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Suicidal behavior and depression among perinatal women: research, prevention, intervention and treatment

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Suicidal behavior and depression among perinatal women: research, prevention, intervention and treatment

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Editorial: Suicidal behavior and depression among perinatal women: research, prevention, intervention, and treatment

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Editorial on the Research Topic

Suicidal behavior and depression among perinatal women: research, prevention, intervention and treatment

The perinatal period, including pregnancy and the first year after childbirth, is often a time of joy and new beginnings. Despite that, for many women, this period also brings significant psychological challenges. Depression and suicidal behaviors among perinatal women are serious issues that affect mothers and their children as well as the family. The studies in this Research Topic dive deep into these challenges by exploring risk factors, causes, and potential interventions that can help women navigate this difficult period more safely and effectively.

Unpacking the risk factors

One of the main themes resulting from the research is the identification of risk factors that contribute to postpartum depression (PPD) and suicidal behaviors. Studies in this Research Topic have examined how different physical and psychological factors can increase a woman's risk. For instance, higher body weight, a history of mental health issues, including major depression, and certain socioeconomic factors have been found to raise the likelihood of developing PPD (Wedajo et al.; Yu et al.). On the other hand, factors like being older at the time of the first birth and having more years of education seem to offer some buffer against these mental health difficulties (Zuo et al.).

Interestingly, another study examined the association between Gut health and postpartum depression (Zhang et al.). The results suggest that the composition of gut bacteria might play a role in either heightening or reducing the risk of PPD and open up possibilities for new treatments that target gut health as a way to help prevent or manage postpartum depression.

Exploring effective interventions

Timing and effective interventions are another major focus of the Research Topic. One study from India (Szajna et al.) highlights a community-based approach in which health workers deliver a simple, acceptable, and effective method of reducing depression symptoms. It is a good example of how low-cost, scalable interventions can make a significant difference, especially in resource-limited settings.

Another study focused on the role of exercise in preventing depression during pregnancy (Liu et al.). The results confirm that regular physical activity plays a vital role in reducing depressive symptoms, especially when started early and maintained throughout the pregnancy. These results reinforce the idea that including exercise in prenatal care routines is needed to support the mental health of expectant mothers.

Addressing challenges in vulnerable populations

Different studies in this Research Topic address the specific mental health challenges among vulnerable populations, including adolescent mothers and women with autoimmune diseases. For instance, Miafo et al. reported on the high rates of mental disorders and suicidal risk among young mothers. These findings highlight the urgent need to make mental health services accessible to adolescent mothers, especially in areas where these challenges are most common.

Another study examined the association between postpartum depression and autoimmune diseases (Yu et al.), indicating that PPD may raise the risk of developing conditions such as type 1 diabetes and Hashimoto's thyroiditis. These findings emphasize the need for comprehensive monitoring of both mental and physical health among postpartum women to help prevent long-term complications.

Improving screening and support systems

The need for better screening and support systems is another key theme. One study examined the effectiveness of different screening questions for detecting suicidal risk among perinatal women (Dudeney et al.). The findings show that many women were uncomfortable with direct language about suicide, which poses challenges for healthcare providers in identifying those at risk. The results underscore the urgent need for more sensitive and culturally appropriate screening tools to ensure no woman slips through the cracks.

A study conducted in Ethiopia on self-harm among postnatal mothers attending immunization clinics highlights the prevalence of this issue and its associated risk factors (Wedajo et al.). The authors suggested that healthcare providers need to be more attentive in recognizing and addressing the signs of self-harm to improve the overall health outcomes for these women.

Moving forward

This Research Topic provides a comprehensive look at the complexities of perinatal depression and suicidality. From understanding the underlying risk factors to exploring effective interventions, these studies highlight the challenges and the potential for significant improvement in perinatal mental health. As we continue to learn from these studies, there is a promising future where we can build better support systems for women during the perinatal period and reduce the incidence of these serious mental health issues.

To move further, research in the future might need to broaden the horizons and include risk factors beyond the individual. Much needs to be done to understand the social and environmental factors and thus include interventions that do not only address the needs of the group with the highest mental health needs but rather rely on public health approaches. The perinatal period brings along many normative yet manageable changes if we have appropriate and broad support available, including psychological, relational, social, and related systems. This highlights the need for further research to address these gaps in knowledge and guide future interventions and policies in the field of perinatal mental health.

We would like to thank all the contributors to this Research Topic for their valuable insights and dedication to improving our understanding of the mental health challenges in perinatal women. We also encourage continued collaboration and innovation in this field.

Author contributions

SH: Writing – review & editing, Writing – original draft. YG: Writing – review & editing, Writing – original draft. VP: Writing – review & editing, Writing – original draft.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Causal effects of potential risk factors on postpartum depression: a Mendelian randomization study

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Background: Postpartum depression (PPD) is a type of depressive episode related to parents after childbirth, which causes a variety of symptoms not only for parents but also affects the development of children. The causal relationship between potential risk factors and PPD remains comprehensively elucidated.

Methods: Linkage disequilibrium score regression (LDSC) analysis was conducted to screen the heritability of each instrumental variant (IV) and to calculate the genetic correlations between effective causal factors and PPD. To search for the causal effect of multiple potential risk factors on the incidence of PPD, random effects of the inverse variance weighted (IVW) method were applied. Sensitivity analyses, including weighted median, MR-Egger regression, Cochrane's Q test, and MR Pleiotropy Residual Sum and Outlier (MR-PRESSO), were performed to detect potential Mendelian randomization (MR) assumption violations. Multivariable MR (MVMR) was conducted to control potential multicollinearity.

Results: A total of 40 potential risk factors were investigated in this study. LDSC regression analysis reported a significant genetic correlation of potential traits with PPD. MR analysis showed that higher body mass index (BMI) (Benjamini and Hochberg (BH) corrected $p = 0.05$), major depression (MD) (BH corrected $p = 5.04E-19$), and schizophrenia (SCZ) (BH corrected $p = 1.64E-05$) were associated with the increased risk of PPD, whereas increased age at first birth (BH corrected $p = 2.11E-04$), older age at first sexual intercourse (BH corrected $p = 3.02E-15$), increased average total household income before tax (BH corrected $p = 4.57E-02$), and increased years of schooling (BH corrected $p = 1.47E-11$) led to a decreased probability of PPD. MVMR analysis suggested that MD ($p = 3.25E-08$) and older age at first birth ($p = 8.18E-04$) were still associated with an increased risk of PPD.

Conclusion: In our MR study, we found multiple risk factors, including MD and younger age at first birth, to be deleterious causal risk factors for PPD.

KEYWORDS

postpartum depression, causal factors, mental disorder, Mendelian randomization, linkage disequilibrium score regression

1 Introduction

Postpartum depression (PPD), also termed postnatal depression, is a type of depressive episode related to childbirth with a variety of symptoms of mood changes, negative attitudes to life, and mental and psychiatric changes, with few severe cases showing suicidality (1). The diagnostic criteria of PPD comprise five or more symptoms, such as depressed mood, loss of

previous interest, weight or appetite alteration, somnipathy, fatigue, attention deficit, and feeling worthless or guilty (2). PPD occurs in approximately 13% of women, which may cause severe consequences for mothers and their children (3). Moreover, the reported overall incidence of paternal PPD between 3 months and 12 months after birth was about 10.4% (4), which suggested that both new parents may suffer from this common psychiatric disorder. Apart from causing mental disorders or even suicides of parents, the risks of PPD on children have been well-investigated, and it suggested that children with parents experiencing PPD are more likely to suffer from depressive disorders (5). Regarding the risk factors associated with PPD, a variety of research found that multiple factors, including a history of mental illness, hormonal changes, and social factors, were related to PPD (1, 6). The causal relationship between potential risk factors and PPD is still unelucidated, and a comprehensive exploration of the causal effects of factors on PPD would be helpful for the intervention of PPD.

Mendelian randomization (MR) is a useful way to infer a causal relationship, using genetic variants as instrumental variants (IVs) to estimate the causal assumption between exposure and outcome (7). Due to the random allocation of genetic variants, MR is less susceptible to other confounding factors and reverse causation that can impede causal inference in conventional observational studies (8). Multivariable MR (MVMR) takes pleiotropy among multiple exposures into account, which is an extension of univariable MR and is important for pleiotropic pathways (9). Thus, accumulating research has taken advantage of MR to gain insights into the causes of multiple diseases (10). Recently, MR analysis initially demonstrated a potential causal relationship between opioid use and the risk of PPD. In turn, PPD was also associated with a higher risk of opioid and non-opioid analgesic use (11). Another recent study investigated the causal association between PPD and cerebrovascular diseases and cognitive impairment, and the result recommended that cognitive impairment was a significant outcome induced by PPD (12). In addition, modifiable risk factors, such as body mass index (BMI) and glucose, are usually considered exposures that may be associated with diseases in MR analysis (13). However, the causal association of other potential risk factors, particularly modifiable risk factors with PPD, still remains unclear.

In the present study, we focused on the association of various potential risk factors and modifiable factors with PPD. Based on the summarized data of the genome-wide association study (GWAS), we investigated the genetic correlations between 40 potential risk factors and PPD by linkage disequilibrium score regression (LDSC) analysis and then performed a two-sample MR analysis.

2 Materials and methods

2.1 Study design

A procedure of MR analysis was established to investigate a causal relationship between potential risk factors and PPD. Figure 1 shows the procedures of our study. The principles of selecting potential risk factors were as follows: First, we sought out a review of the PPD (14), which mentioned the risk factors of PPD, including history of mental illness (psychiatric disorders), hormonal changes (sex hormones), and social factors (socioeconomic Factors). Another study reported the association between thyroid function and PPD (15). Second, we investigated the modifiable risk factors frequently used as exposures in MR analysis, including BMI, blood pressure, glucose and lipids, and diet hobbies such as smoking, drinking alcohol, tea, and coffee. Third, we added some risk factors that may be involved in the pathogenesis of depression, including disorder of sleep (16) and inflammatory processes (inflammatory biomarkers) (17). In total, there were 40 potential risk factors.

Three major assumptions were utilized. First, there existed a direct correlation between the IVs of potential exposures and the PPD (Relevance). Second, the confounders cannot confound the IVs of exposures (Exchangeability). Finally, the IVs have no direct connection to the outcome except through exposure (the exclusion restriction).

2.2 Sources of exposures and PPD in GWAS data

We obtained data on exposures from the GWAS data. The exposure factors of this study are as follows: BMI, total testosterone, bioavailable testosterone, sex hormone binding globulin, estradiol, coffee intake, tea intake, average total household income before tax, age at menarche[1] (18–20), Schizophrenia (SCZ) (21), autism spectrum disorder (22), bipolar disorder (23), major depression (MD) (24), attention-deficit/hyperactivity disorder (25), anxiety (26), diastolic blood pressure, pulse pressure, systolic blood pressure (27), glycated hemoglobin, fasting glucose, fasting insulin, 2-h glucose (28), triglycerides, low-density lipoprotein cholesterol-c, high-density lipoprotein cholesterol-c, apolipoprotein A-I, apolipoprotein B (29), free thyroxine4, thyrotropin (TSH), incTSH/hypothyroidism, decTSH/hyperthyroidism (30), 25 hydroxyvitamin D (31), C-reactive protein (32), smoking initiation (SI), cigarettes per day, alcohol consumption (33), years of schooling (33), age at first sexual intercourse, age at first birth (34), and insomnia (35). Next, the GWAS data of PPD were obtained from the European cohort: the FinnGen study round 8 (36). The FinnGen study is dedicated to combining genome information with digital healthcare data (37). The criterion in FinnGen was based on the 10th edition of the International Classification of Diseases criteria, in which participants with delivery history (O15) diagnosed with F32, F33, or F530 were identified as PPD. A total of 13,657 PPD cases and 236,178 controls were enrolled in the dataset. GWAS summary data of PPD and all risk factors are presented in Table 1. It is worth noting that the ethnicity of the population of attention deficit/hyperactivity disorder was European, North American, and Chinese, and the ethnicity of other GWAS data was European. Given that the diagnostic criteria of the PPD included a history of delivery, we speculated that the gender of this study was restricted to biological females. We elected GWAS of sex hormones, free thyroxine, and TSH of female-only participants as the rest of the studies did not provide gender-specified data.

1 https://gwas.mrcieu.ac.uk/

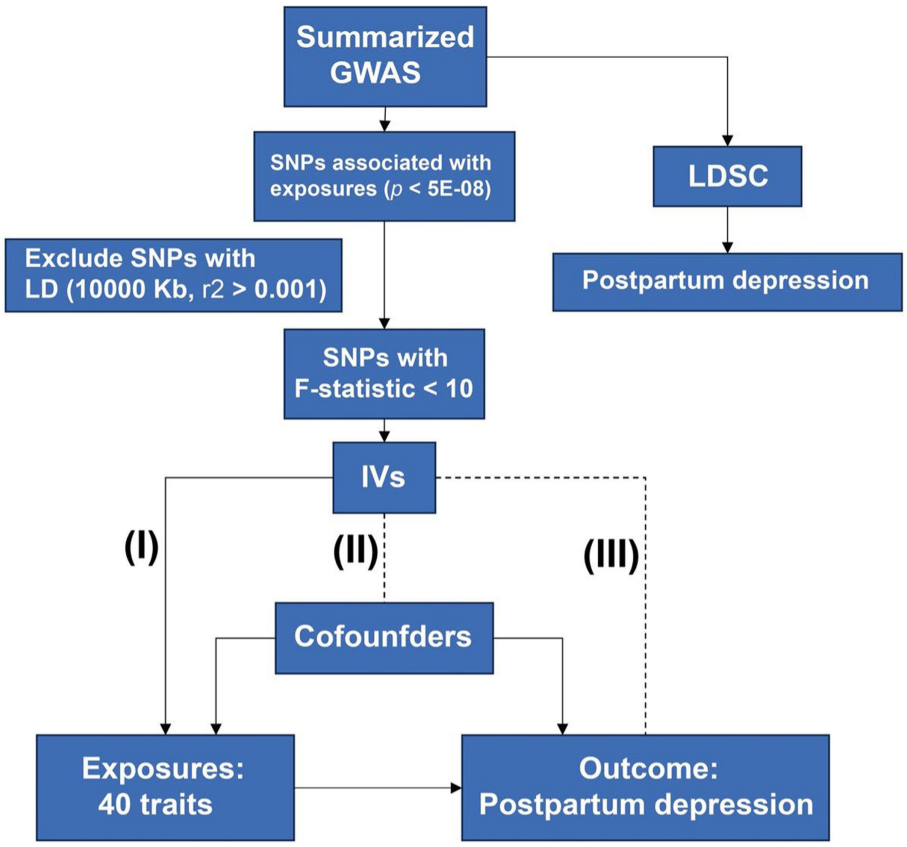

FIGURE 1
Design of the study. Procedures of MR are shown in this flow chart. Three principles of MR were listed: the IVs must be associated with exposure (I) and not be associated with confounders (II) and outcome (III). MR, mendelian randomization; GWAS, genome-wide association studies; SNP, single nucleotide polymorphism; IV, instrumental variant; LDSC, linkage disequilibrium score regression.

2.3 Linkage disequilibrium score regression

To screen the heritability of each trait and the genetic correlations between effective causal factors and PPD, LDSC regression was conducted by the regression slope using GWAS summary data (38). The European Ancestry 1,000 Genomes LD reference panel was used as a reference.

2.4 Genetic instruments selection

To select the qualified IVs, only single nucleotide polymorphisms (SNPs) associated with each exposure at a genome-wide threshold ($p < 5E-08$) were elected. A less strict threshold of 5E-06 was applied if less than four IVs were involved in the inverse variance weighted (IVW) analysis. SNPs with linkage disequilibrium were filtered based on the European ancestry 1,000 Genomes LD reference panel, with $r2 > 0.001$ on the clump window of 10,000 kb to keep the IVs independent from each other. The F-statistic of each SNP was calculated, and any SNP with a low F-statistic (< 10) was removed to avoid weak instrument bias. SNPs significantly associated with outcome ($p < 5E-08$) were excluded as they violated the third principle of MR assumption. SNPs that passed these precedes and existed in the GWAS of outcome were harmonized to avoid a mismatch of alleles based on allele frequencies for palindromes (19).

2.5 Mendelian randomization analysis

We used IVW to analyze the causal relationship of 40 potential risk factors in the PPD (7). In addition, weighted median, MR-Egger regression, heterogeneity test, Cochrane's Q test, and MR-PRESSO were utilized to assess the robustness of IVW results. We appraised the heterogeneity using Cochran's Q statistics and I^2 statistics (39), and if heterogeneity exists ($p < 0.05$), the results should coincide with results estimated by IVW (39). In the pleiotropy test, intercepts calculated by MR-PRESSO were used to assess the horizontal pleiotropy of valid IVs; $p > 0.05$ meant a lower probability of horizontal pleiotropy existence (40). Outliners were detected and removed by MR-PRESSO. The validation of causal inference between exposures and PPD depended on the same tendency of IVW and weighted median and MR-Egger analyses, besides no horizontal pleiotropic effect existing. To control potential multicollinearity, multivariable MVMR was conducted with significant results of the IVW method as exposures. For MVMR, the IVs must be associated with at least one of the exposures, independent of

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TABLE 1 Description of GWAS statistics included in the present study.

Outcome and potential risk factors	Traits	Sample size	PMID or data source	Population	Sex
	PPD	249,835 (13,657 cases and 236,178 controls)	https://risteys.finregistry.fi/endpoints/O15_POSTPART_DEPR	European	-
Psychiatric disorders	SCZ	127,906 (52,017 cases and 75,889 controls)	35396580	European	M/F
	Autism Spectrum Disorder	46,350 (18,381 cases and 27,969 controls)	30804558	European	M/F
	Bipolar disorder	34,950 (7,647 cases and 27,303 controls)	27329760	European	M/F
	MD	500,199 (170,756 cases and 329,443 controls)	30718901	European	M/F
	Attention deficit/hyperactivity disorder	55,374 [20,183 cases (1,084 non-European cases) and 35,191 controls (997 non-European cases)]	30478444	European, North American, and Chinese	M/F
	Anxiety	17,310	26754954	European	M/F
Overweight	BMI	454,884	MRC-IEU (https://gwas.mrcieu.ac.uk/, GWAS ID: ukb-b-2303)	European	M/F
Blood pressure	Diastolic blood pressure	810,865	33230300	European	M/F
	Pulse pressure	810,865		European	M/F
	Systolic blood pressure	810,865		European	M/F
Glucose	Glycated hemoglobin	146,806	34059833	European	M/F
	Fasting glucose	200,622		European	M/F
	Fasting insulin	151,013		European	M/F
	2-h glucose	63,396		European	M/F
Lipids	Triglycerides	441,016	32203549	European	M/F
	LDL-c	440,546		European	M/F
	HDL-c	403,943		European	M/F
	Apolipoprotein A-I	393,193		European	M/F
	Apolipoprotein B	439,214		European	M/F
Sex hormones	Total Testosterone	199,569	MRC-IEU (https://gwas.mrcieu.ac.uk/, GWAS ID: ieu-b-4864)	European	F
	Bioavailable Testosterone	180,386	MRC-IEU (https://gwas.mrcieu.ac.uk/, GWAS ID: ieu-b-4869)	European	F
	Sex hormone-binding globulin	214,989	MRC-IEU (https://gwas.mrcieu.ac.uk/, GWAS ID: ieu-b-4870)	European	F
	Estradiol	53,391	MRC-IEU (https://gwas.mrcieu.ac.uk/, GWAS ID: ieu-b-4872)	European	F
Thyroid function	Free thyroxine	26,954	30367059	European	F
	TSH	29,670		European	F
	incTSH/hypothyroidism	53,323 (3,340 cases and 49,983 controls)		European	M/F
	decTSH/hyperthyroidism	51,823 (1,840 cases and 49,983 controls)		European	M/F
Inflammatory biomarkers	Serum 25-Hydroxyvitamin D levels adjusted BMI	417,580	32242144	European	M/F
	C-reactive protein	575,531	35459240	European	M/F

(Continued)

TABLE 1 (Continued)

Outcome and potential risk factors	Traits	Sample size	PMID or data source	Population	Sex
Habits	SI	632,802 (311,629 cases and 321,173 controls)	30643251	European	M/F
	Cigarettes per day	337,334		European	M/F
	Alcohol consumption	941,280		European	M/F
	Coffee intake	428,860	MRC-IEU (https://gwas.mrcieu.ac.uk/, GWAS ID: ukb-b-5237)	European	M/F
	Tea intake	447,485	MRC-IEU (https://gwas.mrcieu.ac.uk/, GWAS ID: ukb-b-6066)	European	M/F
Socioeconomic Factors	Years of schooling	766,345	30038396	European	M/F
	Average total household income before tax	397,751	MRC-IEU (https://gwas.mrcieu.ac.uk/, GWAS ID: ukb-b-7408)	European	M/F
	Age at first sexual intercourse	397,338	34211149	European	M/F
	Age at first birth	542,901		European	M/F
	Age at menarche	243,944	MRC-IEU (https://gwas.mrcieu.ac.uk/, GWAS ID: ukb-b-3768)	European	M/F
Sleep	Insomnia	453,379	30804566	European	M/F

F, female; M, male; MRC-IEU, the Medical Research Council Integrative Epidemiology Unit; HDL-c, high-density lipoprotein cholesterol-c; LDL-c, low-density lipoprotein cholesterol-c; MD, major depression; BMI, body mass index; PPD, postpartum depression; SCZ, schizophrenia; SI, smoking initiation; TSH, thyrotropin.

all confounders of any exposure and independent of the outcome (41). Least absolute shrinkage and selection operator regression were utilized to avoid potential bias caused by multicollinearity.

2.6 Statistical analysis

All the statistical analyses were performed using R-4.2.3[2] with R packages. The R packages included the two-sample MR package (19), MR-PRESSO package (40), and LDSC package[3] (38, 42, 43). To control type I error, BH (Benjamini and Hochberg) correction was employed in both LDSC and IVW analyses. The BH-adjusted $p < 0.05$ was considered strong evidence, while the standard $p < 0.05$ was identified as suggestive evidence. Scatter plots and forest plots were used for the visualization of MR results.

2.7 Ethical approval

The data from public sources of our study had been granted ethical approval by their own institutional review boards and thus it did not require ethical approval from our institutional review board.

2 https://www.R-project.org/

3 https://github.com/mglev1n/ldscr

3 Results

3.1 Linkage disequilibrium score regression

We performed LDSC to analyze genetic correlations between potential causal factors and PPD. The heritability of SNPs for each exposure factor with a range of 2 to 36% is listed in Supplementary Table S1. Among 40 factors, half of them were associated with PPD even following BH correction, as listed in Table 2.

3.2 IVs selection

SNPs were selected for each pair of exposure and outcome, and detailed information on all SNPs was listed in the Supplementary Table S2. We defined the qualified IVs as only SNPs associated with each exposure at a genome-wide threshold ($p < 5E\text{-}08$). Due to the lack of IVs at the genome-wide significance with anxiety, autism spectrum disorder, and estradiol as exposure, the threshold of 5E-06 was applied in the three analyses. The total F-statistic of all pairs was above 10, indicating strong IVs.

