis within the GDM subgroup identified factors independently associated with comorbid depression: prior depression history (OR = 4.82), low social support (Social Support Rating Scale [SSRS] score < 33, OR = 3.67), and poor glycemic control (HbA1c ≥ 5.8%, OR = 2.91). These findings support the "metabolic-psychiatric comorbidity model": glycemic variability-induced somatic symptoms (e.g., fatigue, polyuria) may exacerbate emotional distress, while depression-related hypothalamic-pituitary-adrenal (HPA) axis hyperactivity could further impair pancreatic function via Cor overproduction, creating a "hyperglycemia-hypercortisolism-depression" vicious cycle [28]. Importantly, adverse pregnancy history and elevated E2/P/Cor levels were independently associated with both GDM onset and comorbid depression within the GDM population. (interaction $P < 0.01$). Mechanistically, adverse pregnancy outcomes may influence mental health through dual pathways: ① miscarriage/fetal anomaly history inducing post-traumatic stress and heightened anxiety sensitivity; ② chronic inflammatory state associated with repeated pregnancy loss may affect limbic system function [29, 30]. These findings indicate that GDM patients with comorbid depression face not only the metabolic challenges of pregnancy-related glucose dysregulation but also experience elevated levels of emotional distress, anxiety, and psychosocial impairment compared to their non-depressed counterparts, underscoring the need for concurrent metabolic and psychological screening in GDM patients with adverse pregnancy histories, implementing dual cardiac-metabolic and mental health management ("dual-heart care").

Based on these findings, we propose a tiered intervention framework integrating biomedical, psychological, and social dimensions:

Primary Prevention: Targeted screening for high-risk groups (pre-pregnancy BMI ≥ 24 kg/m², PCOS, or diabetes family history) with early OGTT pre-screening and dynamic E2/P/Cor monitoring during first trimester. Integrate SSRS into routine prenatal checks, combining Hamilton Depression Scale-17 (HAMD-17) and Pregnancy Pressure Scale (PPS) for psychological assessment in individuals with SSRS < 33, depression history, or unplanned pregnancy. Secondary Intervention: Multidisciplinary care including individualized glycemic targets (e.g., HbA1c < 5.6%) prioritizing diet-exercise protocols: Mediterranean-style diet (40-50% carbohydrates) with postprandial moderate exercise (e.g., 30-minute walking/prenatal yoga) [31]. Short-term metformin or insulin sensitizers may be considered for marked hormone elevation (E2 > 2000 pg/mL, Cor > 580 nmol/L) with close monitoring of hormone-glucose interplay. Cognitive