3.3 IVW analysis of potential risk factors for PPD

Our results of MR analyses indicated that among 40 potential risk factors, eight of them had a significant causal relationship with the PPD. The functionalities of SNPs, such as higher BMI (odds ratio

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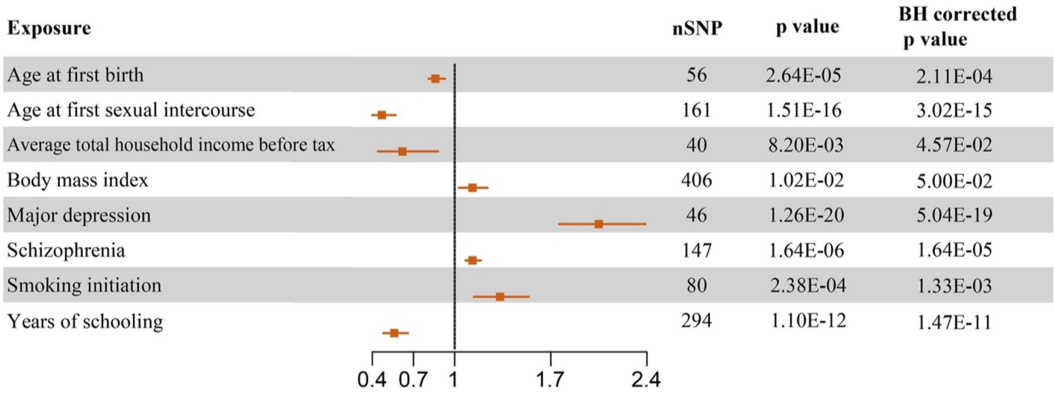
TABLE 2 Genetic correlation between PPD and potential risk factors.

P1	P2	rg	se	*p*-value	BH-corrected *p*-value
PPD	SCZ	0.285	0.038	1.11E-13	4.93E-13
	Autism Spectrum Disorder	0.516	0.064	9.02E-16	5.15E-15
	Bipolar disorder	0.267	0.058	4.58E-06	1.31E-05
	MD	0.623	0.053	3.98E-32	7.96E-31
	Attention deficit/hyperactivity disorder	0.516	0.064	9.02E-16	5.15E-15
	Anxiety	0.075	0.062	0.227	0.350
	BMI	0.162	0.034	1.41E-06	4.34E-06
	Diastolic blood pressure	−0.029	0.077	0.701	0.802
	Pulse pressure	0.037	0.070	0.596	0.711
	Systolic blood pressure	0.013	0.065	0.837	0.881
	Glycated hemoglobin	0.015	0.055	0.793	0.858
	Fasting glucose	0.039	0.057	0.499	0.689
	Fasting insulin	0.092	0.061	0.134	0.223
	2-h glucose	0.033	0.093	0.721	0.802
	Triglycerides	0.120	0.033	2.67E-04	6.67E-04
	LDL-c	−0.024	0.039	0.551	0.710
	HDL-c	−0.088	0.035	0.012	0.027
	Apolipoprotein A-I	−0.064	0.036	0.072	0.125
	Apolipoprotein B	0.020	0.038	0.604	0.711
	Total Testosterone	−0.028	0.044	0.523	0.698
	Bioavailable Testosterone	−0.004	0.045	0.931	0.955
	Sex hormone-binding globulin	−0.051	0.045	0.251	0.372
	Estradiol	−0.268	0.259	0.301	0.430
	Free thyroxine	−0.062	0.032	0.058	0.105
	Thyrotropin	0.560	0.234	0.017	0.034
	Hypothyroidism	0.550	0.230	0.017	0.034
	Hyperthyroidism[a]	NA	NA	NA	NA
	Serum 25-Hydroxyvitamin D levels adjusted BMI	0.083	0.040	0.037	0.071
	C-reactive protein levels	0.208	0.037	2.01E-08	6.70E-08
	SI	0.353	0.042	5.14E-17	4.11E-16
	Cigarettes per day	0.257	0.043	2.75E-09	1.00E-08
	Alcohol consumption	0.133	0.043	0.002	0.005
	Coffee intake	−0.184	0.050	2.18E-04	5.83E-04
	Tea intake	0.069	0.048	0.151	0.241
	Years of schooling	−0.348	0.038	2.34E-20	2.34E-19
	Average total household income before tax	−0.359	0.055	5.04E-11	2.02E-10
	Age at first sexual intercourse	−0.480	0.042	2.18E-30	2.91E-29
	Age at first birth	−0.646	0.053	3.23E-34	1.29E-32
	Age at menarche	0.018	0.034	0.589	0.711
	Insomnia	0.370	0.047	2.86E-15	1.43E-14

[a]Error occurred in performing linkage disequilibrium score regression, where a negative heritability existed in the genetic covariance matrix.
BH, Benjamini and Hochberg; PPD, postpartum depression; MD, major depression; BMI, body mass index; SCZ, schizophrenia; SI, smoking initiation; HDL-c, high-density lipoprotein cholesterol-c; LDL-c, low-density lipoprotein cholesterol-c.

(OR) = 1.13 (1.03, 1.24), BH corrected $p = 0.05$), MD (OR = 2.05 (1.76, 2.39), BH corrected $p = 5.04E-19$), SCZ (OR = 1.13 (1.08, 1.19), BH corrected $p = 1.64E-05$), and earlier SI (OR = 1.33 (1.14, 1.54), BH corrected $p = 1.33E-03$), were associated with the increased risk of PPD. On the contrary, we also found that increased age at first birth (OR = 0.86 (0.81, 0.93), BH corrected $p = 2.11E-04$), older age at first



Exposure	nSNP	p value	BH corrected p value
Age at first birth	56	2.64E-05	2.11E-04
Age at first sexual intercourse	161	1.51E-16	3.02E-15
Average total household income before tax	40	8.20E-03	4.57E-02
Body mass index	406	1.02E-02	5.00E-02
Major depression	46	1.26E-20	5.04E-19
Schizophrenia	147	1.64E-06	1.64E-05
Smoking initiation	80	2.38E-04	1.33E-03
Years of schooling	294	1.10E-12	1.47E-11

FIGURE 2
Forest plots of causal effect estimates based on Mendelian analysis. The significant results of causal inference of eight potential risk factors on PPD in random effect IVW analysis were plotted. SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval.

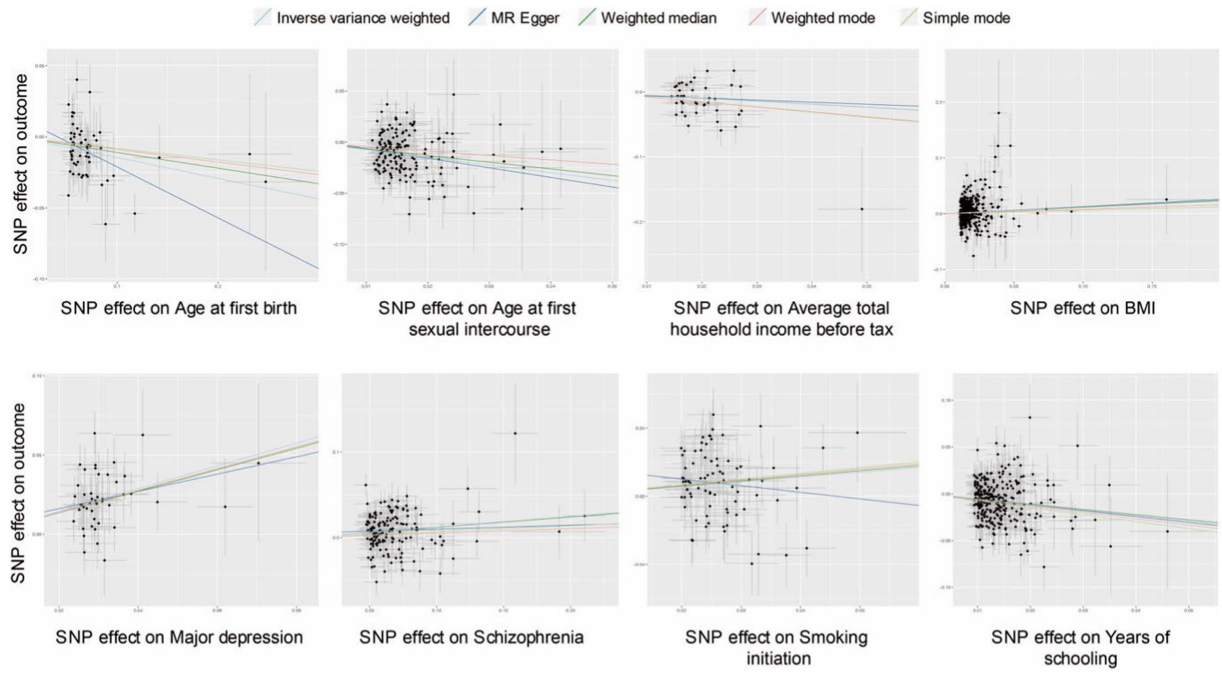


FIGURE 3
Scatter plots of causal effect inference for effective causal factors on PPD, respectively. SNP, single nucleotide polymorphism; BMI, body mass index.

sexual intercourse (OR = 0.47 (0.4, 0.57), BH corrected $p = 3.02E-15$), increased average total household income before tax (OR = 0.62 (0.44, 0.88), BH corrected $p = 4.57E-02$), and increased years of schooling (OR = 0.56 (0.48, 0.66), BH corrected $p = 1.47E-11$) led to a decreased probability of PPD. While no significant causal relationship was found between the other 32 exposures and PPD. Complete results are available in Figure 2 and Supplementary Table S3.

3.4 Sensitivity analysis of MR

The scatter plots of effective exposures with causal effects on PPD are presented in Figure 3. Apart from SI showing a discrepant correlation with PPD between MR Egger and IVW analysis and weighted median analysis (Figure 3), the rest of the effective causal effectors all presented a clear causal relationship with a similar tendency, which was in line with each corresponding forest plot (Figures 2, 3). Heterogeneity was detected in six causal factors identified by IVW, which are as follows: age at first sexual intercourse, average total household income before tax, BMI, SCZ, SI, and years of schooling. The pleiotropy test showed no horizontal pleiotropy in all analyses ($p > 0.05$). MR-PRESSO analysis suggested outliners were presented in the following exposures: average total household income before tax, BMI, SCZ, and years of schooling, deleting those that did not affect the results. The complete results of the sensitivity analysis are available in Supplementary Table S4.

TABLE 3 MVMR analysis of eight significant causal factors.

Exposure	n(SNP)	OR (95% CI)	*p*-value
Age at first sexual intercourse	55	1.05 (0.73–1.52)	0.790
Age at first birth	11	0.81 (0.72–0.92)	8.18E-04
Years of schooling	123	0.89 (0.60–1.32)	0.568
MD	18	1.63 (1.37–1.94)	3.25E-08
SI	18	0.92 (0.75–1.14)	0.4598
SCZ	43	1.05 (0.99–1.12)	0.112
BMI	227	0.90 (0.79–1.01)	0.081
Average total household income before tax	11	0.97 (0.63–1.47)	0.869

MVMR, multivariable Mendelian randomization; SNP, single nucleotide polymorphism; MD, major depression; BMI, body mass index; SCZ, schizophrenia; SI, smoking initiation.

3.5 Multivariable Mendelian randomization

We conducted an MVMR analysis with eight potential causal factors identified by IVW analysis. IVs were selected from shared SNPs of all exposure GWAS (Supplementary Table S5). None of these exposures were excluded after the least absolute shrinkage and selection operator regression. Taking all eight factors into account, genetically predicted MD was still associated with an increased risk of PPD (OR = 1.63 (1.37, 1.94), $p = 3.25E-08$). In contrast, older age at first birth was associated with a lower risk of PPD (OR = 0.81 (0.72, 0.92), $p = 8.18E-04$). The rest of the factors were not significant. Detailed information is listed in Table 3.

4 Discussion

In the present MR study, we found that higher BMI, MD, SCZ, and earlier SI increased the risk of PPD. On the contrary, the risk factors of increased age at first birth, older age at first sexual intercourse, increased income, and higher education level led to a decreased probability of PPD. In sensitivity analysis, contradictory results of SI were reported, which should be interpreted with caution. The other 32 risk factors did not show a statistically causal correlation with PPD. Adjustment for all eight significant traits in the MVMR model further found that MD and older age at first birth were still associated with an increased risk of PPD. Thus, our study shed fresh light on multiple causal factors associated with PPD.

Younger maternal age was reported to be associated with an increased risk of PPD in women (44). There was an MR analysis illustrating that the older age of first birth was a protective factor for mental disorders (45). Consistently, we found a negative causal relationship between age at first birth and PPD; thus, we suggested that relatively late-to-be parents may be less likely to develop PPD. Early sexual intercourse was associated with mental health outcomes (46). A novel MR study established a risky causal relationship between early sexual intercourse and MD (47). In our study, we initially brought forward that the experience of early sexual intercourse exerted a deleterious effect on PPD. As one of the social determinants, higher education level is identified as a protective factor for PPD (48). Our study also suggested that longer years of schooling were negatively associated with the risks of PPD, which was readily understandable as the higher the level of education, the higher the capability to withstand health and wealth risks. Whether income level or urbanization is associated with depression remains controversial (49). Here, we found that a lower average total household income before tax was associated with an increased risk of PPD. This conclusion needs further investigation using genetic biobanks of middle- and low-income countries. Based on these results, clinicians and parents should take advantage of these viable socioeconomic factors to prevent PPD, such as avoiding earlier first birth and immature sexual intercourse and acquiring a higher education level and a higher income.

Regarding the negative causalities of PPD, we found that modifiable risk factors, both higher BMI and earlier SI, significantly increased the likelihood of PPD. Recently, MR analysis has already found a promoting role of BMI in the risk of MD. In addition, it suggested that depression increases the genetic susceptibility to high BMI (50), which means a positive feedback between BMI and depression and needs the clinician's close attention and intervention. Combined with our findings, further clinical trials should investigate the effect of preventing PPD by getting rid of excess weight. Non-smoking has been considered a protective causal factor in the incidence of MD (51). This was consistent with our MR results, which indicated a direct effect of earlier SI on an increased risk for PPD. As the risk factors above are relatively easy to modify, we postulate that reducing BMI and postponing SI may decrease the risk of PPD. Although insomnia was associated with an increased risk of perinatal depression (52), we did not conclude a causal relationship between insomnia and PPD. An observational study reported that 11% of women and 8% of men had PPD after the first birth, and it was partly attributed to postpartum sleep deprivation (53). In contrast, our finding suggested no causal effect of insomnia on PPD. Although insomnia is prevalently comorbid with depression, and treating insomnia is beneficial to the mood of patients (54, 55), further research is warranted to identify the role of insomnia in the pathogenesis of PPD.

Finally, we reported that a history of MD increased the risk of PPD, which was in line with previous findings (56, 57). In addition, there was evidence of a positive causal effect between SCZ and PPD in our study. An observational study suggested that PPD and postpartum psychosis were related to a higher risk of SCZ (58). Our MR analysis further strengthened the robustness of the positive causal connection between mental disorders, such as SCZ and MD, and the risk of PPD. More than half of women with PPD have a

comorbidity of bipolar disorder, which usually being misdiagnosed or neglected (59). In our study, we did not conclude a causal relationship between these two diseases. We speculated that the negative result may be related to limited cases, distinct diagnostic criteria, and sequencing depth for bipolar disorder. Anyway, future studies should try to illustrate the association between bipolar disorder and PPD. Subsequently, we conducted an MVMR analysis to control potential multicollinearity. We included all eight significant traits from the IVW analysis, of which the MR Egger analysis showed that SI had an opposite direction compared to IVW and weighted median analysis, which should be interpreted with caution. In addition, BMI did not reach a significance following BH correcting. Importantly, compared to univariable MR, the effect of MD and older age at first birth on the increased risks of PPD were still observed. Thus, our study brought forward the most important causal factors of PPD, which may help future studies to better prevent and treat PPD.

Our study has limitations. First, the data sources are mainly from participants with European ancestry; thus, our result inevitably may not adapt to different ethnic groups, and the non-European participants in the GWAS of attention-deficit/hyperactivity disorder might lead to biases in results due to variations in allele frequencies and genetic associations among different populations and ancestry-specific effects. Second, the causal relationship of our findings does not conduct external verification as we only obtained one GWAS data of PPD. Therefore, we utilize more approaches to promote the robustness of our results, such as using the MR egger and weighted median analysis. In addition, one of the limitations of the methodology of MR is the potential confounding of the genetic variants and the outcome (Violation of IV condition two: exchangeability). Other than that, another bias of MR analysis that is uneasily corrected is the selection bias (10). In all, we should be prudent with our findings of MR because of the limitations above.

In summary, our MR analysis provided suggestive evidence of the protective effect of older age at first birth and older age at first sexual intercourse, higher education, and higher income on the risk of PPD. We also suggested that higher BMI and a history of MD and SCZ were hazardous causal factors for PPD. In addition, MD and older age at first birth were independently related to the increased risks of PPD. These novel shreds of evidence may help to guide the prevention and intervention strategies for PPD.

Data availability statement

Publicly available datasets were analyzed in this study. See Table 1 for detailed information. Further inquiries can be directed to the corresponding author.

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

Author contributions

MZ: Conceptualization, Data curation, Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. ZW: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. WL: Data curation, Methodology, Validation, Visualization, Writing – review & editing. SC: Formal analysis, Investigation, Validation, Writing – review & editing. YunY: Data curation, Formal analysis, Investigation, Project administration, Validation, Writing – review & editing. YuaY: Funding acquisition, Supervision, Validation, Writing – review & editing. QM: Data curation, Supervision, Validation, Writing – review & editing. YL: Conceptualization, Funding acquisition, Investigation, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2023.1275834/full#supplementary-material

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Glossary

BMI	body mass index
BH	Benjamini and Hochberg
IV	instrumental variant
GWAS	genome-wide association study
IVW	inverse variance weighted
LDSC	linkage disequilibrium score regression
MD	Major depression
MR	mendelian randomization
MVMR	multivariable MR
OR	odds ratio
PPD	postpartum depression
SCZ	schizophrenia
SI	smoking initiation
SNP	single nucleotide polymorphism
TSH	Thyrotropin

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Teenage pregnancy: focus on people with mental disorders

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Introduction

Teenage pregnancy is a global phenomenon caused by multiple and complex factors that can have serious health, social and economic consequences. It was reported in 2020 that there are about 21 million pregnancies per year among girls aged 15-19 in low - and middle-income countries, about 50% of which are unintended, and about 12 million end up giving birth (1). Globally, the adolescent birth rate declined from 64.5 per 1,000 women in 2000 to 42.5 per 1,000 women in 2021 (2). Despite the global decline in adolescent fertility, the rate of change is uneven across regions and there are large differences in fertility between countries and across regions within countries. A study in the United States population noted that adolescent pregnancy accounts for approximately 6% of the maternal population and is higher among those with lower education or lower economic status (3). In China, a large sample survey noted that teenage pregnancies accounted for 1.54% of maternal pregnancies under the age of 35, which is significantly lower than in Western countries (4). And the relaxation of China's one-child policy may also have had an impact on teenage pregnancy. Early pregnancy and childbearing increase the risk to both the mother and her newborn. Compared to young adult pregnant women, teenage mothers are at higher risk of abortion, stillbirth, eclampsia, puerperal endometritis and systemic infections, and babies born to teenage mothers are at higher risk of low birth weight, preterm birth and severe neonatal diseases. While some progress has been made worldwide in reducing adolescent first birth rates, progress has been slower among adolescents with mental disorders and other vulnerable groups, contributing to growing inequalities (5, 6). This article focuses on the risks that teenage pregnancy poses to health and social outcomes, especially for adolescents with mental health problems. It is also noted that current prevention measures are often insufficient to provide the necessary care to vulnerable adolescents. At the end, we conclude by drawing on observations and evidence from global sources to support a robust set of nationally-bound proposals in China.

Mortality rate in teenage pregnancy

The Global Adolescent Mortality Report noted that despite a rapid decline in maternal deaths as a proportion of total deaths, complications from pregnancy and childbirth remain among the leading causes of death among girls aged 15-19 years globally (7), and results obtained in the Chinese adolescent population are consistent with this (8). WHO data stated that the leading causes of maternal death were hemorrhage (27.1%), hypertensive disorders (14.0%) and sepsis (10.7%), which accounted for more than half of all causes of death (9). In the China Population Survey, adolescent maternal mortality rates have generally declined rapidly across Chinese provinces, with the adolescent maternal mortality ratio (MMR; number of maternal deaths per 100 000 livebirths) for 10-14 year old declining from 76.4 (66.1-88.3) in 1990 to 6.8 (6.0-7.7) in 2017, and from 1465.3 (1270.3-1675) in 1990 to 69.8 (60.7-81.5) in 2017 for adolescent maternal deaths aged 15-19 years, with hemorrhage and hypertensive disorders being the two leading causes of maternal mortality (10). A Canadian study noted that maternal age 19 years and younger was an independent influencing factor for severe maternal morbidity (11). Compared to mothers aged 20-34 years, mothers aged 10-19 years had a higher risk of preterm delivery, stillbirth, small for gestational age, and neonatal death, while the risk of cesarean delivery and gestational diabetes was lower (4).

Stillbirth in teenage pregnancy

The higher rate of stillbirths in teenage pregnancies is likewise a problem that cannot be ignored. Stillbirth rates are significantly higher for adolescent pregnancies among 10–19-year-olds compared to adult pregnancies (4). A recent systematic review reported that stillbirth rates have declined in 114 countries worldwide since 2000, but progress in reducing them has been slow, with significant pre-country disparities in stillbirth prevention, particularly in low- and middle-income countries (12). The survey indicated that maternal mortality rates in Africa have declined from previous levels, but only North Africa is close to the UN Sustainable Development Goal that the global maternal mortality ratio should be less than 70 deaths per 100,000 live births (13). A former research covering eight countries in South Asia also showed that adolescent maternal fertility and neonatal mortality rates are higher and significantly associated with local health care payment (14). Higher stillbirth rates in adolescent pregnancies can place a considerable burden on their health, families and society.

Teenage pregnancy with mental disorders

Teenage pregnancy is gaining attention and focus, but little is being mentioned about the current status of teenage pregnancy with mental disorders. The sexual and reproductive health of adolescent psychiatric patients has been largely overlooked. A large sample study in Canada noted that girls with severe mental disorders had significantly smaller decreases in fertility compared to adolescents without mental disorders (5). However, adolescents with mental disorders were more likely to experience risky sexual behavior and were at higher risk for sexually transmitted infections than adolescents without mental disorders (6). One study noted that 26.3% of women with mental disorders aged 15-25 years had been pregnant, 95.2% of which were unintended, while 25.5% tested positive for sexually transmitted infections (STI) (15). In another small sample study, it was found that 78.3% of adolescents with mental disorders had ever had sex, 22.5% had been previously pregnant, and 18.6% tested positive for STI (16). Furthermore, women with mental illness are more likely to have recurrent abortions, sexually transmitted infections, cancers of the reproductive system, contraception and emergency contraception than women without mental illness (17). Current evidence indicated that the rate of pregnancy and STI infection seems to be higher among adolescent girls with mental disorders, which seriously affects their own health.

Associated and postoperative pregnancy complications

In terms of pregnancy complications, women with mental disorders are more likely to have recurrent abortions, pregnancy terminations, gynecological disorders, sexually transmitted infections, and reproductive cancers. However, the sexual and reproductive health needs of women with mental disorders are far from being met compared to the healthy female population, constituting a serious health inequality (17). In terms of specific diseases, pregnancies in schizophrenic population had a higher risk of maternal pre-eclampsia, gestational hypertension, gestational diabetes (18), preterm birth, stillbirth, infant mortality, maternal metabolic risk (19), venous thromboembolism, abnormal birth weight size for gestational age (20), and a higher incidence of neonatal morbidity. For this population, there might be a need for more intensive care hospital resources, more meticulous perinatal care and more complex interventions (20). Secondly, miscarriage and abortion rates were significantly higher in women with schizophrenia, especially in patients who are young (<25 years), have multiple births, and have a history of prior substance abuse (21). On the other hand, maternal major depression was associated with preterm birth and small for severe gestational age; maternal bipolar disorder was associated with preterm birth and large for severe gestational age, and both mood disorders were correlated with higher risk of congenital malformations, neonatal morbidity, and neonatal readmission (22). Meta-analysis also noted that maternal risk of stillbirth or neonatal death was significantly higher in mothers with depression, anxiety, or severe mental disorders (23).

Despite strong evidence of significantly higher maternal pregnancy and delivery complications for women with mental

disorders, related interventions are progressing more slowly and the sexual and reproductive health needs of these vulnerable populations are difficult to secure. In addition, the information available on adolescent pregnancy with mental disorders is extremely limited. The limited evidence points to a significantly higher incidence of teenage pregnancy in mental disorders, with roughly one in five to one in three patients having had an unplanned pregnancy (15, 16, 24). Moreover, children of teenage mothers were more likely to be affected by their mothers' psychiatric disorders, making them a high-risk group for mental disorders (25). In addition, the high rate of unplanned pregnancies observed in adolescents also suggests that teratogenicity should be considered when prescribing psychotropic drugs to adolescent girls, as exposure to psychotropic drugs in early pregnancy may harm the developing fetus, and often the fact of pregnancy is difficult to detect in time in adolescents with unplanned pregnancies.

Factors associated with teenage pregnancy

There are numerous factors associated with adolescent pregnancy, such as early marriage, risky sexual behavior, substance use, family experiences of adolescent childbearing, and lack of sex education and health services. Early marriage is one of the main causes of teenage pregnancy, as it is difficult for girls who marry early to make their own choices about delaying childbirth or using contraceptives, which in turn has a negative impact on the health of children who marry at an early age and their children. Studies have shown that offspring of teenage mothers were also more likely to become teenage parents and that offspring of teenage mothers were prone to poorer educational achievement and lower life satisfaction, resulting in socially and economically risky generational chains (26). The Guttmacher Institute survey have revealed that the higher teenage pregnancy rates tend to be related with lower educational attainment or lower economic status (27). Otherwise, previous study had shown that the prevalence of disability was significantly higher among men and women who married as children, especially among those who married under the age of 16 (28). In addition, WHO reported that sexual abuse against children increases the risk of unintended pregnancy and that at least one in eight children in the world has been sexually abused before 18 years old (29). Despite the current marked decline in fertility among girls aged 15-19, WHO and related agencies survey shown that little progress has been made in preventing adolescent pregnancy, abortion, maternal mortality, sexually transmitted infections, and HIV, particularly among the mentally challenged adolescent population (2, 5, 6).

Gaps in data on teenage pregnancy with mental disorders in China

In China, there is a significant lack of research on teenage pregnancy with mental disorders, resulting in gaps in data and significant disparities across the entire continuum of family, school, community, social, legal, and official policies. Adolescents need and have the right to comprehensive sexuality education and easier access to contraceptive information and services, and the number of early pregnancies and births among girls can be reduced by measures such as a minimum age for marriage. At the same time, girls with mental disabilities who become pregnant need access to quality prenatal care. The "Central Subsidy for Local Health Funding for the Management and Treatment of Serious Mental disorders Project", commissioned by the Department of Disease Control of the Ministry of Public Health of China in 2004 and undertaken by the Mental Health Center of the Chinese CDC, is a disease management project for patients with serious mental disorders. Its purpose is to strengthen mental health construction and other aspects, specifically: (1) registration and assessment of patients with severe mental disorders, and follow-up of patients with risky behavioral tendencies; (2) provision of free primary medication for mental disorders to poor patients with risky behavioral tendencies; free laboratory tests; emergency treatment of patients; free emergency hospitalization; unlocking and treatment of locked patients (3); management and treatment of severe mental disorders program Training of relevant personnel. From the specific inclusion of information entries, it is clear that for patients with severe mental disorders, their pregnancy is not included in the content of the disease management survey (30), while for adolescent patients with severe mental disorders most provinces and municipalities adopt a natural strategy of not recording and following up, and knowledge about the management of this population's condition or pregnancy is even more lacking.

Proposals

There should be several initiatives for teenage pregnancy with mental disorders. First, families and schools should strengthen education on contraception and reproductive health for adolescents to reduce the rate of unprotected sex and unwanted pregnancies. Adolescents have a significantly higher risk of pregnancy mortality and complications than adults, but access to health care for adolescent mothers is relatively limited, especially among those with mental disorders. Therefore, the provision of counseling and perinatal health services by health care professionals to adolescent primigravida and their families with flexible and appropriate perinatal health programs based on adolescent primigravida risk factors will help improve the health of adolescent primigravida and their infants. According to studies, increasing health care expenditures and reducing adolescent female fertility may contribute to a reduction in maternal and neonatal mortality (14). There is a need to focus on improving the education of adolescents and removing economic barriers that prevent them from accessing maternal health services (31). Second, diverse public health facilities and community-based adolescent parenting and child care programs, such as breastfeeding, economic, parenting, and nutritional support, should be established, improved, but this

link is currently quite weak, and those pregnant women with severe mental disorders have difficulty participating in and accessing these simple, decentralized resources. However, community-based psychiatric rehabilitation services have largely come to a complete halt since the outbreak of the COVID-19 epidemic, and community-based rehabilitation for mental health in the post-epidemic era is at a new beginning. Third, the law should focus on protecting the personal rights of underage mothers, strictly reduce and control the incidence of sexual assault on the underage population, take legal action or hold the assailants legally responsible, provide timely medical care and psychological support to victims and related witnesses, and do its best to alleviate their physical and psychological trauma. Moreover, in order to further reduce the sexual abuse suffered by minors, in May 2020, the Supreme People's Procuratorate of the People's Republic of China, the Ministry of Education, and other departments jointly issued the Opinions on Establishing a Compulsory Reporting System for Cases of Aggression against Minors (for Trial Implementation) to establish a compulsory reporting system for cases of aggression against minors. According to the national law, when a pregnant girl under 14 years of age is registered to the hospital, the hospital will compulsorily report to the public security authorities or the procuratorial authorities if the medical staff is confronted with possible aggression against minors and the risk of wrongful aggression (32). Minors are theoretically going to hospitals after being assaulted, and hospitals and doctors often serve as the first to know about minors being assaulted, and the implementation of a mandatory reporting system in this part of the hospital can directly determine the effectiveness of the system's implementation. This reporting system is a major measure of national protection for adolescents. At present, it is still being gradually promoted, and it is worth further deepening the understanding and practical application of the general population and professionals. Lastly, at the national level, the disease management system for people with mental disorders should be further improved to provide more health care services and interventions for people with perinatal mental disorders in order to promote basic reproductive health for the population at large. The health care system should promote further investigation of the current status of teenage pregnancies with mental disorders to obtain relatively credible and realistic data, which in turn can identify creative solutions to provide better clinical care and medical services for this vulnerable population.

Author contributions

ZL: Writing – original draft, Writing – review & editing. SL: Investigation, Software, Writing – review & editing. RY: Data curation, Investigation, Writing – original draft, Writing – review & editing. SC: Conceptualization, Formal Analysis, Writing – original draft, Writing – review & editing. GY: Data curation, Investigation, Software, Writing – original draft. YL: Data curation, Methodology, Writing – review & editing. HL: Project administration, Supervision, Writing – original draft, Writing – review & editing.

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Conflict of interest

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Acceptability and content validity of suicidality screening items: a qualitative study with perinatal women

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Background: Suicide is a leading cause of death for perinatal women. It is estimated that up to 50% of women with mental health issues during pregnancy and/or after birth are not identified, despite regular contact with healthcare services. Screening items are one way in which perinatal women needing support could be identified. However, research examining the content validity and acceptability of suicide-related screening items with perinatal women is limited.

Aims: This study sought to: (i) assess the acceptability and content validity of 16 suicide-related items that have been administered and/or validated in perinatal populations; and (ii) explore the potential barriers and facilitators that may affect how women respond to these items when administered during pregnancy and after birth.

Methods: Twenty-one cognitive and semi-structured interviews were conducted with pregnant and postnatal women in the UK. The sample included women who had experienced self-reported mental health problems and/or suicidality during the perinatal period, and those who had not. Interviews were transcribed verbatim, and a coding framework based on the Theoretical Framework of Acceptability was applied to explore the data using deductive and inductive approaches.

Results: Findings indicated that the acceptability and content validity of suicide-related items were largely unacceptable to perinatal women in their current form. Women found terms such as 'better off dead' or 'killing myself' uncomfortable. Most women preferred the phrase 'ending your life' as this felt less confronting. Comprehensibility was also problematic. Many women did not interpret 'harming myself' to include suicidality, nor did they feel that abstract language such as 'leave this world' was direct enough in relation to suicide. Stigma, fear, and shame was central to non-disclosure. Response options and recall periods further affected the content validity of items, which created additional barriers for identifying those needing support.

Conclusions: Existing suicide-related screening items may not be acceptable to perinatal women. Maternity practitioners and researchers should consider the

phrasing, clarity, context, and framing of screening items when discussing suicidality with perinatal women to ensure potential barriers are not being reinforced. The development of specific suicidality screening measures that are acceptable, appropriate, and relevant to perinatal women are warranted.

KEYWORDS

suicide, perinatal, pregnancy, postpartum, screening, acceptability, qualitative, content analysis

1 Introduction

Maternal suicide is a devastating global issue, accounting for up to one fifth of deaths during the perinatal period in high-income countries (HICs) (1–4) and contributing to pregnancy-related mortality in lower- and middle-income countries (LMICs) (5). In the UK, suicide is the leading direct cause of death for women between six-weeks and one-year post pregnancy, a figure that has tragically remained largely unchanged for over a decade (6, 7). Furthermore, the incidence of maternal death due to mental health related causes has increased over the past few years, now accounting for almost 40% of all deaths during the perinatal period, with many women having experienced multiple adversities (7, 8). Evidence also indicates that approximately half of women suffering from mental health problems and/or those at risk of suicide during the perinatal period are not identified, despite regular contact with maternity services (9, 10). It is therefore imperative that multi-sector approaches for understanding and addressing the potential risk factors and barriers that might prevent perinatal women from disclosing suicidal thoughts and/or behaviours are established. Such efforts may help to lessen the occurrence of preventable maternal deaths and improve outcomes for both women and their babies.

Pregnant women and new mothers are now recognised as a high-risk priority group in the UK cross-government suicide prevention plan for England (11). This strategy aims to reduce suicide rates through targeted and tailored interventions over the next five-years. The most recent report highlighted the importance of screening for mental health problems during pregnancy and after birth and suggested that care providers take an active role in exploring the risk factors for suicide at every perinatal contact. However, universal screening for common perinatal mental health problems is not currently recommended in the UK (12), despite evidence that this approach can lead to both a reduction in perinatal depression and anxiety symptoms (13) and is associated with increased referral rates and engagement with the appropriate services (14). Instead, the National Institute for Health and Care Excellence (NICE) (15) suggests that midwives ask about women's mental health and wellbeing at their first antenatal booking appointment and at all subsequent contacts throughout the perinatal period using the Whooley questions (16) and/or the Generalized Anxiety Disorder Scale-2 (GAD-2) (17, 18). If a woman positively endorses either of these measures, a further assessment using psychometric self-report measures such as the Edinburgh Postnatal Depression Scale (EPDS) (19) or Patient Health Questionnaire-9 (PHQ-9) (20) can be conducted.

However, suicidal ideation and/or self-harm ideation is not routinely discussed with women receiving maternity care unless there is pretext for it, e.g., a prior history of suicidal and/or harming behaviours, if the woman is already receiving specialist care, or has self-disclosed. To date, no self-report screening measures of suicidality have been specifically designed for use with pregnant and postnatal women. When there is concern for a woman's mental health, the presence or absence of suicidal and/or self-harm ideation is often identified in the context of screening for depression and/or other common mental health problems because: (i) suicidality and depression are frequently comorbid (2, 21); (ii) depression is a risk factor for suicide (22); (iii) many depression measures include an item that asks about suicidal and/or self-harming ideation (23); and (iv) screening measures are relatively quick to administer and complete. However, although depression screening has become a proxy for identifying possible suicidality in perinatal women, it is important that the broader implications of this approach are not overlooked. Whilst depression and suicidal ideation and/or suicide behaviours do overlap, suicidality can occur without the presence of depression (and vice versa), thus screening for perinatal suicidality using depression measures alone may result in cases being missed (24–26). Furthermore, suicide is a multifaceted phenomenon, characterised by a highly complex interplay of biology, psychology, environment, and culture (27). Hence, using a single item to capture the presence or absence of suicidal ideation and/or suicidal behaviours has clear limitations. Approaches for identifying suicidality need to consider numerous psychosocial factors as part of a comprehensive assessment, and distinguish between suicidal ideation (which can include both passive thoughts about a desire to die, and/or active thoughts about ending your own life by suicide), suicide plans, and suicide behaviours because these are distinct processes, with differing implications in terms of mitigating risk and developing individual care plans (28). NICE (29) do not recommend that risk assessment tools are used to predict future suicide, nor should they be used to determine who is offered treatment or not.

Psychometric validity and reliability of tools for identifying mental health problems in pregnancy and after birth needs to be rigorously tested in diverse settings and contexts (30). However, a recent systematic review (23) indicated that the validity and reliability of measures that have been used to identify suicidality in perinatal women is limited, and nearly all were either items or subscales on a measure for depression. Research should continue to evaluate the psychometric properties of suicidality measures in perinatal populations to ascertain the suitability of their use. It is equally important to explore the content validity and acceptability of screening measures to perinatal women because this may affect their appropriateness and uptake. Content validity is generally assessed by looking at how well a measure captures the construct (s) it is meant to represent, particularly in terms of its relevance, comprehensiveness, and comprehensibility to the target population (31). However, approaches for defining and assessing acceptability are more varied. Whilst it is now widely recognised that acceptability should be a key consideration in the development, evaluation, and implementation of healthcare interventions, there has been a lack of agreement or guidance regarding how it should be measured, and the use of existing theory is often overlooked (32). These inconsistencies can inhibit the comparison of acceptability across intervention types and settings, and limit evidence-based policy and or practice recommendations.

Research has examined the acceptability of perinatal mental health interventions and/or screening using various methods, including: (i) semi-structured interviews/focus groups to explore experiences, attitudes and/or perceptions (33); (ii) cognitive interviews to measure comfort, ease, recall, and confidence in answering depression case-finding questions (34); (iii) self-report surveys/questions to measure usefulness, comfort etc (35); and, (iv) uptake as an indicator of acceptability (36). Perinatal mental health assessment and commonly used measures appear to be acceptable to pregnant and postnatal women given certain conditions (37–39). For example, care providers need to explain the purpose, outcome, and follow-up procedures of mental health screening to perinatal women because this can influence their willingness to engage (40). Likewise, factors such as the mode of administration, individual comfort levels, relationship with healthcare professionals, and stigma, guilt, shame, and fear associated with perinatal mental health problems can affect acceptability and prevent women from answering screening measures honestly, which creates additional barriers for identifying those who might require support (39, 41–46).

Considering these barriers, it is unsurprising that identifying suicidality in perinatal women poses an even greater challenge. This is further exacerbated by the complex risk factors associated with suicidal ideation and behaviours (47, 48) and mitigating women's fears regarding the potential consequences of disclosing suicidality e.g., unwanted intervention, hospitalisation, and/or concerns that their child will be taken away. Whilst there are a few studies that have explored and theorised women's experiences of suicidality during the perinatal period (49–52), there is little literature that has specifically examined how pregnant and postnatal women feel about suicide-related items that are embedded into mental health screening measures or how acceptable these items are to them. Some studies have found that perinatal women from LMICs are hesitant to answer item-9 from the PHQ-9 ("Thoughts that you would be better off dead or of hurting yourself in some way") due to religious beliefs (53) and/or because they find it uncomfortable (54), and other research has highlighted that there may be ambiguity regarding item-10 from the EPDS ("The thought of harming myself has occurred to me") because this may not be interpreted to include suicidal ideation (37, 55). Furthermore, there is no universal consensus regarding the operational definition of suicidal ideation, which may create confusion in terms of identifying passive or active intent (56), and variations in language use/the phrasing of items may also play a significant role in perpetuating or reducing stigma and fear, and/or addressing cultural differences.

Therefore, given that the acceptability of suicide-related screening items is understudied in perinatal populations, and that research using an existing theory of acceptability to explore perinatal mental health screening measures is limited, it is important to adopt an established and structured approach to conducting research in this area to ensure methodological rigour. This will help to generate new knowledge and contribute to the systematic enquiry of acceptability in the perinatal mental health and suicide literature. The Theoretical Framework of Acceptability (TFA) (32) offers a systematic and evidence-based approach for evaluating the acceptability of healthcare interventions, from both the perspective of those receiving and/or those delivering the intervention. The TFA defines acceptability as a multifaceted construct, comprising of seven domains (affective attitude, burden, ethicality, intervention coherence, opportunity costs, perceived effectiveness, and self-efficacy, see Table 1 for construct definitions) that can be applied at different timepoints (before, during or after an intervention) to assess the prospective, concurrent, or retrospective acceptability of an intervention. Perinatal research has used the TFA to assess acceptability in a variety of healthcare contexts (e.g., 57–61), including the use of exposure therapy among pregnant women with elevated anxiety (62), and a systematic review on the acceptability of implementing patient reported measures in routine maternity care (63). However, the authors know of no research that has used the TFA to assess the acceptability of suicide-related screening items to perinatal women. Using the TFA should provide valuable insights regarding the content validity of these items for identifying suicidal ideation and/or suicidal behaviours in perinatal women and it might also highlight some of the barriers and facilitators that influence how women respond to them.

Hence, the aims of this study were to: (i) assess the acceptability and content validity of 16 different suicide-related items that have been administered and/or validated in perinatal populations using the TFA; and (ii) explore the potential barriers and facilitators that may affect how women respond to these items when they are administered during pregnancy and after birth. These items were specifically selected from self-report measures for depression and/or common mental health problems because they have previously been used in perinatal populations as either a single item or as a subscale to identify suicidal ideation and/or behaviours (23). It is therefore

TABLE 1 Constructs of the adapted Theoretical Framework of Acceptability (TFA) (32).

TFA construct	Definition Sekhon et al. (32)	Definition as applied to this study
Affective attitude	How an individual feels about the intervention	How an individual feels about the item (e.g., do they feel comfortable with the item, do they like the phrasing of the item, is the item distressing in any way)
Burden[1]	The perceived amount of effort that is required to participate in the intervention	The amount of (cognitive) effort required to understand the item and how it works (e.g., is the item clear or confusing in any way, do they find the item too difficult to answer, is it a good fit for asking about suicidality)
Intervention coherence[1]	The extent to which the participant understands the intervention and how it works	
Opportunity costs[2]	The extent to which benefits, profits or values must be given up by engaging in the intervention	How confident a participant is that they could answer this item (and/or answer it honestly) in light of their own value systems, motivation, and the potential costs/benefits of their response (e.g., is there anything that would prevent them from answering this item)
Self-efficacy[2]	The participant's confidence that they can perform the behaviour(s) required to participate in the intervention	
Ethicality[2]	The extent to which the intervention has a good fit with an individual's value system	
Perceived effectiveness	The extent to which the intervention is perceived as likely to achieve its purpose	The extent to which the item is perceived as likely to serve its purpose (e.g., do they think this item is useful or effective for identifying suicidality in perinatal women)

Superscript numbers [(1,2)] indicate that theses TFA constructs were clustered in this research.

important to assess how acceptable their use is to perinatal women, for both clinical and research purposes.

2 Materials and methods

2.1 Design and participants

This was a qualitative study using cognitive interviewing and semi-structured interviews to examine the acceptability and content validity of existing suicide-related screening items to perinatal women. All interviews took place online (e.g., Microsoft Teams or Zoom) or via the telephone, depending upon the participants preference.

The sample size for this study was guided by the Information Power approach (64). This approach suggests that five key areas should be considered when establishing a sample size estimation: (i) study aim(s); (ii) sample specificity; (iii) use of established theory; (iv) quality of dialogue; and (v) analysis strategy. It was anticipated that approximately 20 women would be suitable to meet the sample size requirements above. The final sample consisted of 21 participants.

Participants were pregnant and postnatal women (up to two-years postnatal), aged 18 or over, living in the United Kingdom, who were able to speak and understand English. The sample included both women who had experienced mental health problems and/or suicidality during the perinatal period in the past, and those who had not. Women who were experiencing current (self-reported) suicidality were not eligible to take part.

2.2 Recruitment and data collection

Of the 21 participants, most (n = 16) were recruited via social media (e.g., Twitter/X), and five were recruited via word of mouth. After making initial contact with the lead researcher (ED), eligible participants were sent an information pack which included a consent form, participant information sheet, and resource list to enable an informed decision about participation in the study. Once a participant had provided their informed consent, a convenient time was scheduled for them to take part in a one-to-one interview with ED, who was experienced in conducting qualitative interviews on sensitive topics and in identifying and signposting suicide risk.

A topic guide was developed by ED and RC, which comprised two parts. The first part of the interview used cognitive interviewing techniques to examine the acceptability and content validity of 16 suicide-related items taken from seven different depression and/or mental health screening measures, which have previously been administered and/or validated in perinatal populations (23). Participants were asked to sequentially read out each item (and its corresponding response options) and to 'think aloud' when verbalising their thoughts on the item to the researcher. Participants were not asked to answer the screening items directly, as our interest was in their thoughts about the application of these items in the 'real world' context, not in their responses to them per se. The researcher also used relevant probes to further explore the TFA constructs (as outlined in Table 1). The second part of the interview was a semi-structured interview about the broader implications of suicidality screening during the

perinatal period. Detailed findings from this part of the interview are reported elsewhere.

Interviews lasted approximately 90 minutes, were audio-recorded, and transcribed verbatim and deidentified. Participants were reminded throughout the study that their participation was entirely voluntary and that they could withdraw from the study at any stage, up until the point of data analysis, without needing to provide a reason. All participants completed their interviews in full, with no obvious or reported adverse effects.

2.3 Measures

The 16 suicide-related items were taken from seven different screening measures of psychological distress, depression, and anxiety. Items were chosen because they have previously been administered and/or validated in perinatal populations to identify suicidal ideation and/or suicidal behaviours (23). A descriptive summary of the included measures/items is presented in Table 2. Six items were from the Inventory of Depression and Anxiety Symptoms (IDAS) (66) suicidality subscale. Five items were from the Postpartum Depression Screening Scale (PDSS) (67) suicidal thoughts scale. One item each was taken from: the Edinburgh Postnatal Depression Scale (EPDS) (19); the Patient Health Questionnaire-9 (PHQ-9) (20); the Self-Reporting Questionnaire-20 (SRQ-20) (68); the Beck Depression Inventory (BDI) (65); and the Ultra-Short Maternal Mental Health Screen (Ultra-Short) (69).

2.4 Data analysis

The deidentified transcripts were uploaded to NVivo 14 (70) for analysis. Using principles of the framework approach (71, 72), data were initially analysed using deductive content analysis, which is suitable for interpreting qualitative data in line with an existing framework or theory.

TABLE 2 Descriptive summary of measures.