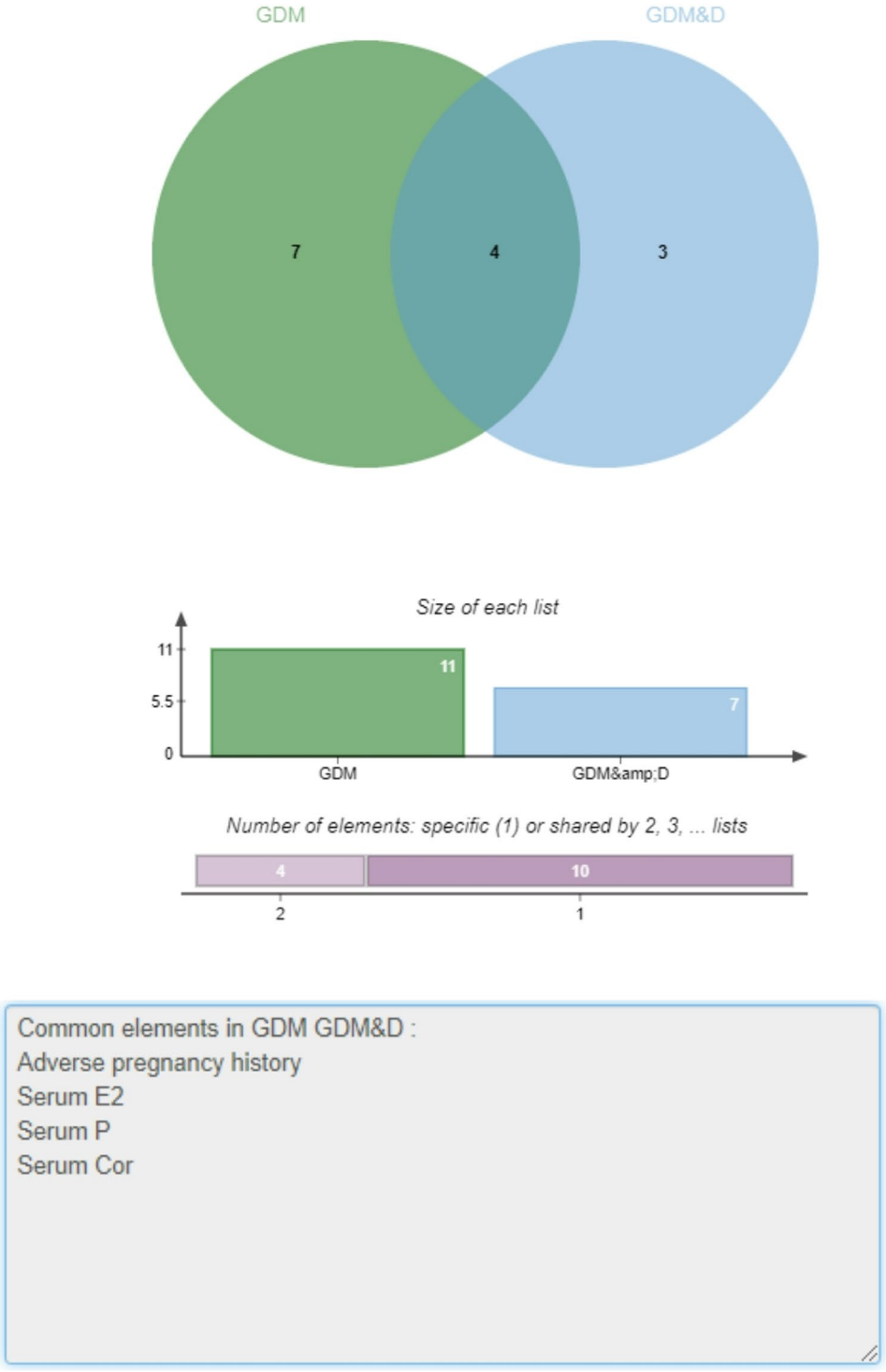


Fig. 1 Wayne Diagram for analysis of interactive influencing factors

restructuring for catastrophic thinking in adverse pregnancy history cases, stimulus control/sleep restriction therapy for insomnia, and peer-support groups to enhance self-efficacy [32]. Tertiary Support: Family education programs (nutrition preparation, emotion recognition training) to improve household support. Community-based free glucose monitoring devices and psychological hotlines. Development of GDM management apps integrating glucose tracking, exercise logging, teleconsultation, and AI-driven depression risk alerts. Quaternary Optimization: Policy advocacy for including GDM depression screening in essential public health

services and expanding insurance coverage. Pilot "hospital-community" referral systems prioritizing specialist mental health referrals for patients with poor glycemic control and SSRS < 33.

Strengths of this study include the relatively large sample size, comprehensive clinical and psychological data collection, and the integrative analytical approach combining biomedical, behavioral, and hormonal variables. Moreover, the study was conducted within a standardized prenatal care system, minimizing potential disparities in care delivery and increasing the representativeness of the findings.

This study also has several limitations. First, the retrospective design limits causal inference, and associations identified cannot establish temporal relationships. Second, the lack of postpartum follow-up data precludes assessment of the long-term metabolic and psychological outcomes among GDM patients. Third, hormone levels were measured at a single time point, which may not fully reflect the dynamic endocrine fluctuations across gestation. Fourth, the lack of an a priori sample size calculation may limit the study's ability to detect subtle effects or interactions. Although the overall cohort was sizable ($n = 746$), the relatively low GDM incidence (11.26%) led to a smaller analytic sample ($n = 84$), especially for subgroup analyses. Notably, this GDM rate is consistent with previous population-based studies in China reporting rates between 9% and 15%, supporting the generalizability of our findings [33–35]. Post hoc power analysis suggested adequate power for major associations but insufficient sensitivity for smaller effects. This limitation is typical of retrospective studies, where sample size depends on available data. Future prospective studies with planned power estimation are needed to validate these findings.

Conclusion

GDM and comorbid depression result from biopsychosocial interactions, necessitating integrated prevention systems. Early high-risk screening, dual metabolic-psychological interventions, and enhanced social support networks may disrupt the "metabolic dysregulation-psychological stress" cycle, improving maternal and offspring long-term outcomes.

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Authors' contributions
Yan Wang and Yunxia Quan conceived and designed the study. Yan Wang collected and analyzed the clinical data. Yunxia Quan performed statistical analyses and interpreted the results. Yan Wang and Yunxia Quan contributed to drafting and revising the manuscript. All authors reviewed and approved the final manuscript.

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Data availability
The datas used and/or analyzed during the current study are available from the corresponding author.

Declarations

Ethics approval and consent to participate
This study was approved by the ethics committee of Shijiazhuang Maternal and Child Health Hospital and in accordance with the Declaration of Helsinki. All participants signed an informed consent form prior to the start of the study, acknowledging their understanding of the study's purpose, procedures, potential risks, and benefits.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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