Measure, item	Description of measure	Item content	Response options [scoring]	Recall period
Beck Depression Inventory (BDI), item-9*	21-item scale to screen for depression symptoms and severity	"I don't have any thoughts of killing myself", "I have thoughts of killing myself, but I would not carry them out", "I would like to kill myself", "I would kill myself if I had the chance"	Choose one of the statement options [0 to 3]	Past seven-days
Edinburgh Postnatal Depression Scale (EPDS), item-10*	10-item scale to screen for postnatal depression symptoms and severity	"The thought of harming myself has occurred to me"	"Never" [0], "Hardly ever" [1], "Sometimes" [2], "Yes, quite often" [3]	Past seven-days
Inventory of Depression and Anxiety Symptoms (IDAS), item-7*	64-item scale to screen for depression and anxiety symptoms	"I had thoughts of suicide"	"Not at all" [1], "a little bit" [2], "moderately" [3], "quite a bit" [4], "extremely" [5]	Past two-weeks
Inventory of Depression and Anxiety Symptoms (IDAS), item-9*	64-item scale to screen for depression and anxiety symptoms	"I hurt myself purposely"	"Not at all" [1], "a little bit" [2], "moderately" [3], "quite a bit" [4], "extremely" [5]	Past two-weeks
Inventory of Depression and Anxiety Symptoms (IDAS), item-14*	64-item scale to screen for depression and anxiety symptoms	"I thought about my own death"	"Not at all" [1], "a little bit" [2], "moderately" [3], "quite a bit" [4], "extremely" [5]	Past two-weeks
Inventory of Depression and Anxiety Symptoms (IDAS), item-15*	64-item scale to screen for depression and anxiety symptoms	"I thought about hurting myself"	"Not at all" [1], "a little bit" [2], "moderately" [3], "quite a bit" [4], "extremely" [5]	Past two-weeks
Inventory of Depression and Anxiety Symptoms (IDAS), item-41*	64-item scale to screen for depression and anxiety symptoms	"I cut or burned myself on purpose"	"Not at all" [1], "a little bit" [2], "moderately" [3], "quite a bit" [4], "extremely" [5]	Past two-weeks
Inventory of Depression and Anxiety Symptoms (IDAS), item-43*	64-item scale to screen for depression and anxiety symptoms	"I thought that the world would be better off without me"	"Not at all" [1], "a little bit" [2], "moderately" [3], "quite a bit" [4], "extremely" [5]	Past two-weeks
Patient Health Questionnaire-9 (PHQ-9), item-9*	9-item scale to screen for depression symptom prevalence and severity	"Have you had thoughts that you would be better off dead, or of hurting yourself in some way?"	"Not at all" [0], "several days" [1], "more than half the days" [2], "nearly every day" [3]	Past two-weeks

(Continued)

TABLE 2 Continued

Measure, item	Description of measure	Item content	Response options [scoring]	Recall period
Postpartum Depression Screening Scale (PDSS), item-7*	35-item scale to screen for postnatal depression symptoms	"I started thinking that I would be better off dead"	"Strongly disagree" [1], "disagree" [2], "neither disagree nor agree" [3], "agree" [4], "strongly agree" [5]	Past two-weeks
Postpartum Depression Screening Scale (PDSS), item-14*	35-item scale to screen for postnatal depression symptoms	"I've thought that death seemed like the only way out of this living nightmare"	"Strongly disagree" [1], "disagree" [2], "neither disagree nor agree" [3], "agree" [4], "strongly agree" [5]	Past two-weeks
Postpartum Depression Screening Scale (PDSS), item-21*	35-item scale to screen for postnatal depression symptoms	"I wanted to hurt myself"	"Strongly disagree" [1], "disagree" [2], "neither disagree nor agree" [3], "agree" [4], "strongly agree" [5]	Past two-weeks
Postpartum Depression Screening Scale (PDSS), item-28*	35-item scale to screen for postnatal depression symptoms	"I felt that my baby would be better off without me"	"Strongly disagree" [1], "disagree" [2], "neither disagree nor agree" [3], "agree" [4], "strongly agree" [5]	Past two-weeks
Postpartum Depression Screening Scale (PDSS), item-35*	35-item scale to screen for postnatal depression symptoms	"I just wanted to leave this world"	"Strongly disagree" [1], "disagree" [2], "neither disagree nor agree" [3], "agree" [4], "strongly agree" [5]	Past two-weeks
Self-Reporting Questionnaire-20 (SRQ-20), item-17	20-item scale to screen for mental disorders	"Has the thought of ending your life been on your mind?"	YES/NO [1/0]	Past 30-days
Ultra-short Maternal Mental Health Screen (Ultra-Short), item-4	4-item scale to measure common perinatal mental disorders	"Has the thought of committing suicide often occurred to you?"	YES/NO [1/0]	Past month

* measure has been validated in perinatal populations.
Measures: Beck Depression Inventory (BDI) (65); Edinburgh Postnatal Depression Scale (EPDS) (19); Inventory of Depression and Anxiety Symptoms (IDAS) (66); Postpartum Depression Screening Scale (PDSS) (67); Patient Health Questionnaire-9 (PHQ-9) (20); Self-Reporting Questionnaire-20 (SRQ-20) (68); Ultra-Short Maternal Mental Health Screen (Ultra-Short) (69).

2.4.1 Theoretical framework of acceptability

Following a familiarisation of the interview transcripts, ED and RC developed a coding framework based on the TFA constructs to inform the analysis. Sekhon et al. (32) suggest that the seven constructs may cluster or influence each other (Figure 3, p.8). Based on the initial coding, the decision was made to cluster the constructs of 'burden and intervention coherence' into one unique domain, and 'opportunity costs, self-efficacy, and ethicality' into another. Here, the construct of 'burden' was interpreted to be less associated with how much time or expense was required to answer each individual suicide-related item (as these were relatively short) and more related to the amount of cognitive burden (e.g., effort) that was required to understand the item and how it worked ('intervention coherence'). The constructs of 'opportunity costs, self-efficacy, and ethicality' were clustered because together they related to how confident a participant might feel answering the item (and/or answering it honestly) in light of their individual value systems and the potential costs or benefits that may be associated with their response. 'Affective attitude' and 'perceived effectiveness' remained as single constructs. By conceptualising the constructs in this way, the researchers were able to assess the concurrent acceptability (e.g., as experienced in real time) and the prospective acceptability (e.g., if applied in the real world) of each suicide-related item in relation to the research aims. Definitions of the TFA constructs as applied to this study are presented in Table 1. In addition, the categories of 'response options' and 'recall period' were also included in the coding framework as relevant aspects of content validity.

The indexing procedure for each transcript involved: (i) selecting the data associated with the first suicide-related item (e.g., EPDS, item-10) and coding it under a corresponding heading (e.g., EPDS, item-10); (ii) coding all occurrences related to each of the framework categories for the item under the corresponding heading (e.g., 'affective attitude', 'perceived effectiveness' etc.); and (iii) applying positive (+), negative (–) and/or neutral/indifferent (+/-) codes to the data within each category. This process was repeated for all 16 suicide-related items across each transcript, and the data were then extracted into a matrix format using an Excel spreadsheet. This enabled the researchers to examine the number of positive, negative, and neutral/indifferent coding instances per item across all constructs and participants. Lastly, inductive coding was also applied to the qualitative data within each of the positive, negative, and neutral/indifferent categories to explore and generate themes within each of the domains.

The entire dataset was initially coded by ED and RC, with AZ independently coding 20% of the transcripts (adhering to the procedure above). Any areas of contention were discussed, and all minor coding discrepancies were revised as needed to ensure the trustworthiness of the analysis. ED and RC met regularly

throughout the analytic process to discuss and review the coding as it progressed, and all coauthors agreed on the finalised main themes without disagreement. Reporting follows the guidelines set by the Consolidated Criteria for Reporting Qualitative research (73).

3 Results

3.1 Sample characteristics

Twenty-one perinatal women took part in this study. Three were pregnant at the time of their interview and 19 had a child under the age of two. One participant was both pregnant and had a child under the age of two. For 14 women, this was either their only child or first pregnancy. Most women were in their 30s (range 29 – 42 years, mean age 33.9). Twenty women spoke English as their first language and the cultural background of participants was predominantly White British. Nineteen women held a bachelor's degree or higher qualification. Participant demographics are presented in Table 3.

TABLE 3 Sample characteristics (n = 21).

Sociodemographic variable	*M (range)* or *n* (%)
Age	33.9 (29 – 42 years)
Perinatal phase (at time of interview)	
Pregnancy	2 (9%)
Postnatal (≤ 24-months)	18 (86%)
Pregnant and postnatal*	1 (5%)
Number of additional children	
0	14 (67%)
1	4 (19%)
2	3 (14%)
Mental health problems and/or suicidal thoughts during most recent pregnancy and/or after birth	
Yes	17 (81%)
No	4 (19%)
Mental health problems and/or suicidal thoughts at any other time in life	
Yes	13 (62%)
No	8 (38%)
Treatment and/or intervention for mental health problems at any time in life (including perinatal period)	
Yes	15 (72%)
No	3 (14%)
Not applicable	3 (14%)
English as first language	
Yes	20 (95%)
No	1 (5%)
Education	
Secondary school (e.g., GCSE, SVQ level 1)	1 (5%)
Post-secondary (e.g., A-level, National Diploma	1 (5%)
Bachelor's degree, or equivalent	8 (38%)
Master's degree, or equivalent	7 (33%)
Doctorate	4 (19%)
Cultural background	
(White) English/Welsh/Scottish/Northern Irish/British	16 (77%)
(White) Irish	2 (9%)
Any other White background	2 (9%)
(Mixed/multiple ethnic groups) White and Asian	1 (5%)

*One participant was pregnant at the time of interview and had a child under two years old.

Seventeen women self-reported that they had experienced mental health problems (including anxiety and depression) and/or suicidal thoughts during their current or most recent pregnancy and/or after the birth of their baby. Of these 17 women, five had not experienced any mental health problems and/or suicidal thoughts prior to their pregnancy. Thirteen women reported that they had experienced mental health problems and/or suicidal thoughts prior to their most recent pregnancy. Of these 13, 12 women also experienced poor mental health during the perinatal period, and only one participant did not. Over two-thirds of the women reported that they had received treatment and/or support for their mental health problems, but it is unclear when this was accessed (e.g., it could have been at a time prior to pregnancy and/or during the perinatal period).

3.2 Main findings

In the following sections, key themes related to each of the TFA constructs are discussed under the corresponding heading. Findings are presented using quantitative data from cognitive interviews, and qualitative data from semi-structured interviews. The participants thoughts regarding the response options and recall periods for the suicide-related items are also reported.

The number of positive, negative, and neutral/indifferent codes that were identified for each item using the TFA constructs as applied in this study are presented in Supplementary Table 1. Supplementary Table 2 displays the number of positive, negative, and neutral/indifferent codes that were identified in relation to the response options and recall periods for each item or subscale. Both tables also present illustrative quotes per item, response option and recall period.

3.2.1 Affective attitude

This construct is concerned with how women felt about the different suicide-related items. Whilst all participants expressed that it was important and necessary for healthcare professionals to ask about suicidal thoughts and/or behaviours at regular intervals throughout pregnancy and after birth, differences in how the items were worded influenced their level of comfort and reactions to them.

Item wording and content.

Many women were uncomfortable with items that used words such as 'dead' (PHQ-9, item-9; PDSS, item-7) 'death' (PDSS, item-14) or 'kill' (BDI, item-9). These words felt upsetting and confronting to them because they emphasised the finality of what thinking about suicide might result in.

> "I personally do find that one a bit more of a confronting question, even just with it being 'dead' at the end of the sentence, that's quite a triggering word I think for someone who maybe does have suicidal ideation, yeah, that's a bit more

> of an uncomfortable question, 'cos 'dead' that's the final bit isn't it, there's nothing after that." (p8).

Instead, women preferred the phrase 'ending your life' because this language felt slightly softer, and it focussed more on the process of suicide rather than the outcome (SRQ-20, item-17). By phrasing the item in this way, women said they would feel less defensive and more likely to engage in an honest conversation about how they were feeling.

> "I'd receive this [SRQ-20, item-17] much better, if someone said to me 'has the thought of ending your life been on your mind' I'd be like 'well no, it hasn't been on my mind' but I think if it had been on my mind, I think I'd probably be more inclined to say 'yes', I think it probably would open up a conversation because it's more gentle, and in a way, it just feels less intrusive." (p7).

Women were also more comfortable with items that asked about thoughts of 'harming yourself' (EPDS, item-10) or 'hurting yourself' (IDAS, item-15) because these terms felt more open to interpretation. As such, the women did not feel like they would be admitting to something specific if they endorsed these items, which was less frightening. However, an important caveat to this was that nearly all women interpreted 'harming or hurting' as non-suicidal self-harm.

> "For me, that would be quite specific for self-harming, you know, even if I was suicidal at that point, I wouldn't ever think that question had anything to do with me, I would be thinking 'oh no, that's self-harm." (p4).

Women expressed mixed feelings about using the word 'suicide' (IDAS, item-7; Ultra-Short, item-4). For some women, this word seemed too direct and clinical, whereas for others it made the item easier to receive because it felt less personal. Two women said that using the word suicide was helpful to them because they might 'talk themselves out' of answering questions that used more indirect or 'fluffy' language. Likewise, items that used subjective and/or overly emotive language were largely disliked. Many women stated that the phrases 'the only way out of this living nightmare' (PDSS, item-14) and 'the world would be better off without me' (IDAS, item-43) were unnecessarily dramatic. Not only was this language viewed as unsuitable, but women also felt that it might not necessarily describe their experiences. As one woman said:

> "I don't like the term 'living nightmare', that feels like putting words in someone's mouth in a very extreme way, you know, even if I was feeling suicidal, I would be tempted to disagree with that one because, calling it a 'living nightmare' might not necessarily describe my experiences." (p3).

Some women also felt that using words such as 'wanted to' (PDSS, item-21, and item-35) or 'on purpose/purposely' (IDAS, item-9, and item-41) in relation to suicidal and/or harming thoughts and behaviours was inappropriate. They suggested that these words may reinforce feelings of shame and indirectly place a negative onus onto the woman for engaging in harming behaviours. One woman further highlighted how the use of 'purposely' reflects a lack of understanding regarding what living with harming thoughts and/or behaviours might look like:

> "Purposely' gives it an assumption that you know what you're doing, and when you're in a decline of mental health, you don't really know what you're doing, it makes it sound like there's been thought behind it, but when I did it [harming myself], it was always done in a frantic, very 'on the spot' moment, never from a 'I'm thinking about doing this, I'm going to go and set it up to do that, I'm now going to hurt myself' so yeah, I think 'purposely' gives a really big assumption and it also detracts away from what actually an illness is like, you don't do things 'purposely', you don't even realise that you're doing it until the act is done, and then you get all the shame and things like that afterwards, you don't have control over it." (p9).

3.2.2 Burden and intervention coherence

This construct is concerned with how much cognitive effort was required for the women to understand and/or complete each item, and the extent to which this may affect their views regarding how the item worked to identify suicidal thoughts and/or behaviours. Overall, the clarity of items appeared to be problematic. This related to both the basic structure of sentences and comprehending the implicit meaning of concepts and phrases. Many women said that these issues might cause confusion and difficulty when attempting to answer the items because they would not understand what was being asked of them.

Ambiguity of terms and phrases.

Women found it easier to understand short and direct items, rather than those which contained abstract and/or complex terms. Women suggested that it was important to use plain English, and correct grammar to ensure comprehensibility, particularly for those who may not speak English as a first language and/or struggle with literacy. Many women commented positively on the relatability of items that used more 'everyday' language, however they also felt that sometimes these were unclear for identifying suicidal thoughts. For example, women found the phrase 'leave this world' (PDSS, item-35) ambiguous. Some suggested that this could mean leaving their current situation or home environment, or simply needing a break, and that they would not know how to respond to this item.

> "This feels a bit more like esoteric, it feels too subjective, like 'what does that mean [?]', is it in like, abandon family, leave [hometown] like, or is it just voicing views on like 'I've found it really hard being a mum, I found it really hard entering into this new world of parenthood', or does it mean like, 'I want to commit suicide' [?], I mean most people will probably be like 'I'm not really sure what that means' so I don't know if you'd 'disagree or agree' because I'm not really sure what this is

> actually getting at." (p21).

Likewise, many women found words in the item content such as 'often' (Ultra-Short, item-4), 'occurred to you' (Ultra-Short, item-4; EPDS, item-10), and 'on your mind' (SRQ-20, item-17) too broad and subjective. One woman commented:

> "Occurred to you often' [?], that's really gonna limit peoples answers because you're gonna have somebody who thinks 'well how often is often, how much is often, what is often [?]' you know, is that once a week out of the past month, every single day, or just once [?], for me, just once is enough, but it couldn't be considered to be 'often' in this context, so I would just get rid of 'often." (p13).

Concept definitions and the implications of nuance.

Many women struggled to understand the definitions of 'hurt myself' (IDAS item-9 and item-15; PHQ-9, item-9; PDSS, item-21) or 'harm myself' (EPDS, item-10). Most women interpreted 'hurting or harming myself' to mean non-suicidal harm, but some were unsure as to whether this encompassed both physical and/or psychological harm, intentional or unintentional harm, and to what degree. Women felt that these terms needed far more clarity.

> "I mean 'harming' can be a complete range of different methods to different people, I think that's quite broad, it could be emotional, physical, and I would think that the emotional and the physical would be treated differently in terms of 'harm', so I think there could be some struggle to answer that question in terms of how people interpret it … the stereotypical-ness of it is that you probably think immediately of the physical, of actually doing something to your body externally as opposed to turning to alcohol, turning to drugs, so I think it would be better if it was more granular in what it was asking for, I think it needs to be probably written out directly, of what the different things could be." (p9).

Women had mixed feelings about whether suicidal and non-suicidal harm should be enquired about in the same item. Some women suggested that having a broad item about 'harming' or 'hurting' oneself may capture more people in need of support, whereas others saw 'suicidality' and 'harming' as two distinct phenomena that should be asked about independently. Likewise, whilst women said that it was important to identify and distinguish between a desire to die versus intentionally ending your own life, several women felt that the compound item 'have you had thoughts that you would be better off dead or of hurting yourself in some way' (PHQ-9, item-9) should be separated. They felt that this item was potentially asking too much e.g., passive and active suicidal ideation, non-suicidal self-harm, or a combination, which could be confusing and make it difficult to answer. A further implication was how a positive endorsement to this item might be interpreted. Some women highlighted that they may have had thoughts relating to one part of the item and not the other, and might not feel comfortable about being associated with both aspects.

> "I feel like it's better to ask them as two separate questions actually because I think the detail is good to have, whether it's one or the other, and some people when reading this question might think 'oh, well I don't think I'm better off dead, but I have thought about hurting myself in some way' and so they might kind of dismiss it or not answer it, so yeah, I think it's better to separate them out because they might feel strongly about not answering one of them in that way and that might steer them to give a less accurate answer of how they're feeling." (p6).

3.2.3 Opportunity costs, self-efficacy, and ethicality

This construct is concerned with how confident the women were about answering the different items (and/or feeling confident to answer them honestly) in light of their own value systems, motivation and the potential costs/benefits of their responses. Overarchingly, women talked about the stigma associated with suicidality and their fears concerning the consequences of disclosure.

Stigma, shame, and judgement.

For many women the concept of suicide had very negative connotations. Women expressed that the stigma associated with suicide might create a barrier to them answering these items, and/or answering them honestly and they were afraid of the consequences of endorsement (e.g., interventions from social services and/or having their baby taken away). This was particularly heightened for items that included the word 'suicide' or 'committing suicide' (IDAS, item-7; Ultra-Short, item-4), 'dead' (PHQ-9, item-9; PDSS, item-7), 'death' (PDSS, item-14) or 'kill' (BDI, item-9).

> "That's a really big thing to disclose to anyone, and especially if you are pregnant or if you've just had a baby, like your first thought would be 'are they gonna take my baby away from me, does this mean I'm gonna end up having lots of interventions', I would be like 'is it safe for me to answer this question or is it going to open pandora's box, is the help gonna be helpful [?]'… but yeah, I think that for me, the biggest barrier would be thinking 'does this mean that social services are gonna get involved' and that would terrify me, so that would really put me off if I'm being honest." (p10).

Other women further highlighted the implications of using the word suicide in terms of religion and cultural differences.

> "Suicide' has got such a negative connotation, especially if you're religious, suicide is a word that like basically, if you do it, you are super bad, you go to hell and everything else, so yeah, it's one of these judgemental words that can make people feel taken aback

> from telling the truth and being honest about the answers". (p2).

Women also talked about how the experience of suicidality stood against the traditional narratives of motherhood. This inner conflict created feelings of shame and guilt. As such, women may not want to answer suicide-related items through a fear of being perceived and/or judged as a bad mother.

> "When you have like a child, there's that feeling of guilt, you feel bad about what's going on and you don't necessarily want to admit that you're feeling down or you're struggling because it's meant to be like the best time ever … and I think there's that conflict there of feeling like you should be feeling great and you've got this amazing joy in your life and everyone says 'oh, just enjoy every moment' and all of that kind of stuff … so it kind of just goes against the whole narrative around having a baby and what it's meant to be like … it would be hard to like properly admit that or answer that honestly because of all the wider conflicts as like a new mum." (p7).

The importance of context and framing.

Some women found broader items (e.g., 'the thought of harming myself has occurred to me', EPDS, item-10) less frightening to be asked, they felt more confident in their ability to answer these honestly and suggested that these types of items might be useful for 'opening up a conversation'. The women also talked about the importance of context, framing and normalising suicide-related items, and providing more information about why these questions were being asked as this would help to facilitate a more honest dialogue with healthcare professionals.

> "You need a very sensitive introduction to a question like this, or to a whole questionnaire maybe, something like 'we know that new parents can have thoughts about harming themselves, we want to find out if this is something that you've experienced so that we can put in place the right support for you', I think you are more likely to kind of take it in if someone says it to you … normalising the fact that these thoughts can occur for new parents is important." (p3).

3.2.4 Perceived effectiveness

This construct is concerned with the extent to which women perceived the items as likely to serve their purpose. It is important to acknowledge that the 'effectiveness' of these items for identifying suicidal thoughts and/or behaviours is profoundly embedded within and influenced by the other TFA constructs, and heavily dependent upon additional factors such as context and individual differences. Bearing these significant implications in mind, the women did offer insights regarding the potential usefulness or relevance of some items for identifying suicidal thoughts and/or behaviours.

Many women felt that items related to 'harming or hurting yourself' were unclear and may not be useful or relevant for identifying suicidal thoughts as they would associate them more with self-harm. Likewise, items that used vague and/or abstract terms were not perceived to be particularly helpful, and nearly all women felt that the item 'I thought about my own death' (IDAS, item-14) would be ineffective for asking about suicidality. As one woman said:

> "So, that doesn't speak to me necessarily about suicide, you know, 'I thought about my own death' is thinking about when you might die, what might happen when you die, and if you're pregnant or have just had children, then you may well think quite a lot about your own death, so yeah, I don't think that would pick up on suicide at all." (p17).

Despite the directness and heightened negative undertone of terms such as 'suicide' or 'dead', some women did feel that these words were more likely to be effective for identifying suicidal thoughts, because it was clearer what the item was asking.

> "I think it's clear and direct [IDAS, item-7], which I think if you're trying to identify women that are likely or thinking of suicide, that's quite a good one." (p20).

Likewise, women saw potential utility in the phrase 'ending your life' (SRQ-20, item-17) for identifying suicidality because they felt that it was very specific, and it would capture the more active suicidal thoughts as opposed to passive thoughts about not wanting to be here anymore.

> "This one is better than the previous ones because its 'ending your life', the language is softer, and it's more direct, so with 'ending your life', the implication is that you would do it rather than just, you know, you not being around anymore." (p13).

A few women also commented on the issue of interpreting items for those who don't speak English as a first language and suggested that the word 'suicide' may not be as easily translatable as other terms, which may result in women from this demographic being missed.

> "I'm also just thinking as well about mums for whom English isn't their first language, and actually, 'death' and 'dying' are words that we probably come across a little bit more often, and so someone who isn't completely fluent in English might be more likely to understand a question that's asking about 'death and dying', rather than 'suicide' as I don't know how 'suicide' translates to other languages." (p3).

3.2.5 Response options

Response options for the items varied, and women were asked to comment on their appropriateness and comprehensibility in relation to the item. Broadly, women preferred a frequency-based scale (e.g., 'never' to 'every day'), or a dichotomous response choice

(e.g., 'yes' or 'no') to an agreement scale (e.g., 'strongly disagree' to 'strongly agree') or severity-based scale (e.g., 'not at all' to 'extremely'). However, the women also felt that it was important and necessary to follow-up all responses other than 'no', 'never', 'strongly disagree' and so on with a more in-depth conversation.

Many women felt that frequency-based response options were appropriate for answering difficult and sensitive items because these offered scope for disclosing some amount of thoughts based on individual comfort levels.

> "I think having a scale is good, because it allows people to not commit fully 'cos if you can like almost say 'a bit' then people feel a bit safer saying that 'cos they're not saying 'I've definitely felt it all the time, but it's just like 'a bit." (p1).

However, some women expressed that being asked to rate suicidal thoughts on a scale was inappropriate for identifying highly personal and distressing feelings, because this felt like a 'tick box' exercise. They explained how 'yes or no' response options were more validating of their experiences (SRQ-20, item-17; Ultra-Short, item-4).

> "These would be better off as 'yes or no', because you're making someone feel valid in that really strong and upsetting and difficult feeling they're having, asking them to rate it is very odd way of approaching it I think." (p17).

Several women also struggled to differentiate between response options such as 'hardly ever' and 'sometimes' (EPDS, item-10) because these terms were too subjective and ambiguous. Likewise, whilst some women liked the clarity of being specifically asked how many days they had experienced suicidal thoughts (PHQ-9, item-9), others felt that it was challenging for perinatal women to quantify how often these thoughts had occurred.

> "I don't really respond well to these, having to specifically pin-point it to a day, because when you are in those kind of head spaces, and especially having like a baby and stuff, when you're tired, you're not counting days, it's either going to be really frequent or it's not, yeah I don't think you're gonna be counting to see if it's 'half the days' or not." (p8).

Most women had strong negative reactions to the agreement-type and severity-based response options. Women said that using the terms 'agree or disagree' (PDSS, subscale) felt like a work performance review or generic questionnaire and was highly inappropriate for such a sensitive topic. They also stated that there was no benefit to having the option of 'neither disagree or agree', nor did they understand how to differentiate between 'agree' and 'strongly agree'. Similarly, the women found the severity-based options (IDAS, subscale) very confusing, and not fitting at all for the types of questions that were being asked.

> "I mean, 'I had thoughts of suicide, a little bit' I just can't imagine what thoughts of suicide 'a little bit' are [?], the rating thing isn't any good I don't think, and 'extremely', something about that doesn't sit well either, I mean apart from the fact that it doesn't make sense, I think if I was sitting down filling in a questionnaire, and I was feeling extremely suicidal, it just wouldn't feel comfortable to me that wording." (p17).

Women had mixed feelings about the statement-based response choices (BDI, item-9). Despite all women disliking the content of this item (e.g., 'killing myself'), some did see value in the format because it provided a distinction between passive versus active thoughts and intent. Other women said that this style included too much information to process, which would make them feel overwhelmed.

3.2.6 Recall period

The recall period for the items ranged from 'the past seven-days' to 'the past month'. Women were asked to provide their thoughts on these timeframes to explore appropriateness and relevance to the items. Overall, the women felt that the recall period for suicide-related screening items should be longer rather than shorter, although some did comment that shorter recall periods may be necessary and/or useful in certain instances (e.g., to monitor symptom changes for those in specialist care).

The women's preference for wider timeframes was largely due to an overarching concern that people may be missed if the recall period was limited to seven-days or two-weeks. Several women talked about the fluctuating nature of suicidal thoughts and highlighted that these may vary significantly from one day to another. As such, women felt that some suicidal thoughts might not be captured by a shorter timeframe because people may interpret this literally and therefore not disclose anything that had happened outside of the specified period.

> "You might think, 'well, at the start of the month, I was not in a good place, but this week I feel better' so then, you know, you could answer 'never', because it's asking about the past seven-days and you're just sort of like getting missed, especially someone like me, I do sort of have these like episodes, where I'll be well for a few weeks, and then I can sort of like dip again, so very specifically seven-days I could answer 'never', so it's tricky really." (p14).

Some women also expressed that putting a time restriction on these types of questions could minimise and devalue their experience of suicidal thoughts. These women said that they might assume that suicidal thoughts were not important to maternity caregivers unless they had occurred within the specified timeframe, which may then deter them from disclosing sensitive and difficult information in case it was dismissed.

> "I actually think it should be over a longer period because in a way it's quite dismissive isn't it, if I had thought about harming myself, I don't know whether I'd feel a bit like 'oh maybe I shouldn't say anything' or I might feel like 'oh maybe it doesn't matter if it was over seven-days ago 'cos it's not as important." (p7).

Lastly, whilst most women thought that applying some type of timeframe was necessary when asking about suicidal thoughts and/or behaviours, they also felt that this needed to be contextualised to their current situation. Several women suggested that a more appropriate framing of these items might be to ask 'since pregnancy or since your baby was born, have you…' because this would provide both a suitable recall period and it would situate the items in terms of being a pregnant woman or new mother.

> "Rather than have it kind of in a timeframe, it almost needs to be like 'since you've been pregnant or since birth', do you know what I mean [?], 'cos it's more about your experience of the pregnancy itself than it is about the time, so I'm wondering that for all the questions really." (p21).

4 Discussion

This study assessed the acceptability and content validity of 16 suicide-related items with pregnant and postnatal women using the TFA, and two additional categories of 'response options' and 'recall period'. It also explored the barriers and facilitators that affected women's reactions and responses to these items. This is the first time that the acceptability of different suicide-related items has been examined in perinatal populations, and the first time that the TFA has been applied in this context. Novel findings of this research are that the suicide-related items assessed in this study were largely unacceptable to pregnant and postnatal women. This finding is contrary to research that suggests more general perinatal mental health screening and/or common screening measures are acceptable to perinatal women (37–39). Therefore, this study makes an important contribution to the literature in the following ways: (i) it offers insight into how perinatal women feel about different suicide-related items that are embedded within measures that screen more widely for depression and/or other mental health problems (including their response options and recall periods); (ii) it highlights factors that may facilitate or prevent perinatal women from answering suicide-related items, and/or answering them honestly; and (iii) it provides a nuanced understanding regarding the utility and appropriateness of using these screening items to identify suicidal ideation and/or suicidal behaviours in perinatal women, which may be valuable and relevant in both research and clinical settings.

The TFA provided a structured and meaningful approach for exploring the acceptability of suicide-related items with perinatal women. Some of the TFA constructs were collapsed in this study to create a coding framework that was suitable for assessing the participant data in line with the study design and research aims (see Table 1). Clustering the components in this way allowed for greater depth in understanding how different aspects of acceptability affected the content validity of items, and it provided scope for identifying barriers and facilitators to disclosure when applying these items in the 'real world' context. The results suggested that word choice and the terms used to characterise suicide affected women's comfort with and comprehension of the items, and their willingness to engage.

In the following sections, the findings related to the TFA constructs for each suicide-related item or subscale have been summarised to provide an overall assessment of their acceptability. The corresponding response options and recall periods are discussed in terms of their key strengths and weaknesses. The clinical implications of applying these measures in practice is also considered.

SRQ-20, item 17.

Overall, women were most comfortable with SRQ-20, item-17, which asks 'has the thought of ending your life been on your mind'. Women said that the phrase 'ending your life' felt slightly softer than other terms and made the item less confronting to answer honestly. Women also saw potential utility in this item and its response options ('yes/no') for identifying suicidal thoughts in perinatal women, although some felt that the latter part ('on your mind') was confusing and should be modified or removed.

EPDS, item-10.

Similarly, women generally found EPDS, item-10, less upsetting than other items. However, many interpreted 'harming myself' to mean non-suicidal self-harm, and did not think the item was specific enough for identifying suicidal thoughts. This finding is in line with previous research that also highlighted the ambiguity of this item (37, 55). Furthermore, whilst most women felt that frequency-based response options were appropriate, some struggled to differentiate between 'hardly ever' and 'sometimes', which created additional confusion in answering the item accurately.

PHQ-9, item-9.

Women had mixed feelings about PHQ-9, item-9. Some women thought that asking about suicide and self-harm in one item was useful, whereas others felt that these needed to be addressed separately. Several women said they would not know how to answer this item, and/or would not feel comfortable doing so because it was attempting to ask too much. Likewise, the phrase 'better off dead' was largely disliked. Women found this distressing and said that it may prevent them from answering the item. Previous research has observed similar hesitancy from perinatal women towards PHQ-9, item-9 (53, 54), but it was not clear whether this related to the specific item wording or to the topic of suicide more broadly. Differentiating the terms 'several days' and 'more than half the days' and having to quantify their answers was problematic.

PDSS, suicidal thoughts subscale.

The PDSS suicidal thoughts subscale comprised five items. Generally, women found these items to be overly emotive or dramatic, and/or too abstract for identifying suicidal thoughts in

perinatal women. Women also thought that the agreement response option, was unsuitable because it felt generic and undermined the seriousness of the topic. They further struggled to understand what determined 'strongly disagree' from 'disagree' or 'strongly agree' from 'agree' and did not see value in the option of 'neither disagree or agree' for items related to suicide and/or self-harm.

IDAS, suicidality subscale.

The IDAS suicidality subscale comprised six items. Asides from item-43 ('the world would be better off without me') and item-14 ('I thought about my own death'), women found these items relatively direct and clear. However, most women felt that three of these items (item-9, item-15, and item-41) were self-harm specific, and unlikely to be effective at identifying suicidal thoughts. Likewise, all women were uncomfortable with item-41 'I cut or burned myself on purpose' and felt that this type of question should only be asked as part of a comprehensive assessment, and not used for screening. Women also largely disliked the severity scale response options. For example, the response option of 'extremely' in answer to item-7 'I had thoughts of suicide' did not appear to make sense, nor was it befitting to the item.

BDI, item-9 and the Ultra-Short Maternal Mental Health Screen, item-4.

Women had the strongest negative reactions to BDI, item-9, and item-4 from the Ultra-Short, which use the terms 'killing myself' and 'committing suicide', correspondingly. These items also elicited the most concern from women in terms of perpetuating stigma and inciting fear about the consequences of disclosure. Nearly all women felt that these items were inappropriate for identifying suicidality in perinatal women and they would not want to answer them.

Recall period.

Recall periods for the items ranged from 'seven-days' to the 'past month'. Many women felt that longer timeframes should be applied to these items to avoid cases being missed, prevent women's experiences being minimised and to contextualise these items around being a pregnant or postnatal woman. Several women suggested using the phrase 'since pregnancy' or 'since the birth of your baby' (or similar) as they found this more relatable to their current situation, and easier to reflect upon in terms of when and/or how frequently thoughts were happening.

4.1 Implications for practice and future research

Many suicide-related items that are embedded into existing screening measures for depression and/or other mental health problems may be unacceptable to perinatal women in their current form. Identifying pregnant or postnatal women who may be experiencing suicidal ideation and/or suicidal behaviours poses several challenges in the maternity care context. Pressures due to financial constraints, a lack of resources, staff shortages and increasing demands and expectations are common across health services. Maternity care practitioners often have little time during routine appointments to enquire about mental health problems with perinatal women, which further increases the potential for cases being missed. Whilst common mental health problems are not universally screened for during pregnancy and after birth in the UK, screening measures do offer a pragmatic approach for identifying women who may require additional support. These measures are generally brief and easy to administer, with a relatively small burden upon resources. However, healthcare professionals and researchers should be aware of the limitations of using the measures assessed in this study to identify possible suicidality in pregnant or postnatal women because the content, comprehensibility and appropriateness of these items and their corresponding response options and recall periods may create and/or reinforce barriers to women's disclosure. There may be some value in using screening measures to identify the presence or absence of suicidal ideation in perinatal women as part of a stepped approach for identifying those who may require additional support, but the development of specific measures that are acceptable to perinatal women for this purpose is warranted. Such measures should not be used to assess suicide risk, predict future behaviours and/or determine treatment outcomes, but instead to indicate that further comprehensive psychosocial assessment might be necessary. New measures should be developed in accordance with evidence-based guidelines such as the Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) (74) and in collaboration with perinatal women. It is also important for maternity care practitioners to consider the framing of suicide and/or self-harm questions when engaging in discussions with perinatal women because wider evidence suggests that subtle differences in wording and communication style can influence and create additional barriers to disclosure (75–77). Adopting a sensitive, open, and non-judgemental approach may help to foster a trusting and safer environment for perinatal women to share their thoughts and feelings.

Furthermore, research is needed to explore perinatal women's experiences and views on the broader implications of discussing suicide in maternity care settings. This is important because many women commented on the influence of context upon their willingness to disclose suicidal ideation and/or behaviours. Factors including how suicide-related screening questions might be administered, when and/or how frequently they might be asked, and who should ask them, continuity of care, referrals to specialist services and general knowledge about perinatal mental health conditions may be relevant for developing appropriate and acceptable approaches for identifying suicidality in pregnant or postnatal women. Likewise, cultural differences, religious beliefs, language and translation issues, and social factors may create unique challenges for identifying women from different ethnic and minority groups, and future research should explore the wider barriers and facilitators, and the acceptability of suicide-related measures with women from more diverse backgrounds. It would also be useful to examine the acceptability of suicide-related items with pregnant and postnatal women in treatment settings as their views may differ from those identified in non-clinical samples.

4.2 Strengths and limitations

Using a theoretical framework to explore the acceptability of suicide-related items with perinatal women is an important strength of this research. Compared to more general approaches for

assessing acceptability, the TFA provided a systematic and comprehensive approach for informing the study design and materials, and analysing the in-depth interview data, which enabled key components of acceptability to be explored. Furthermore, given that suicidal ideation and/or behaviours are still highly stigmatised, and that recruiting pregnant women or women with a new baby poses unique challenges, the sample size and inclusion of participants from across the UK were also significant strengths of this study.

Several limitations of this study also need to be acknowledged. Firstly, using the TFA to assess the acceptability of different suicide-related items was a novel approach. The TFA was originally developed to assess the acceptability of healthcare interventions rather than measurement scales per se, hence there was a scarcity of literature or clear guidelines for how the TFA could be applied in this context. In this study, some of the TFA constructs were clustered to create an appropriate framework for exploring the data in line with the research aims. This may have affected the findings because not all constructs were assessed as unique and independent components of acceptability. Likewise, previous research has reported overlap and/or ambiguity differentiating some of the TFA constructs in certain contexts (58, 61), and similar interrelatedness was identified here. This was particularly evident for 'perceived effectiveness' which was heavily embedded within and influenced by the other TFA constructs. Therefore, the utility of 'perceived effectiveness' as a distinct component for assessing the acceptability of screening measures may be limited, and more suited to healthcare interventions with clearer behavioural and/or treatment outcomes. Secondly, the suicide-related items used in this study were taken from several wider measures of depression, anxiety and/or psychological distress. Examining these specific items in isolation to the full measurement instrument(s), and outside of their intended context, may also be a limitation of this research. The utility of these items when asked in conjunction with their counterpart items may be more acceptable and relevant for identifying wider mental health problems in perinatal women. Likewise, items from the PDSS suicidal thoughts subscale (five items) and the IDAS suicidality subscale (six items) were assessed as standalone items and not in combination together for identifying suicidality. Therefore, the relevance, comprehensibility, acceptability, and appropriateness of some of these items may have been affected. Similarly, women were not asked to directly comment on the use of depression measures to screen for suicidal ideation and/or behaviours, so the broader acceptability of this approach cannot be inferred. Lastly, the sample comprised mainly White British pregnant and postnatal women with a high level of education. As such, the views of women from more diverse ethnic, cultural, social, and religious backgrounds is required.

4.3 Conclusions

This study assessed the acceptability and content validity of suicide-related screening items with pregnant and postnatal women using the TFA. Whilst all participants agreed that it was important and necessary to ask about suicidal thoughts and behaviours during the perinatal period, the findings from this research suggest that many existing suicide-related items that are embedded into wider measures of depression and/or other common mental health problems are unacceptable to perinatal women in their current form. Item-17 from the SRQ-20 may have some utility for identifying suicidal ideation in clinical and research settings, although modifications to the latter part of the item ('on your mind') should be considered. Maternity practitioners and researchers need to be cautious about using the measures explored in this study for identifying suicidal ideation and/or behaviours in perinatal women because their content, comprehensibility, and appropriateness may create and/or reinforce barriers to disclosure. Stigma, perceived judgement, and a fear of the consequences of disclosure are significant factors that may prevent women from being honest about how they are feeling. More research is needed to explore the acceptability of discussing suicidality in maternity care settings, and the development of specific screening measures for identifying suicidal ideation in perinatal women are warranted. Such measures may help to facilitate the early identification of those who may require additional assessment and support, which may lead to better outcomes for women, their children, and families.

Data availability statement

The datasets generated and analysed during the current study are not publicly available due to the sensitive nature of the data. Requests to access the datasets should be directed to Elizabeth Dudeney, elizabeth.dudeney@city.ac.uk.

Ethics statement

The studies involving humans were approved by School of Health and Psychological Sciences Research and Ethics Committee (SHPS REC) at City, University of London (reference number, ETH2122-0757). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study prior to their interview, and they had the opportunity to withdraw from the study at any time up until the point of data analysis, without needing to provide a reason.

Author contributions

ED: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft. RC: Conceptualization, Formal analysis, Supervision, Writing – review & editing. SA: Conceptualization, Supervision, Writing – review & editing. RM: Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2024.1359076/full#supplementary-material

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Feasibility and acceptability of a community health worker administered behavioral activation intervention for postpartum depression: a single arm pilot study from India

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Introduction: Women in India experience high rates of postpartum depression (PPD), with minimal availability of screening or treatment. India has an extensive network of community health workers, known as accredited social health activists (ASHAs). While they are knowledgeable about most maternal–child health problems, they have minimal knowledge about PPD. We trained ASHAs to deliver a simple home-based intervention, behavioral activation (BA), which involves individuals in activities that are sources of positive reinforcement to counter depression. The research questions guiding this study were as follows: 1) What are the feasibility and acceptability of ASHAs screening for and delivering a brief behavioral activation intervention addressing PPD among women in Belagavi, South India? 2) What impact did the brief behavioral activation intervention have on PPD?

Methods: The mixed methods evaluation used interviews with participants and interventionists, and depression scores were assessed before and after the evaluation. After a 2-day training with 17 ASHAs that focused on understanding PPD, screening using the Edinburgh Postnatal Depression Scale (EPDS), and implementing the BA protocol, ASHAs and researcher supervisors screened the mothers 6–12 weeks postpartum presenting at pediatric immunization clinics. Mothers who screened positive were invited to participate in an ASHA-led 5-week BA intervention, with ASHAs visiting the mothers' homes. We assessed post-intervention EPDS scores and conducted satisfaction assessments and individual interviews.

Results: All 26 women who screened positive on the EPDS agreed to be enrolled in the study. All participants had a significant reduction ($p < 0.001$) in PPD scores. Both ASHAs and mothers had high enthusiasm for the intervention methods and activities.

Discussion: This ASHA-delivered BA intervention was found to be feasible, acceptable, and effective in treating PPD in rural Indian mothers. This corroborates literature that demonstrates the efficacy of a BA intervention among individuals with generalized depression in South Asia. In communities with minimal mental health resources, interventions led by trained community workers have the potential to address PPD.

KEYWORDS

postpartum depression, South India, behavioral activation, community-health worker, maternal mental health

Introduction

Postpartum depression (PPD) is a worldwide phenomenon, with women from all demographic, cultural, and religious groups affected. Estimates suggest that globally 17% of women experience PPD, with low- and middle-income countries (LMICs) reporting a higher prevalence than high-income countries (1). These disproportionate rates are concerning, as many LMICs lack the resources necessary for screening, identification, and treatment of mental illness. In India, a meta-analysis estimated a 22% PPD prevalence rate, with results as high as 31% in South India (2). While genetic history and medical history are contributory factors, social environment also plays a role in PPD. In India, for example, preference for a male child, domestic violence, and economic difficulties are contributing factors, as well as local practices for postpartum mothers such as limiting food and drink and restrictions on leaving the house or socializing for several months (3, 4).

Defined as part of a more comprehensive diagnosis that includes depressive symptoms emerging during pregnancy or after childbirth, PPD symptoms and illness trajectory vary. When untreated, 30%–50% of women will experience ongoing symptoms as long as 1 year postpartum (5). Maternal consequences may include poor quality of life, impaired social and family relationships, risky behaviors such as substance use, and, in extreme cases, completed suicide. Infant consequences include impaired maternal bonding, breastfeeding complications, difficulty with weight gain, developmental delays, and risk for maternal maltreatment (6). Proactive screening and effective treatment are essential to decrease the risk of adverse outcomes for both mother and child.

Behavioral activation (BA), an individual-level treatment for depression, was developed by Lewison and colleagues in the, 1970s (7). BA assists depressed individuals with reengagement in their lives through focused activities that address patterns of avoidance, withdrawal, and inactivity. The program was designed to help individuals with engagement and positive reinforcement to counter depression (8). Randomized controlled trials in India have demonstrated that psychosocial interventions such as BA developed in high-income countries can be modified and delivered by non-physician health workers in LMICs (9). For example, a lay counselor-delivered BA intervention with 495 community-dwelling adults (75% of whom were women) diagnosed with moderately severe to severe depression in Goa, India, was found to significantly lower symptom severity when compared to usual care (10).

Recent reductions in maternal mortality provide the opportunity to shift focus to address maternal mental health problems including PPD (11). The Indian Mental Healthcare Act of, 2017 outlined objectives to increase universal access to mental health care, congruent with the United Nations' Sustainable Development Goals (Goal 3-Health) (11). While a welcomed policy, continued barriers exist to implementing feasible, sustainable, broad-reaching initiatives to improve maternal mental health outcomes. Access to mental health services is one barrier, with a widely reported ratio as low as 0.75 psychiatrists per population of 100,000 (12). Complex help-seeking patterns, the result of culturally derived norms, including stigma, misconceptions, and knowledge deficits related to mental illness, all limit care-seeking behaviors (13). Stigma and negative attitudes toward patients with mental illness are also documented among healthcare workers (14). Issues specific to pregnancy and PPD include the lack of screening protocols as part of the standard of care, hesitancy to treat PPD with pharmacological modalities, minimal ability to refer, and maternal stigma, all of which necessitate an innovative approach to timely and effective identification and treatment (15).

Community health workers (CHWs), known as accredited social health activists (ASHAs), are trained as part of India's National Rural Health Mission and are equivalent to CHWs found globally. ASHAs serve as gatekeepers for maternal health initiatives, having familiarity and rapport with women in their community (16). ASHAs conduct routine visits with women in both the prenatal and postnatal periods as part of usual care delivery. ASHA maternal–child health training content is broad and provides only minimal information about mental health in general or about PPD specifically. Integration of ASHAs for screening and delivering BA for women with PPD may serve as a strategy to optimize health outcomes among postpartum women, addressing barriers in India and other LMICs.

The two research questions guiding this study were as follows:

- What are the feasibility and acceptability of ASHAs screening for and delivering a brief behavioral activation intervention addressing PPD among women in Belagavi, South India?
- What impact did the brief behavioral activation intervention have on PPD?

Methods

We implemented a single-arm pilot study using mixed quantitative and qualitative measures to explore the feasibility of using ASHAs to screen for and deliver a brief behavioral intervention aimed at treating PPD and to assess the acceptability of the intervention among women testing positive for postpartum depression.

We obtained approval for this study from the Thomas Jefferson University Institutional Review Board, the Institutional Ethics Committee of the KLE Academy of Higher Education and Research (Ref: 70121010), and from the Karnataka State Government Department of Health and Family Welfare, which oversees ASHA role responsibilities. The interprofessional research team from both US- and India-based academic institutions included a nurse midwife, a psychiatrist, a public health nurse-researcher, a psychiatric nurse practitioner, and mental health and community nursing faculty.

Training

A total of 17 ASHAs working locally were recruited to participate in a 4-day training on the campus of an India-based affiliated university. ASHAs were compensated for their transportation to the university and for their time in training. Permission for their participation was obtained from local supervisors. Training materials were developed by the research team, based on a review of the literature and findings from a qualitative study of local stakeholders (4). Content included an oral assessment of perceptions, knowledge, and experiences related to PPD using interactive lectures, videos, role-playing, and storytelling. Details about the study protocol, the ASHAs' role in the study, therapeutic communication methods, and the responsible conduct of research were also presented. All training materials were designed for the education and literacy levels of the ASHAs.

Recruitment

Eligibility criteria for potential participants included women who a) were 6 – 12 weeks postpartum, b) had no self-reported history of previous substance use disorder or psychiatric illness, c) were 18 years of age or older, and d) could read and write in the local dialects of Kannada or Marathi and screened positive for mild to moderate PPD. Exclusion criteria were 1) women who answered affirmatively to a question indicating thoughts of self-harm) and 2) women with severe depression (scores on the screening instrument of more than 14). Women with either of these exclusion criteria were referred to the team psychiatrist.

To identify an appropriate sample, researchers and ASHAs used local primary health centers. These centers are the main entry point for primary health services throughout India; each is responsible for the care of approximately 30,000 Indians. The researchers and ASHAs together attended 38 pediatric vaccination clinic sessions between May and November, 2022 at seven primary health care (PHC) clinics in Belagavi, Karnataka, India. Women who met eligibility criteria and indicated an interest in screening worked with researchers and ASHAs to review the informed consent document. To ensure ASHAs' comfort in completing these tasks, researchers initially assisted the ASHAs and then gradually assumed a more passive role, available for questions.

Intervention

ASHAs visited postpartum women enrolled in the study for five weekly visits. At each visit, the ASHAs asked the women to select five activities that they would do daily from a list of culturally appealing activities such as cooking a new recipe, having a 10-minute phone conversation with a friend, or knitting a hat for the baby. At subsequent visits, ASHAs reviewed the activities in which the women had participated, made goals for the upcoming week, and assessed progress from the previous week using a weekly activity log. At each visit, ASHAs also asked if participants had any thoughts of self-harm or harm to others. Each ASHA was assigned a designated member of the research team who was readily available by phone, should participants answer in the affirmative. Researchers made random visits with the ASHAs to ensure adherence to the study protocol.

Data collection instruments

To screen for PPD and identify women whose screening indicated the presence of depressive symptoms, we used the Kannada language version of the Edinburgh Postnatal Depression Scale (EPDS). Screening with the EPDS is standard of practice in the USA and is commonly used in many LMICs (17). The scales' 10 items ask frequency of symptoms (e.g., "I feel anxious or worried for no good reason; I have been so unhappy that I have had difficulty sleeping") with four levels of responses ("not at all; not very often; sometimes; and yes, most of the time"). Possible scores range from 0 to 30, with scores of 10 or greater indicating minor or major depression. The validity of a Kannada-language version of the EPDS has been demonstrated in past research.

Intervention feasibility for participants was assessed by self-report and completion of intended and actual BA activities in the adapted Participant Weekly Behavioral Activity Log. Acceptability was assessed using the Behavioral Activation Intervention Acceptability Survey (BAIAS) (18), an eight-item (one open-ended and seven Likert-scored questions) instrument for ASHAs by the System

Usability Scale (19). Higher scores on each of these instruments suggest greater feasibility and acceptability of the intervention. Open-ended individual and group interviews with both participants and ASHAs also addressed both feasibility and acceptability.

All instruments were translated into the local language of Kannada by researchers who have previously provided this work, back-translated to ensure accuracy, and pilot-tested before program implementation.

Feasibility and acceptability were also assessed 1 month after completion of the intervention with two focus group interviews with ASHAs to capture their perspectives about their role as PPD screeners and as BA interventionists.

Data collection

ASHAs collected the baseline screening information from postpartum women using the EPDS at vaccination clinics. Researchers were present during screening to ensure adherence to the screening protocol and provide feedback as needed. For women who screened positive and participated in the intervention, ASHAs collected a follow-up EPDS score at women's homes at the final visit to assess intervention efficacy. Members of the research team conducted individual interviews with each participant following the 5-week intervention. To assess ASHAs' perspectives on the feasibility of PPD screening and intervention implementation, ASHAs participated in a focus group 2 weeks after the completion of the final participant visit. All interviews were held in a private room at the local PHC.

Multiple attempts were made to ensure the privacy of data collection, with mothers invited to be interviewed in separate rooms or outdoor areas. In a few cases, the interview was conducted in the presence of the patient's mother.

Data analysis

Quantitative data were entered into a REDCAP database by one member of the research team (VN) and transferred to a SAS 9.4 program (20). Before conducting the pre-test/post-test analysis, we created a difference variable by subtracting the pre-PPD score from the post-PPD score for each participant. We generated a paired t-test to compare the pre-assessment with post-assessment results for PPD score. For this method of analysis to be valid, we assumed that the data were symmetrically distributed around the mean. Using the univariate procedure in SAS, we checked for significant violations of the normal assumptions. In addition, we performed Wilcoxon signed rank tests, which require no parametric assumption. For the categorical predictors with small cell sizes, we also considered the non-parametric Wilcoxon rank sum test. A significance level was set at the alpha = 0.05 level.

Researchers transcribed the qualitative data verbatim from audio recordings and translated them into English. We analyzed transcriptions using NVivo software version, 13 (21). Two independent investigators (AS and PK) experienced in qualitative research open-coded the transcripts. We reviewed codes with the principal investigator/author to resolve any discrepancies. The research team identified major themes and selected relevant quotes. To ensure trustworthiness, credibility, transferability, dependability, and confirmability, researchers adhered to the tenets of Lincoln and Guba (22).

Results

Over the screening period, we screened 83 postpartum women. One woman disclosed thoughts of self-harm and was immediately referred to the psychiatrist researcher who offered treatment at the affiliated tertiary care institution. Twenty-six of the 83 women (31%) screened positive for PPD. There were no demographic differences between women who did and did not screen positive. No eligible women declined screening. After two of the 26 moved, 24 women participated in and completed the intervention.

Of the 24 women who completed the intervention, the average age was 27 years (range 20–35, SD 4.9); 15 (62.5%) had an elementary education, and 10 (38.9%) had secondary school education; 21 (87.5%) were Hindu, and three (12.55%) were Muslim. This was a first child for 10 (41.7%) women. These and other descriptors are presented in Table 1.

All participants had highly significant changes ($p < 0.001$) in PPD scores (mean change −10.63, SD 1.44). Similar results were obtained by both the non-parametric Wilcoxon signed rank test and the paired t-test.

BAIAS showed high acceptability with an average of 4.32 (SD 0.89). All 24 participants completed the activities on their weekly Behavioral Activity Log, also suggesting high acceptability. Qualitative results from ASHAs and participants suggested enthusiasm for the training and intervention components.

From the ASHAs:

> *ASHA #3: Initially, we were concerned about administration of the EPDS. This was resolved during training by performing role play based on various scenarios from the training officers and later [by working with] the participants.*

> *ASHA #5: After training, we were much more confident in screening through the EPDS and [doing] the intervention through role play.*

> *ASHA #8: The tool [EDPS] was in the local language which made it easy to screen the mothers.*

> *ASHA #2: All ASHA workers need to be trained. These Activities were non-pharmacological and don't involve any risk.*

> *ASHA #10: If more ASHAs were trained … it is helpful in preventing PPD by regular BA activities.*

From the mothers:

> *Mother #9: I felt confident day by day doing the BA, as these activities were simple and was able to complete the tasks each day. This boosted my self-confidence.*

> *Mother #8: It was a good experience. It strengthened my personality and my mood.*

> *Mother #19: Activities were so simple and free from hassle.*

> *Mother #2: I encountered no such problems [when engaging in BAI activities]. All activities were so simple and easy to perform at home along with baby care.*

Discussion

The results of this pilot study suggest that community health worker-administered behavioral activation interventions have the potential to address PPD in settings with minimal mental health resources.

The very high levels of acceptability and completion of activities among participants were surprising. While it is not possible to discount the social acceptability of responses to questions, that is, that ASHAs and participants stated what they thought the research team wanted to hear, it is likewise possible that the BA model is actually very patient-friendly and feasible to implement. This latter possibility is supported by the findings in a recent community-based Randomized controlled trial in which 83.9% of participants in the BA arm completed their assignments (23). Similarly, studies of BA with cancer patients found completion rates of 76.2% and 77.3% (24, 25).

TABLE 1 Demographics of Sample.

Education	
Primary	15/62.55%
High school	8/33.3%
Graduate	1/ 4.2%
Number of chidren	
One	10/41.7%
Two	7/29.2%
>Two	7/29.2%
Sex of Baby	
Female	14/58.3%
Male	10/41.7%
Religion	
Hindu	21/87.5%
Muslim	3/12.5%
Planned pregnancy	
Yes	15/62.5%
Baby complications	
Yes	2/8.3%
Maternal complications	
Yes	5/20.8%
Mean EPDS scores at baseline	11.75 ±1.22

The surprisingly high change in scores of all participants on the EPDS suggests either a highly effective community-based intervention or the negative feelings and mood swings experienced by many new mothers are transient as the result of hormonal changes and sleep deprivation. While our positive screening rate of 31% was consistent with that found by other researchers in southern India (2), a randomized controlled trial with a larger sample size and serial assessments of the mental health status of new mothers is necessary to understand the natural history of PPD and the role of community-based interventions to address this problem.

Our positive feasibility and acceptability results provide preliminary evidence that the ASHA role can be expanded to include screening for PPD. ASHAs have familiarity with women in their communities, and their current workload involves routine visits with women in both the prenatal and postnatal periods. They also have positive attitudes about community mental health issues and have worked to expand mental health services in selected communities during the COVID-19 pandemic (26). However, such role expansion must be coupled with adequate training, supervision, and compensation to be scalable and sustainable (16).

This study had several limitations. We did not have a mechanism to confirm women's participation in the daily BA activities; however, the ASHAs had trusted interpersonal relationships with the women with whom they work, and participants would feel comfortable disclosing non-adherence. The lack of a control group that would provide information about the natural history of PPD means that we cannot state that the intervention was responsible for changes in depression scores. Though the lack of privacy might have affected the validity of some cases, the results are still generalizable to the Indian population where privacy in clinical settings is still not a regular practice. The small sample made an effect size difficult to calculate.

This community health worker-mediated behavioral activation intervention was found to be feasible and acceptable in treating PPD in rural Indian mothers. Large-scale, controlled studies are needed to confirm these findings.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Thomas Jefferson University IRB and KLE University Ethics Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

AS: Funding acquisition, Writing – original draft, Writing – review & editing. BT: Funding acquisition, Writing – original draft, Writing – review & editing. VN: Writing – original draft, Writing – review & editing. GU: Writing – original draft, Writing – review & editing. MS: Writing – original draft, Writing – review & editing. SD: Writing – original draft, Writing – review & editing. UK: Writing – original draft, Writing – review & editing. SP: Writing – original draft, Writing – review & editing. SR: Writing – original draft, Writing – review & editing. VS: Supervision, Writing – review & editing. PK: Funding acquisition, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Magnitude of self-harm and associated factors among postnatal mothers attending immunization clinics at public health facilities in Boneya Boshe Woreda, Western Ethiopia, 2023: institution-based cross-sectional study design

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Background: Self-harm is a preventable, but a leading, cause of maternal morbidity and mortality all over the world, with a significant impact on healthcare systems.

Objective: To assess the magnitude of self-harm and associated factors among postnatal mothers attending immunization clinics.

Methods: An institution-based cross-sectional study was employed among postnatal mothers attending infant immunization clinics at public health facilities in Boneya Boshe Woreda, Western Ethiopia, 1 October to 30 October 2023. A pretested, face-to-face interviewer-administered structured questionnaire prepared by Kobo Toolbox was used to collect the data. Both bivariable and multivariable logistic regression analyses were done. The level of significance was declared at p-value <0.05 with a 95% CI.

Results: Among the 423 mothers enrolled in the study, 415 of them finally participated, at a response rate of 98.10%. The magnitude of self-harm was 12.53% (95% CI: 9.33, 15.73). Involvement of husband in maternity and child healthcare (AOR = 1.90; 95% CI: 1.12, 2.10), depression (AOR = 2.79; 95% CI: 2.14, 6.94), loneliness (AOR = 2.49; 95% CI: 1.15, 5.40), postpartum intimate partner violence (AOR = 2.15; 95% CI: 1.01, 4.54), average monthly income (AOR = 3.70; 95% CI: 2.17, 10.50), and postnatal care (AOR = 2.72; 95% CI: 1.28, 5.80) were significantly associated factors.

Conclusion and recommendations: The study sought a magnitude of self-harm that was slightly higher than the previous study conducted in the northern part of Ethiopia. Therefore, healthcare providers should focus on identified factors during postnatal care to overcome them. Similarly, the concerned body should

develop an effective strategy based on the identified factors to pay attention to postnatal mothers.

KEYWORDS

self-harm, immunization clinics, Boneya Boshe, infant immunization, postnatal mothers

Introduction

Self-harm is an intentional in which a person causes harm to their own selves as a coping mechanism when gripped by difficult or distressing thoughts and feelings. It most frequently takes the form of cutting, burning, or non-lethal overdoses. However, it can also be any behavior that causes injury to the victim, whether it is low or high (1, 2). The term self-harm encompasses a broad spectrum that includes a wide range of behaviors and intentions, including attempted hanging, impulsive self-poisoning, and superficial cutting in response to intolerable life events in the life process (3).

Self-harm is one of the most common reasons for hospital visits. It is a reflection of distress rather than a diagnosis in itself and is currently increasing among women of reproductive age, particularly during the perinatal period (4, 5). This problem is more common in women than men, which is one of the current global health challenges across the world (6).

During perinatal period, women are at the greatest risk of mood changes as a result of hormonal changes and life stress events related to pregnancy and childrearing processes (7–9). Common mental health problems like suicidal behaviors, postpartum psychological distress, anxiety, and postpartum stress disorders can lead to self-harm during the postnatal period if not identified and managed at an early stage (10–12).

Mental health problems are one of the leading global causes of maternal morbidity and mortality, posing the greatest challenge throughout the world (13). They also manifest as self-harm or thoughts of self-harm. The World Health Organization (WHO) estimates the magnitude of self-harm among the general population at 75.5% in both low-and middle-income countries (14). The studies conducted on postpartum mothers in both low-and high-income countries identified a varied magnitude of the problem that ranges from 4.6 to 27.4% (9, 15–17).

As identified by previous research, mental disorders, substance misuse, younger age, being unmarried, and obstetric and neonatal complications were factors leading to self-harm among postnatal mothers (18–20). In addition, lack of social support, lack of emotional support, and intimate partner violence were the other identified factors (5, 21).

Self-harm has significant consequences for infants, family members, and the healthcare system. In addition, it affects the Sustainable Development Goal agenda, which focuses on ending preventable maternal deaths by 2030 (22). Maternal self-harm leads to poor maternal–infant bonding processes that might affect infant health (15, 23). Similarly, the study identified that maternal self-harm thought causes self-harm thought in the offspring in the future and leads to early discontinuation of breastfeeding, which might increase childhood morbidity (24, 25). Maternal self-harm thoughts can also lead to childhood self-harm and suicidal ideations (26).

During the postnatal period, mothers may suffer from life-threatening health problems, including mental health problems. Even though this problem has a multi-dimensional impact, little attention has been given to it in both high-and low-income countries, which can lag behind the sustainable development goal three that focuses on the eradication of preventable causes of maternal deaths. Little attention has been given to maternal deaths all over the world, including in this specific study area, which is the focus of our research.

Therefore, this study aimed to assess the magnitude of self-harm and associated factors among postnatal mothers attending immunization clinics in public health facilities in Boneya Boshe Woreda, Western Ethiopia, in 2023. The findings of this study can be used as an input by healthcare providers to provide an evidence-based care plan to alleviate it. In addition, it may help the government to prevent maternal deaths related to self-harm and may be used as an input by scholars for further research.

Methods and materials

Study design, area, and period

An institution-based cross-sectional study design was conducted in Boneya Boshe Woreda from 1 October to 30 October 2023. This Woreda is found in the East Wallaga Zone of the Oromia region, which is located 81 km from the capital city of the zone, Nekemte town, and 311 km from the capital city of the country, Addis Ababa. Boneya Boshe Woreda is bordered by Nono Benja Woreda in the south, Gobbu Sayo and Sibu Sire Woreda in the north, Bako Tibe and Ilu Galan in the east, and Wahama Hagalo in the west.

In this Woreda, the total population is 73,227, with 14,925 households in 12 Kebeles. Out of this population, 34,803 are in the reproductive age group, of which 16,206 are women in the reproductive age group. This Woreda has an expected delivery rate of 2,541 per year. The 2022 Woreda Health Bureau report revealed that the total delivery in one year was 2,355. This Woreda has three health centers and 12 health posts, with a total of 68 health professionals to carry out healthcare activities.

Eligibility criteria

All postpartum mothers attending immunization clinics in the first one year after childbirth during data collection period and who

Abbreviations: IPV, intimate partner violence; PNC, postnatal care; AOR, adjusted odds ratio; COR, crude odds ratio.

presented with their infants whose age was from two weeks after birth to one year were included in the study. However, those mothers who were critically ill during the data collection period and not permanent residents of this Woreda were excluded from the study.

Sample size determination and sampling technique

The sample size was determined by using a single population proportion formula based on assumptions of 95% CI, 5% margin of error, and 50% of the proportion of self-harm since there has been no study done on this population in the study area, as follows:

$$n = \frac{\left(Z\frac{\propto}{2}\right)2pq}{d2}.$$

Then

$$n = \frac{(1.96)2(0.5x0.5)}{(0.05)2} = 384.$$

Finally, by adding 10% of the non-response rate, the final sample size of 423 was arrived at for this study. A systematic random sampling technique was used to select the study participants based on the total number of infants attending immunization clinics. Initially, the total number of infants attending three immunization clinics in this Woreda was obtained from the infant immunization logbooks of each health center. Those health centers are Bilo Health Center, Qidame Health Center, and Jawis Health Center. The number of infants attending immunization clinics were 761 from Bilo Health Center, 692 from Qidame Health Center, and 676 from Jawis Health Center 676. Then it was proportionally allocated, and the allocated mothers were selected by a systematic random sampling method as follows (Figure 1).

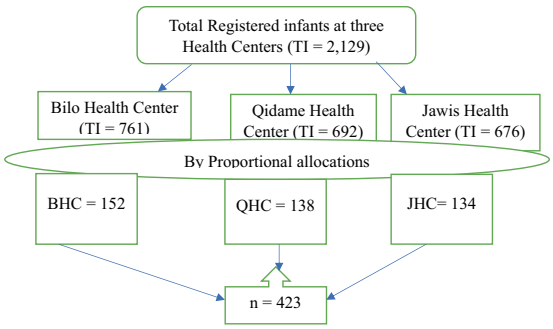

FIGURE 1
Diagrammatic presentation of sampling procedure to assess the magnitude of self-harm among postnatal mothers in Boneya Boshe Woreda, 2023. BHC, Bilo Health Center; QHC, Qidame Health Center; JHC, Jawis Health Center; TI, Total Infant.

Variables of the study

Dependent variable

The magnitude of self-harm was the dependent variable in this study.

Independent variables

Socio-demographic variables include maternal age, husband's age, maternal educational level, husband's educational level, maternal occupation, husband occupation, average monthly income, and family size.

Medical, reproductive history, and substance-related factors

The data collected for the study include the place of delivery, postnatal follow-up, history of adverse pregnancy outcome, maternal history of known diagnosed medical illnesses, history of diagnosed mental health problems during pregnancy, husband's involvement in maternity and child healthcare, husband's index of pregnancy during the current baby, husband's satisfaction with the gender of the current baby, alcohol use by the father and mother of the infant, husband's khat use, and husband's smoking habit.

Psychosocial-related factors

Intimate partner violence during the postnatal period, postpartum depression, maternal social support level, loneliness, and the decision-making power of the mother were explored.

Operational definitions and measurements

Intentional self-harm is the condition in which an individual tries to hurt themselves purposefully. They could indulge in self-injurious behaviors like cutting, burning, hitting, hanging, overdosing, poisoning, banging head on objects, scratching the body, bloodletting (intentional act of an individual to let blood from them for self-hurt), strangulating the neck (the act of an individual to forcing or damaging one's own neck or body for self-hurt), and electrocuting by the mother who intended to harm herself. If she has at least attempted one or more items developed provided in the Self-harm Screening Inventory (SHSI) tool to hurt herself during her first year after childbirth, she is considered to have done intentional self-harm, for which code "1" was assigned. For a mother who has not tried any of the items mentioned in the SHSI tool is considered to have not resorted to intentional self-harm, which was coded as "0" (27).

Partner involvement in maternity and child healthcare: This variable was assessed with nine questions. For each question, the responses were scored between 0 and 1. The total score was 9, with a minimum of 0 and a maximum of 9. Hence, husband's involvement with a score above the median showed that the husband was involved in maternity an child healthcare (28).

Postpartum depression: The women who had an Edinburgh postnatal depression score of greater than or equal to 13 during their first year after childbirth were considered to be depression, and code "1" was given to them; those who scored less than 13 were not considered to have depression symptoms and coded as "0" (29).

Known medical illness: Women diagnosed with chronic medical illnesses like diabetes, cardiac disease, renal disease, hypertension, liver disease, and tuberculosis that are confirmed by doctors at health institutions are considered to have known medical illness (30).

Decision-making power: This was measured by the ability of women to act independently and decide on household activities including their health, their children's health, freedom of movement, and control over finances without asking permission from another person. Depending on the items designed to assess maternal decision-making power, "2" was given if she decides by herself, "1" will be given if she decides jointly with her husband, and "0" was given if it is decided by others. Based on items designed to assess household decision-making power, women who scored above the median were considered to have good decision-making power and coded "1," and those who scored below the median were considered to have poor decision-making power and were coded "0" (31).

Maternal social support: Social support was assessed by three items on the OSLO-3 social support scale. Mothers whose score was 3–8 were considered poor on social support and coded "0". A score of 9–11 signified moderate social support and assigned the code "1", and 12–14 indicated strong social support and code "2" was given (32).

Postpartum Intimate partner violence (PIPV): This was assessed by 13 items developed from an adapted tool to assess domestic violence against women in low-income country settings. It includes physical violence, sexual violence, and psychological violence. Any mother who is the victim of at least one type of PIPV was coded "1" and who was not the victim was coded "0" (33).

Maternal loneliness: The University of California Los Angeles (UCLA-3) 20-item Loneliness Scale (Version 3) was used to measure maternal loneliness during the first year after childbirth. The UCLA-3 20-item Loneliness Scale was used to gather the total score. Based on this tool, code "0" was given for those mothers who scored <28 (no loneliness) and "1" was given for those who scored ≥28 (had loneliness) (34).

History of adverse pregnancy outcome: Mothers who have a history of abortion, neonates with congenital anomalies that are incompatible with life, stillbirth, and/or neonatal death were considered to have adverse pregnancy outcomes for the purpose of this study.

Average monthly income: Based on this income, the mother was categorized as living above or below the poverty line based on the current classification system by the World Bank group. Earning US$1.90 or 97.85 Ethiopian Birr (ETB) or lower per day meant living below the poverty line. At the current exchange rate of US dollar to Ethiopian Birr, for 30 days, earning 2935.5 ETB or lower indicated that the mother was living below the poverty line (35).

Data collection instruments and procedures

In face-to-face interviewers, structured questionnaires prepared by Kobo Tool Box (an innovative open-source platform for collecting, managing, and visualizing data) was administered to collect the data. The tool has a socio-demographic component, reproductive history, maternal and child healthcare services, and psycho-social factors related to the mother. Postpartum intimate partner violence was assessed by 13 items containing sexual violence, psychological violence, and sexual violence (33). Postnatal depression was assessed by a validated Edinburgh postnatal depression tool that was validated in an Ethiopian context (29).

Maternal social support was assessed by a validated OSLO-3 social support scale that contains three items (32), and loneliness was assessed by the University of California Los Angeles (UCLA-3) 20-item Loneliness Scale (Version 3) (34). The outcome variable was assessed by the SHIS tool, which has 20 items to assess self-harm (27). Husband's involvement in maternity and child healthcare was assessed by a tool developed from related literature that has nine items (28). Similarly, decision-making autonomy was assessed by nine items developed from the related literature (31).

Data quality assurance

A pretest was done on 10% of the study participants one month before data collection at Wahama Hagalo Woreda. The internal consistency of the tool was checked and had a Cronbach's α test of 0.79. Initially, the tool was developed in the English language and translated to Afan Oromo for actual data collection, and the Afan Oromo version was retranslated back to English to cross-check the consistency of the tool.

Data was collected from three diploma holder women midwifery health professionals and supervised by three diploma holder women nurses. Training was given for two days on the objectives of the study for data collectors and the training also included participant safety for both data collectors and supervisors. Supervision was carried out by supervisors daily for the sake of clarity, accuracy, and consistency of the data.

Data processing and analysis

The data collected by Kobo Tool Box was exported to SPSS version 25 software for cleaning, coding, and further analysis. Descriptive statistics were done, and the results were presented using diagrams and tables. Both bivariable and multivariable logistic regression analyses were done to identify factors associated with self-harm during the first year after childbirth. Variables with a p-value <0.25 in binary logistic regression analysis were transferred to multivariable logistic regression.

The crude odds ratio (COR) and the adjusted odds ratio (AOR) with a 95% CI were calculated to show association and strength of association, respectively. In multivariable logistic regression analysis, variables with a p-value of <0.05 were reported as statistically significant. The model goodness-of-fit test was done. Finally, the results were presented both in the narrative, diagram, and table forms.

Results

Socio-demographic characteristics

Among the 423 postpartum mothers selected for this study, 415 mothers participated in the study, at a response rate of 98.10%. The study identified that 31.80% of the participants were in the 18–23 age category and 17.00% were in the 41–45 age category. As revealed by

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this study, 53.30% of the mothers were housewives and 57.38% of their husbands were farmers. In addition, 13.50% of mothers have no formal education, and 9.60% of their husbands have no formal education. Furthermore, 51.30% of mothers have an average monthly income below the poverty line, and 47.50% have family sizes greater than or equal to six (Table 1).

TABLE 1 Socio-demographic characteristics of the study participants.

Variables	Categories	Frequency	Percentages/100%
Age	18–23	132	31.80
	24–29	56	13.30
	30–35	66	15.90
	36–40	91	22.00
	41–45	70	17.00
Religion	Orthodox	151	36.40
	Protestant	146	35.20
	Muslim	102	24.50
	Others*	16	3.90
Maternal occupation	Housewife	221	53.30
	Merchant	130	31.30
	Government employed	64	15.40
Occupation of husband	Farmer	238	57.34
	Merchant	111	26.75
	Government employed	66	15.91
Maternal educational status	No formal education	56	13.50
	Primary education	151	36.40
	Secondary education	139	33.50
	Diploma and above	69	16.60
Husband educational status	No formal education	40	9.60
	Primary education	140	33.70
	Secondary education	148	35.70
	Diploma and above	87	21.00
Family size	Less than or equal to 3	95	22.90
	Four to five	123	29.60
	Greater than or equal to 6	197	47.50
Average Monthly income	Below poverty line	202	51.30
	Above poverty line	213	48.70

*Waqefata and Catholics.

Medical, reproductive history, and substance-related factors

As identified by this study, 55.18% of the infants were girls, and 52.00% of the husbands were not satisfied with the gender of their infants. Similarly, 48.00% of mothers did not intend to have the baby during the index of pregnancy. Furthermore, 78.31 and 51.80% of the mothers have antenatal care (ANC) and postnatal care (PNC) follow-up, respectively. From the total study participants, 13.50% of mothers gave birth at home and 10.80% of them have a history of adverse pregnancy outcomes. It was revealed that only 45.10% of husbands were involved in maternity and child healthcare.

In addition, 5.10 and 3.62% of mothers have been diagnosed with medical illnesses and mental illnesses, respectively. Similarly, 2.66% of their husbands have been diagnosed with medical illnesses. Furthermore, 3.90% of mothers have a family history of known diagnosed mental illnesses. Out of the total study participants, 36.39% of mothers and 52.80% of their husbands were alcohol users. Finally, 15.90% of the husband participants consume the khat (Table 2).

Psychosocial-related factors

Out of the total study participants, 13.50 and 32.30% of mothers suffered from postnatal depression and postpartum intimate partner violence. In addition, 41.90 and 17.10% of the mothers enjoyed poor and moderate social support, respectively, during their postnatal period. Similarly, 29.40% of the mothers were lonely and only 31.81% of the mothers have decision-making power over household activities (Table 3).

Magnitude of self-harm among postnatal mothers attending infant immunization clinics

This study revealed that the magnitude of self-harm among postnatal mothers in this study setting was 12.53% (95% CI: 9.33, 15.73) (Figure 2).

Factors associated with self-harm and associated among postnatal mothers attending immunization clinics at public health institutions in Boneya Boshe Woreda, Western Ethiopia, 2023

From the total variables fitted for binary logistic regression at a *p*-value less than 0.25, six variables were significantly associated in the multivariable logistic regression model at a *p*-value less than 0.05 at a 95% CI. Variables significantly associated with self-harm in the final model were husband's involvement in maternity and child healthcare, depression, loneliness, postnatal follow-up, postpartum intimate partner violence, and average monthly incomes.

TABLE 2 Medical, reproductive history, and substance-related factors of the study participants.

Variables	Categories	Frequency	Percentage/100%
Sex of infant	Female	229	55.18
	Male	186	44.82
Husband satisfaction to gender of the infant	Yes	195	48.00
	No	216	52.00
Maternal intention to have baby	No	201	48.40
	Yes	214	52.60
ANC follow-up	No	90	21.69
	Yes	325	78.31
PNC follow-up	No	200	48.20
	Yes	215	51.80
Place of delivery	Home	56	13.50
	Health institution	359	86.50
Husband involvement in maternity and child healthcare	No	228	54.90
	Yes	187	45.10
History of adverse pregnancy outcome	No	45	10.80
	Yes	370	89.20
Maternal known diagnosed medical illness	No	394	94.90
	Yes	21	5.10
Husband known diagnosed medical illnesses	No	404	97.34
	Yes	11	2.66
Maternal known diagnosed mental illnesses	No	400	96.38
	Yes	15	3.62
Maternal family history of known diagnosed mental problem	No	399	96.10
	Yes	16	3.90
Maternal alcohol use	Yes	151	36.39
	No	264	63.61
Husband alcohol use	Yes	219	52.80
	No	196	48.20
Husband's khat use	Yes	66	15.90
	No	349	84.10

ANC, Antenatal care; PNC, Postnatal care.

This study identified that the odds of self-harm among mothers whose husbands do not participate in maternity and child healthcare were 1.90 times higher than those whose husbands participate in the care (AOR = 1.90; 95% CI: 1.12, 2.10). In addition, the odds of self-harm among mothers who have depression were 2.79 times higher than their counterparts (AOR = 2.79; 95% CI: 2.14, 6.94), and the odds of self-harm among mothers who do not have postnatal follow-up were 2.72 times higher than those who follow their postnatal care (AOR = 2.72; 95% CI: 1.28, 5.80).

Similarly, the odds of self-harm among mothers who have loneliness were 2.49 times higher than their counterparts (AOR = 2.49; 95% CI: 1.15, 5.40), and the odds of self-harm among mothers who suffered from postpartum intimate partner violence were 2.15 times higher than those who did not face the problem (AOR = 2.15; 95% CI: 1.01, 4.54). Finally, the study identified that the odds of self-harm among mothers with average monthly income below the poverty line were 3.70 times higher than those who were above the poverty line (AOR = 3.70; 95% CI: 2.17, 10.50) (Table 4).

Discussion

Self-harm is a significant maternal health problem that can be prevented by screening and providing care for those mothers who have risks related to this problem. This study revealed that the magnitude of self-harm thought among postnatal mothers was 12.53%. The finding is comparable with the study conducted in Canada, which reported self-harm at 10.40% (19). However, the findings of this study were lower than those of the studies conducted in Sri Lanka (27.40%) (9), London (16.79%) (7), and the United States

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TABLE 3 Psychosocial-related factors.

Variables	Categories	Frequencies	Percentage/100%
Depression	No	359	86.50
	Yes	56	13.50
PIPV	No	281	67.70
	Yes	134	32.30
Social support	Poor	174	41.90
	Moderate	71	17.10
	Strong	170	41.00
Maternal decision-making power	Poor	283	68.19
	Good	132	31.81
Loneliness	No	293	70.60
	Yes	122	29.40

PIPV, postpartum intimate partner violence.

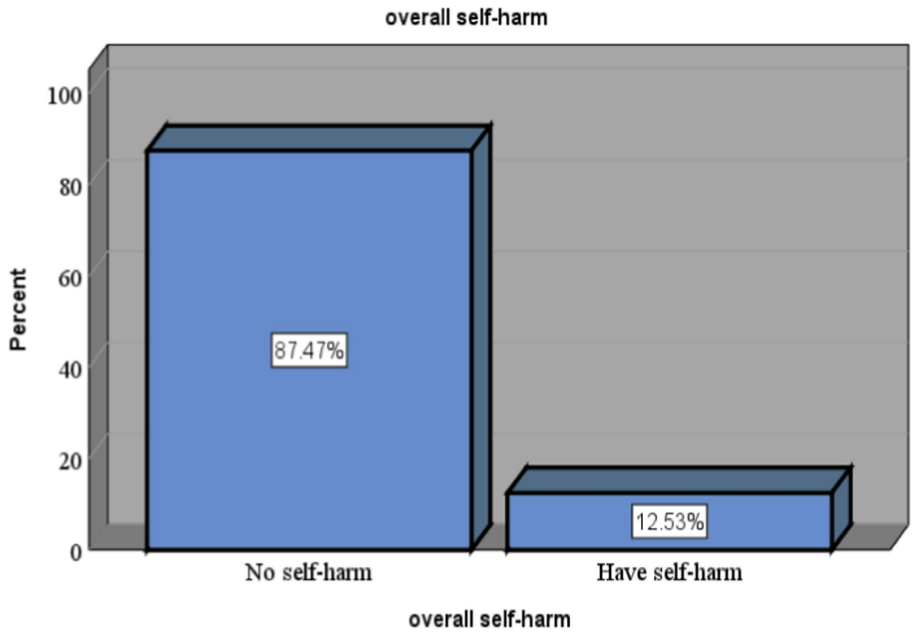

FIGURE 2
Magnitude of self-harm among mothers attending infant immunization clinics in Boneya Boshe Woreda.

(19.3%) (36). The discrepancies might be due to differences in the assessment methods employed and sample size used for the studies, as these three studies used a larger sample size, which might increase the magnitude of self-harm thoughts.

Conversely, the findings of this study are lower than those of the studies conducted in northern Ethiopia (8.5%), South Africa (7%) (37), and Japan (9.1%) (38). The possible justifications for the discrepancies might be also attributed to the study period or years of the studies. The discrepancies between the study conducted in the northern part of Ethiopia and our study might be due to the current market inflation in Ethiopia, which might increase life expectancy and push mothers to self-harm as they are unable to fulfill the economic demands of their family members in the current market situation.

Husband's involvement in maternity and child healthcare is significantly associated with self-harm thoughts during the postnatal period. The possible scientific reason might be that women whose husbands are involved in maternity and child healthcare feel confident that their husbands are with them in any ups and downs of life, which may affect their feelings as a result of physiological changes during childbirth (28). In addition, husbands who are involved in maternity and child healthcare consult the health professionals as they observe emotional and psychological changes in their wives during the postnatal period and have obtained information from health professionals regarding their families' health (39).

Similarly, this study identified that having depression is significantly associated with self-harm thoughts. This evidence is supported by the study conducted in Canada (19). The possible reason might be that depression during the postpartum period pushes mothers to self-harm as a result of the unmanaged postpartum depression, which leads to

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TABLE 4 Factors associated with self-harm among postnatal mothers attending infant immunization clinics.

Variables	Categories	Magnitude of self-harm		COR(95%CI)	AOR(95%CI)
		Yes (52)	No (363)		
Husband involvement in maternity and child healthcare	No	36 (15.8%)	192 (84.2%)	2.00 (1.67,3.74)	1.9 (1.12,2.10)*
	Yes	16 (8.6%)	171 (91.4%)	1	1
Maternal intentions to have baby	No	41 (38.1%)	160 (44.1%)	4.73 (2.35,9.50)	3.76 (0.66, 4.51)
	Yes	11 (48.9%)	203 (55.9%)	1	1
Depression	No	34 (9.5%)	325 (90.5%)	1	1
	Yes	18 (32.1%)	38 (67.9%)	4.53 (2.33,8.80)	2.79 (2.14, 6.94)*
History of adverse pregnancy outcome	No	37 (10%)	333 (90%)	1	1
	Yes	15 (33.3%)	30 (66.7%)	4.50 (2.22,9.12)	2.69 (0.99,7.30)
Loneliness	No	24 (8.2%)	269 (91.8%)	1	1
	Yes	28 (23%)	94 (97%)	3.34 (1.84,6.05)	2.49 (1.15, 5.40)*
Postnatal follow-up	No	35 (17.5%)	165 (82.5%)	2.47 (1.34,4.57)	2.72 (1.28, 5.80)*
	Yes	17 (7.9%)	198 (92.1%)	1	1
Postpartum IPV	No	22 (7.8%)	259 (92.2%)	1	1
	Yes	30 (22.4%)	104 (77.6%)	3.40 (1.90,6.20)	2.15 (1.01, 4.54*)
Average monthly income	Below poverty line	45 (22.3%)	157 (77.7%)	4.41 (3.70, 9.20)	3.7 (2.17, 10.5)*
	Above poverty line	13 (6.13%)	200 (93.88%)	1	1
Social support	Poor	40 (23%)	134 (77%)	4.78 (2.30,9,91)	3.70 (0.59, 8.62)
	Moderate	11 (15.4%)	60 (84.5%)	2.93 (0.09,2.17)	0.34 (0.06, 1.87)
	Strong	10 (5.9%)	160 (94.1%)	1	1
Decision-making power	Poor	43 (15.3%)	238 (84.7%)	2.50 (1.18, 5.30)	2.30 (0.92,5.70)
	Good	9 (6.7%)	125 (93.3%)	1	1

*Significantly associated factors at *p*-value less than 0.05.
IPV, intimate partner violence.

postpartum psychosis, posing a high level of danger for both maternal and infant's health, ending up with postpartum morbidity (7).

The study also revealed that loneliness is significantly associated with self-harm thoughts. Even though there was no evidence to support this finding, loneliness pushes the mothers to self-harm, and as a result, they may feel empty as they lack people around them during the postpartum period. If there are no people around them for support, the anxiety levels of mothers increase, which worsens the thoughts of self-harm as a defense mechanism to be out of their feelings, and loneliness leads to mental health problems (40).

In addition, the average monthly income is a significantly associated factor with thoughts of self-harm during the postnatal period. This finding is supported by the study conducted in northern Ethiopia (21). The reason might be that mothers whose monthly income is below the poverty line might be stressed about their income, which might not be sufficient to support the livelihood of the families. Similarly, they lose hope, which pushes them to take action on their lives if they are unable to fulfill their family's needs due to lack of money to fulfill even their basic needs.

Furthermore, postpartum intimate partner violence is a significant factor associated with self-harm thoughts during the postnatal period. This finding is supported by the study conducted in the northern part of Ethiopia (21). The possible justification might be that mothers who suffer from this problem might fall into psychological crisis as a result of their husband's bad attitude toward them, and those mothers lose hope, which pushes them to life-threatening problems like self-harm thoughts.

Finally, the study identified that postpartum follow-up is a significantly associated factor with maternal self-harm thoughts. As already known, postpartum follow-up is key for the upkeep of maternal and infant health and may help health professionals screen the problem early to take action. Postpartum follow-up is part of the maternal continuum of care, which improves overall maternal health (41). During postpartum follow-up, mothers may consult their health professionals for any mental health problems that may occur during the postpartum period as a result of hormonal and physiological changes related to childbirth.

Limitations and strengths of the study

Since it was a cross-sectional study, it does not identify cause-and-effect relationships. In addition, since it was an institution-based study, it might lead to an underestimation of the magnitude of self-harm thoughts. The study focused on the neglected areas that hold great significance for reducing preventable causes of maternal deaths and assessed important factors that have a great impact on maternal health.

Conclusion and recommendations

This study revealed that the magnitude of self-harm thoughts during the postnatal period was a significant maternal health problem in the study setting. It was identified that the husband's involvement in maternity and child healthcare, loneliness, depression, average monthly income below the poverty line, postpartum follow-up, and postpartum intimate partner violence were factors significantly associated with maternal self-harm thoughts. Husband's involvement in maternity and child healthcare is needed to overcome the problem. In addition, the Ministry of Health should develop an effective strategy for preserving maternal health after childbirth based on the identified factors. The future studies in this direction need to have better study designs and large sample sizes.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The ethical clearance was obtained from the Wallaga University Institute of Health Sciences. Written informed consent was obtained from the study participants after they were informed of the overall nature of the study and its benefits for the mothers and the implications for policymakers.

Author contributions

LW: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing, Funding acquisition. MH: Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. ZA: Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. GT: Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. YW: Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. WG: Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. MAH: Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. AG: Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. ST: Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. SA: Conceptualization, Data curation, Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Gut microbiota and postpartum depression: a Mendelian randomization study

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Background: Increasing evidence suggests a correlation between intestinal microbiota and the gut-brain axis; however, the causal relationship between gut microbiota and postpartum depression (PPD) remains unclear.

Methods: In this study, a two-sample Mendelian randomization (MR) design was employed to analyze the GWAS data of gut microorganisms from the Mibiogen database and PPD data from the UK biobank. Various statistical methods, including inverse variance weighted, MR-Egger, weighted median, weighted model, and MR-PRESSO, were utilized to investigate the causal relationship between gut microbiota and PPD. Additionally, sensitivity analysis was conducted to assess the robustness of the findings.

Results: Through MR analysis, it was found that phylum Actinobacteria (P=0.014, OR=0.971, 95% CI=0.948-0.994) and genus Holdemanella (P=0.023, OR=0.979, 95% CI=0.961-0.997) have protective effects on PPD, while the other two unknown genera, genus Unknown Ids 2001 (P=0.025, OR=0.972,95% CI=0.947-0.996), and genus Unknown Ids 2755 (P=0.012, OR=0.977, 95% CI=0.959-0.995) also has a protective effect on PPD. The sensitivity analysis results indicate that there is no heterogeneity or horizontal pleiotropy.

Conclusion: This study has identified a causal association between Actinomycetota, Holdemanella, and PDD through MR analysis. These findings offer significant contributions to the development of personalized treatment approaches for PPD, encompassing interventions such as dietary modifications or microbiome interventions.

KEYWORDS

Mendelian randomization, gut microbiota, postpartum depression (PPD), causal relationship, w-3

Introduction

Postpartum depression (PPD) is a non-psychotic depressive episode that begins or continues into the postpartum period (1). Postpartum depression is the most common complication of childbirth, affecting women and mother-infant relationships and cognitive and emotional problems in children, with serious consequences for mothers, families, and children (2). Nearly 20% of patients with depression relapse within 20 years of their initial onset, and most people develop suicidal thoughts, with 4% -5% dying from depression-related suicide (3, 4). Not only does it significantly impact the mother itself, but it also affects the quality of life of a family.

Recent studies have shown that the gut microbiota (GM) plays an important physiological role in maintaining gastrointestinal, hormonal, immune, and neural homeostasis (5). The concept of the "microbiota-gut-brain (MGB) axis" has been developed to understand the impact of the gut-brain axis on human homeostasis, particularly in the field of psychiatry (6). There is a close relationship between depression and the microbiota, as recent research suggests that the gut microbiota may have a significant impact on the onset and development of depression. Animal experiments indicate that the gut microbiota can influence brain function and potentially affect behavior. For example, oral administration of Lactobacillus can reduce the expression of pro-inflammatory cytokines and increase the levels of BDNF in the hippocampus, leading to anti-anxiety and antidepressant effects in mice (5).

Evidence from human studies indicates that the gut microbiota of individuals with depression differs significantly from that of healthy individuals, including changes in the abundance of specific bacterial genera and alterations in the overall microbial community structure. Some microbial families have been found to be positively associated with anxiety and depressive symptoms, while others may help alleviate depressive symptoms (7–9). Additionally, the relative abundance of certain bacterial taxa, such as the Firmicutes phylum, appears to be more representative in major depressive disorder (MDD) (6, 10). This association is likely mediated through mechanisms such as regulating inflammation, influencing neurotransmitter synthesis and metabolism, and modulating the gut-brain axis signaling.Overall, the research suggests that the gut microbiota may have a profound impact on the molecular pathways involved in the occurrence and development of anxiety and depression-related behaviors, despite the differences between human and murine microbiomes (11).

Mendelian randomization (MR) is a new approach to exploring the causal relationship between gut microbiota and PPD by constructing working exposure variables using genetic variation to assess the causal relationship between exposure and outcome (12). Due to the random assignment of genes, the influence of other confounding factors is also avoided (13). The Mibiogen database is a bioinformatics platform that can be used for multi-omics data analysis and interactive visualization (14), based on which numerous authors have explored the causal relationship between gut flora and a variety of diseases, including eclampsia (15), adverse pregnancy outcomes (16) and ischemic Stroke (17).

In this study, a two-sample MR Analysis was performed using pooled statistics from genome-wide Association Studies (GWAS) from MiBioGen and the UK biobank consortium to explore specific gut microbiota causally associated with PPD.

Methods

Data sources

We obtained summary statistics of genome-wide association studies of the gut microbiota in mibiogen (18), and the MiBioGen study coordinated 2021S rRNA gene sequencing profiles and genome-wide genotyping data from 18,473 individuals (25 cohorts) and is the largest, multi-ethnic, genome-wide meta-analysis of the gut microbiome to date (19). This study included 211 taxa: 9 phylum, 16 orders, 20 families, 35 families, 131 genera, and 7738 participants of European ancestry, as determined by 16S ribosomal RNA gene sequencing (18). Data for PPD were obtained from the UK biobank, containing 4834 patients and 33173 controls from the European population, containing a total of 11,982,120 SNPs (20). All the people are European.

Genetic variants selection criteria

Based on the screening criteria from previous literature, we chose a stringent threshold of $P<1\times10^{-5}$ to select instrumental variables (IVs) for our analysis. This threshold ensures that only genetic variants with a very low probability of being associated with the outcome are included as IVs, reducing the likelihood of including SNPs with weak or spurious associations.

Additionally, to ensure the independence of each IV, we applied a threshold of $r^2<0.001$ within a window size of 10,000 kb. This step aimed to mitigate the effects of linkage disequilibrium (LD), a phenomenon where genetic variants close to each other on the chromosome are inherited together. By trimming IVs that are in high LD with each other, we aimed to reduce redundancy and remove SNPs that are essentially providing the same information. This helps in ensuring that the selected IVs are truly independent and provide unique information for the analysis.

Furthermore, we removed "echo SNPs" which are SNPs that are redundant due to LD and do not provide additional information beyond the already included SNPs. We also excluded SNPs that were not present in the results from the IVs, ensuring that all SNPs used in the analysis had valid and reliable data available for the research.

By applying these stringent criteria, we aimed to ensure that the selected IVs were robust, independent, and unlikely to be influenced by LD, thus enhancing the quality and reliability of our instrumental variable analysis.

MR analysis

The IVW method is an extension of the Wald ratio estimator based on meta-analysis principles (21). The random effects model

with inverse variance weight was selected as the main MR method. For the flora with causality in IVW ($p<0.05$), four additional methods were selected as supplements (MR Egger, weighted median, simple model, and Weighting pattern). In addition, we conducted a sensitivity analysis of the results. Firstly, we used the MR Egger interception test and the MR PRESSO global test to detect horizontal pleiotropy (22, 23). We reported the heterogeneity of the Wald estimator using the Cochrane Q statistic (24). In addition, a retention analysis was conducted to evaluate the robustness of the results.

All analyses in this study were conducted based on R software (version 4.2.1). The "TwoSampleMR" R package and the "MRPRESSO" R package were used for our MR research.

Results

According to the selection criteria of IVs, a total of 2044 SNPs were used as IVs for 5 levels and 211 sets, including 9 phylum, 16 classes, 20 orders, 35 families, and 119 bacterial genera.

We tested the causal relationship between Gut microbiota and postpartum depression by five MR methods. We identified a causal relationship between four bacterial characteristics and postpartum depression using the IVW method (Table 1, Figure 1). They are phylum Actinobacteria (P=0.014, OR=0.971,95% CI=0.948-0.994), genus Holdemanella (P=0.023, OR=0.979,95% CI=0.961-0.997), genus. unknown. ids. 2001 (P=0.025, OR=0.972,95% CI=0.947-0.996), and genus. unknown. ids. 2755 (P=0.012, OR=0.977,95% CI=0.959-0.995). They contain 15, 11, 10, and 13 SNPs, respectively. Additionally, other methods were used to compare The screened strains were validated, and beta values in the same direction were also obtained, Proving that our results are robust.

We used IVW testing and MR Egger regression to test the Q-statistic results and did not find any heterogeneity in the results. We used MR Egger regression to detect the presence of horizontal pleiotropy in Genus (Table 2). Holdemanella (P=0.04), but no other results showed the presence of horizontal pleiotropy. At the same time, we used the MR-PRESSO algorithm for detection and did not find the existence of horizontal pleiotropy. The forest diagram of causal effects using a single SNP shows that their association with mental illness/traits is not very significant, and sensitivity analysis indicates that there is no single SNP driving causal association signal (Figure 2).

In addition, the MR Steiger directionality test showed that the variance explained by the included bacterial exposure SNP was greater than the mental outcome, indicating a true causal correlation in the direction.

TABLE 1 Causal estimations of gut microbiota on postpartum depression in the MR analysis.

exposure	method	nsnp	b	pval	OR	95%CI
Phylum Actinobacteria id.400	MR Egger	15	-0.050	0.314	0.951	(0.866~1.044)
	Weighted median		-0.030	0.065	0.971	(0.941~1.002)
	IVW		-0.030	0.014	0.971	(0.948~0.994)
	Simple mode		-0.008	0.781	0.922	(0.936~1.051)
	Weighted mode		-0.022	0.435	0.979	(0.928~1.032)
Genus Holdemanella id.11393	MR Egger	11	-0.045	0.139	0.956	(0.906~1.009)
	Weighted median		-0.032	0.010	0.969	(0.945~0.992)
	IVW		-0.022	0.023	0.979	(0.961~0.997)
	Simple mode		-0.039	0.108	0.961	(0.92~1.004)
	Weighted mode		-0.038	0.072	0.963	(0.927~0.999)
Genus Unknowngens id.2755	MR Egger	13	-0.010	0.792	0.990	(0.919~1.066)
	Weighted median		-0.018	0.160	0.983	(0.959~1.007)
	IVW		-0.023	0.012	0.977	(0.959~0.995)
	Simple mode		-0.016	0.451	0.984	(0.946~1.024)
	Weighted mode		-0.016	0.433	0.984	(0.947~1.023)
Genus unknowngenus id.2001	MR Egger	10	-0.117	0.015	0.889	(0.825~0.958)
	Weighted median		-0.035	0.034	0.966	(0.935~0.997)
	IVW		-0.029	0.025	0.972	(0.947~0.996)
	Simple mode		-0.043	0.105	0.958	(0.915~1.004)
	Weighted mode		-0.039	0.153	0.962	(0.916~1.01)

IVW, inverse variance weighted; MR, Mendelian randomization; nsnp, number of single-nucleotide polymorphism;b,bata; OR, odds ratio; SM, Simple mode; 95%CI, 95% Confidence interval.

TABLE 2 Heterogeneity test and horizontal pleiotropy test of gut microbiota on postpartum depression.

exposure¤	method¤	Heterogeneity test¤			horizontal pleiotropy test¤		MR PRESSO¤
		Q¤	Q_df¤	Q_pval¤	egger¶ intercept¤	pval¤	
Phylum¶ Actinobacteria¶ id.400¤	MR Egger¤	9.817¤	13¤	0.709¤	0.001¤	0.665¤	0.788¤
	IVW¤	10.013¤	14¤	0.761¤	¤	¤	
Genus¶ Holdemanella¶ id.11393¤	MR Egger¤	5.851¤	8¤	0.664¤	0.009¤	0.041¤	0.368¤
	IVW¤	11.792¤	9¤	0.225¤	¤	¤	
Genus¶ Unknowngens¶ id.2755¤	MR Egger¤	7.773¤	11¤	0.733¤	-0.001¤	0.722¤	0.817¤
	IVW¤	7.907¤	12¤	0.792¤	¤	¤	
Genus¶ Unknowngens¶ id.2001¤	MR Egger¤	10.343¤	9¤	0.323¤	0.003¤	0.395¤	0.258¤
	IVW¤	11.262¤	10¤	0.337¤	¤	¤	

p value > 0.05 represent no significant pleiotropy. Q_p value > 0.05 represents no significant heterogeneity.
GWAS, genome-wide association study; IVs, instrumental variants; IVW, inverse variance weighted; MR, Mendelian randomization; SE, standard error.

Discussion

In this study, the causal relationship between four bacterial features in the gut microbiota genome-wide association study (GWAS) and postpartum depression (PPD) was demonstrated through Mendelian randomization (MR) analysis. This research is not only significant in understanding the role of the gut microbiota in postpartum depression, but also provides new evidence for the "microbiota-gut-brain (MGB) axis" concept. The gut-brain axis is involved in the shared genetic basis of gastrointestinal and mental disorders, a notion which has been confirmed through comprehensive genomic range analysis (25).

This study identified a causal relationship between four bacterial genera and postpartum depression (PPD), allowing for in-depth exploration of the impact of these microbial changes on function and metabolism. Notably, the research on Actinobacteria

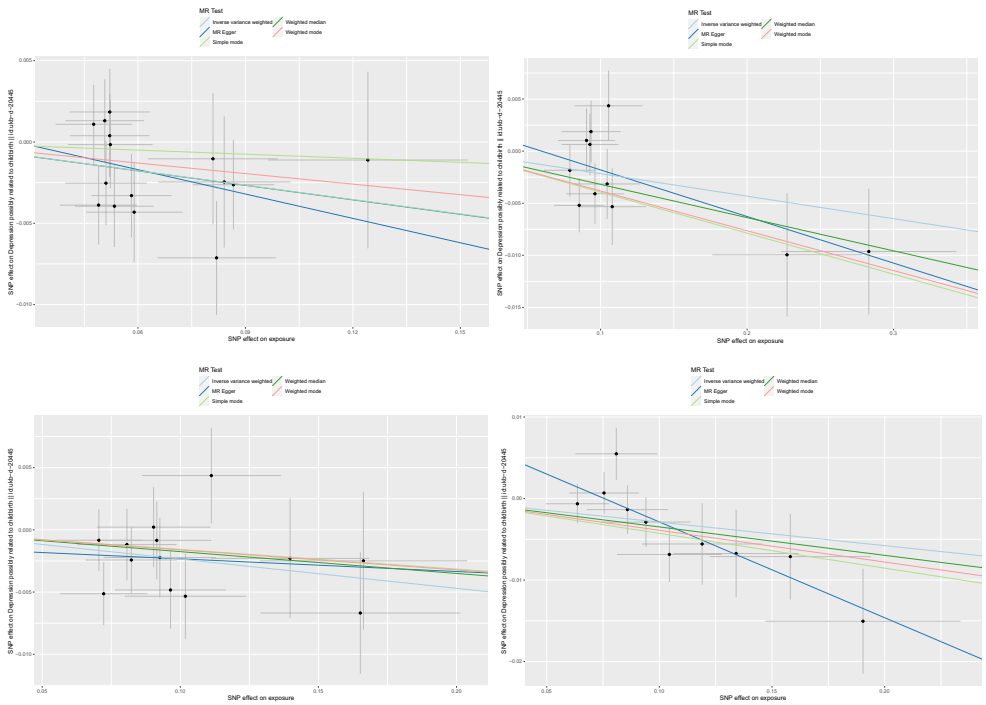

FIGURE 1
Scatter plots for the causal association between gut microbiota and PPD.

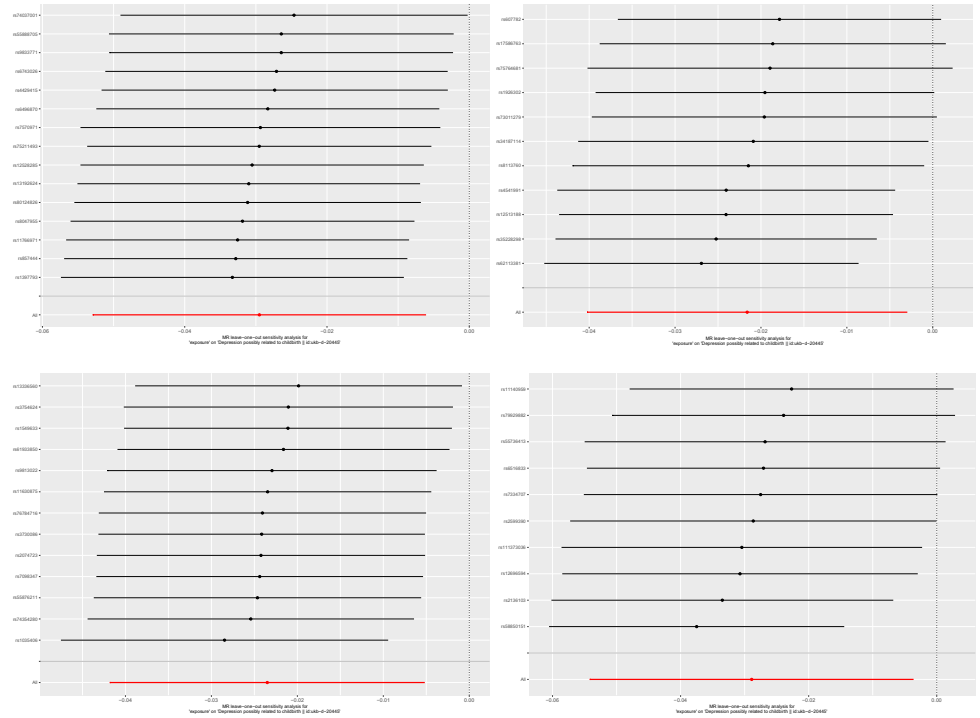

FIGURE 2
Leave-one-out analysis for the causal association between gut microbiota and PPD.

and Holdemanella genera is particularly intriguing. Evidence of the protective role of Actinobacteria as a key member of the gut microbiota against depression continues to accumulate, as demonstrated by Tian et al.'s analysis of the gut microbiota in normal mice and those with PPD, which revealed higher abundance of Actinobacteria (including Bifidobacterium and Corynebacterium) in the normal group compared to the PPD group (26). Previous research has also indicated an association between gut microbiota imbalance and certain mental disorders such as anxiety and depression. Jiang's high-throughput sequencing analysis of 46 depressed patients and 30 healthy controls showed significantly higher abundance of Actinobacteria and Firmicutes in the healthy control group at the phylum level compared to the depressed patients (27). Moreover, previous MR studies have indicated a protective effect of Actinobacteria against major depressive disorder (MDD) incidence (OR 0.88, 95% CI 0.87-0.9) (28). Therefore, bacteria within the Actinobacteria phylum may indirectly influence the onset and development of mental disorders by affecting the balance of the gut microbiota. In fact, Actinobacteria are producers of many important antibiotics (29), including penicillin, tetracycline, and erythromycin, and their increased abundance may compete with pathogens for nutrients and adhesion sites, thereby inhibiting pathogen colonization and growth, and contributing to the maintenance of gut microbiota balance. Additionally, some Actinobacteria may modulate the host's immune system, contributing to immune response regulation and maintaining gut immune system balance. However, further research and exploration are needed to elucidate the specific mechanisms and effects of Actinobacteria in alleviating postpartum depression.

Research on the Holdemanella genus also suggests its potential beneficial impact in reducing the risk of postpartum depression (PPD). In a study on post-stroke depression (PSD), researchers analyzed fecal samples from 232 patients with acute ischemic stroke using 16S rRNA sequencing. The samples were assessed using the Hamilton Depression Rating Scale (HAMD-3). The results indicated a significant decrease in the abundance of Holdemanella genus in PSD patients, and a negative correlation between the abundance of Holdemanella genus and HAMD scores, suggesting a potential beneficial impact of Holdemanella genus in reducing the risk of PSD (30). Furthermore, Jiang's study observed lower abundance of Firmicutes in the gut microbiota of depressed patients compared to healthy controls (7). Additionally, several studies consistently indicate that increasing the levels of the Holdemanella genus is beneficial in reducing the incidence of depression (31, 32). It is worth mentioning that depressed patients often have lower levels of omega-3 fatty acids (33). While there is no consensus on whether supplementing omega-3 alone can effectively alleviate depression, it has been observed that consuming omega-3-rich fish may be associated with increased abundance of Holdemanella genus (27). Could increasing the abundance of Holdemanella genus and reducing the risk of postpartum depression be achieved through omega-3 supplementation? This is purely speculative, but it also provides a new perspective on the role of dietary intervention in preventing postpartum depression.

This study identified a causal relationship between four bacterial features in the gut microbiota genome-wide association study (GWAS) and postpartum depression (PPD) through Mendelian randomization (MR) analysis. Additionally, it suggests that the Actinobacteria and Holdemanella genera may have a potential beneficial impact in reducing the risk of depression. Adjusting the abundance of these microorganisms in the gut microbiota may help improve symptoms of certain mental disorders, providing important evidence for understanding the role of the gut microbiota in postpartum depression.

However, this study also has some limitations. Firstly, the GWAS meta-analysis of the gut microbiota included male and female participants. Even though genetic variants located on the sex chromosomes were excluded from the analysis and adjustments for gender were made, it may still introduce bias (18). Moreover, the majority of the data is from individuals of European descent, potentially introducing interference from racial differences. Therefore, in future studies, we hope to conduct detailed subgroup analyses targeting specific populations to explore the influence of gender on the relationship between the gut microbiota and PDD. Additionally, we aim to conduct in-depth research on specific gut microbiota to understand their association with PDD, and further explore the mechanisms of specific microbiota in PDD through metagenomic analysis and functional experiments, deepening our understanding of the relationship between the gut microbiota and PDD, and providing a scientific basis for more precise intervention measures in the future.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/supplementary material.

Author contributions

JZ: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. LW: Conceptualization, Data curation, Formal analysis, Writing – original draft. HT: Data curation, Formal analysis, Validation, Writing – original draft. WP: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Perinatal mental disorders and suicidal risk among adolescent mothers living in urban areas of Cameroon

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Background: In sub-Saharan Africa the birth rate among teenage mothers is the highest in the world. In 2021, there would be 6,114,000 births for 15–19-year-olds in this part of the world. In Cameroon, the fertility rate among adolescents aged 15–19 is 24%. However, there is a significant lack of data on the mental health of teenage mothers. Given the biopsychosocial conditions of the perinatal period and adolescence, we hypothesise that the prevalence of mental disorders and the risk of suicide is very high in Cameroon. The aim is therefore to determine the prevalence of perinatal mental disorders and suicide risk among adolescent mothers in urban areas of Cameroon.

Methods: Following ethical approval of the submitted protocol, we recruited adolescent mothers and data were collected using diagnostic interviews based on the DSM-5, PDM-2 and MINI guidelines. The types of sampling used were typical and incidental. Data were tabulated with Epidata 3.1 and processed with SPSS 25.

Results: 66.4% of adolescent mothers were diagnosed with a mental disorder and 27.4% with suicidal risk. It was found that there was a link between mental disorders and suicidal risk ($p<0.001$), with mothers at suicidal risk having an 8.4 times greater risk of having a mental disorder (OR=8.423). Linear regression confirmed the statistically significant relationship between perinatal mental disorders and suicidal risk. 31.1% of the total variance in suicidal risk was explained by mental disorders. The regression coefficients for mental disorders with a $p<0.05$ value is: perinatal depression (-0.279), post-partum psychosis (-0.133), trauma disorder (-0.034), generalised anxiety disorder (-0.008) and conduct disorder (-0.020).

Conclusions: Our hypothesis is confirmed, because the prevalence of 66.4% of mental disorders and 27.4% of suicidal risk are significantly high in Cameroon. In some way, the disorders predict suicidal risk, because the less an adolescent mother has one of these pathologies during the perinatal period, the less she will be at risk of suicide. More research of this kind is needed to contribute in providing more data, including solutions to address the morbidity and mortality problems associated with the mental health of teenage mothers.

KEYWORDS

perinatal mental health, perinatal period, perinatal mental disorders, adolescents mothers, suicidal risk, unsatisfied social needs, Cameroon

Introduction

The possibility of becoming pregnant and having a baby is a reality for adolescent girls around the world. This reality is determined by conditions of biological, psychological and social vulnerability. The perinatal period runs from the first day of pregnancy to the end of the baby's first year of life (1–3). The mental disorders, states of psychological distress or perinatal mental problems, studied by the perinatal psychiatry, have a high prevalence and are recognised as major contributors to maternal morbidity and mortality in adolescent girls, and to health and development risks for babies (4, 5). Perinatal psychiatry is a discipline that lies at the interface between adult and child psychiatry. Its aim is to study the mental disorders that occur in one or other of the parents during the perinatal period, as well as the specificities of the development of the foetus, the newborn and the infant in this context. The disorders that appear during this perinatal period and that are dependent on it are called perinatal psychiatric disorders (6). According to the theory of human birth, mental illness can be understood as a pathology of the human relationship immediately after birth and during the first year of life (7). In high-income countries, the prevalence of maternal depression in this population group is 48% (3). In low- and middle-income regions such as sub-Saharan Africa, the perinatal mental health of adolescent mothers is neglected and, in some areas, virtually non-existent. However, some research has been carried out, although not in all areas (8). Yet in sub-Saharan Africa, the birth rate among teenage mothers is the highest in the world. In 2021, there would be 6,114,000 births by 15–19-year-olds in this part of the world (9). However, studies on the prevalence of perinatal mental disorders in sub-Saharan Africa have focused solely on perinatal depression or its symptoms. Prevalence rates ranged from 10.1% to 94% (8). With regard to the problem of suicide in this segment of the population, only two qualitative studies have been carried out in Kenya and South Africa on the factors associated with suicidal behaviour (10). In Central Africa, particularly Cameroon, there is one study on the prevalence of symptoms of perinatal depression (1). In this country, the fertility rate among adolescents aged 15–19 is 24% (11). It therefore seems crucial for us to seek information on the prevalence of perinatal mental disorders and psychological distress in this category of the population. Our hypothesis is that the prevalence of perinatal mental disorders is very high and that these can predict the occurrence of suicidal risk. The aim of our study is to determine the prevalence of perinatal mental disorders and suicidal risk, and the link between the two, in adolescent mothers during the perinatal period, in urban areas in Cameroon. Beforehand, their socio-demographic characteristics and unmet social needs will be identified.

Methods

Determining the prevalence of perinatal mental disorders and suicidal risk, including the relationship between the two, requires a scientifically proven approach.

Ethical considerations

The study procedures were carried out in accordance with the ethical principles and obligations to which researchers are bound by the Declaration of Helsinki (12). All participants were informed of the study and provided written consent. They were informed that if they wished, they could withdraw from the study at any time. Ethical approval was granted by the National Ethics Committee for Human Health Research (CNERHH) in Yaoundé, after evaluation of our research protocol. The approval number is: 2014/03/436/L/CNERSH/SP.

Framework of the study

This study is the research dimension of an action research project, which combines, in a single movement, a research rationale to produce knowledge and an action rationale to act, modify and improve a situation or an activity (13). In Cameroon, the partners involved were: the Ministry of Public Health (MINSANTE), the

Ministry for the Promotion of Women and the Family (MINPROFF), Le Réseaux National des Associations de Tantines (RENATA), Uni-Psy et Bien-Être (UniPsy) an organisation of mental health professionals. And in Geneva, the University of Geneva, Action en Santé Publique (ASP) a non-governmental organisation, the Department of Child and Adolescent Psychiatry (SPEA) of the Geneva University Hospitals and the Worl Health Organisation (WHO). Skills were enhanced by training a team of 71 front-line workers (nurses, social workers, psychology students, junior psychologists). These skills included the use of the World Health Organisation's (WHO) Mental Health Global Action Plan (mhGAP) based on the Diagnostic and Statistical Manual of Mental Disorders (14, 15), the Edinburgh Postnatal Depression Scale (EPDS) (16), the Mini International Neuropsychiatric Interview (MINI) (17), and other data collection instruments (questionnaires, interview guide, risk factor inventory). Supervision was provided by 8 2nd line clinical psychologists and 3 3rd line psychiatrists. The front-line workers administered the data collection tools, and the clinical psychologists and supervising psychiatrists made the diagnoses.

Population and sample

For the purposes of this study, we will refer to all teenage mothers who are pregnant or have a baby aged one year or less, as teenage mothers. Our study population consisted of 1633 adolescent mothers in the perinatal period. Their place of residence was Yaoundé and its environs. With regard to their perinatal status, 827 were prenatal and 783 postnatal. Recruitment was continuous for 4 years 8 months, from April 2014 to December 2018. Inclusion criteria were being aged 20 years or less, pregnant or having a child no older than 12 months. The exclusion criteria were being over 20 years of age, having a child over 12 months of age, not having fully completed the collection tools and not having been clinically assessed. The non-probability sampling technique was chosen. 2 types of sampling were carried out. Typical sampling was used for participants recruited at the hospital and through the personal network of carers, and accidental sampling for those recruited door-to-door (18).

Procedure, tools and data collection

The research protocol was drafted, corrected and submitted for ethical approval. A framework for face-to-face and remote discussion was created for the action research project to facilitate the exchange of information and the coordination of the project. Training sessions lasting between three and five days were organised each year for the data collection team. The aim was to teach them how and when to conduct the interview, and to go through the EPDS, including the questionnaire and interview guide. The data was collected by means of directive and semi-directive interviews based on the sub-themes presented in Table 1 below:

Collection tools

The diagnosis of a mental disorder is made by psychiatrists, psychologists or other care providers trained and authorised to do so. It is made using a number of methods based on questionnaires or observations, which are in turn based on tried and tested and scientifically validated theoretical and clinical corpus. This is the case for perinatal and adolescent mental disorders. When it comes to diagnosing adolescents, given the period of development, a certain number of psychopathological symptoms may be observed, when in fact they are not. The diagnosis must take account of both diachronic and synchronic data. This is why, in addition to the presence of signs and symptoms, the diagnosis will take into account parameters such as: the individual's history, environmental circumstances, the degree of rupture with past functioning, family interactions, disturbance of habitual psychic functioning, maladjustment to external reality, biopsychosocial risk factors, the intensity and permanence of signs and symptoms (19). The aim of taking these parameters into account is to increase the reliability and viability of the diagnostic criteria for teenage mothers. We did not find any specific scales for screening and diagnosing perinatal mental disorders in adolescent mothers. The above comments have been taken into account in our work, as can be seen from the above-mentioned evaluation sub-themes (socio-demographic profile, evaluation, perinatal and parental experiences,

TABLE 1 Sub-themes addressed during data collection.

Sub-themes	Contents
Socio-demographic profile	Age, occupation, perinatal status, marital status, religion, sibling rank, level of education, region of origin, living area (whether close to home or not), contacts
Evaluation	Context of the meeting, social needs, perceptions of mental health, baby's psychological and physical state, baby's diet
Perinatal and parental experiences	State of relationship with partner, state of relationship and social interactions with others during the perinatal period, pre-, per- and postnatal experience, changes and evolution of the state of health of the mother and child, transformations linked to parenthood and the quality of the mother-baby relationship.
Psychopathological aspects and mental disorders	Screening and diagnostic tools: Edinburgh Postnatal Depression Scale (EPDS), Mini International Psychiatric Interview (MINI) for suicidal risk, DSM-5 for diagnosing mental disorders, PDM for diagnosing complex psychotrauma and mother-baby relationship disorders, presence or absence of a dysfunctional family (7 open questions are asked for this aspect and the themes are as follows: communication, roles, conflict resolution, material satisfaction, emotional reactions, emotional involvement, behavioural control).
Risk factors for perinatal mental disorders	5 categories: circumstances of pregnancy and motherhood, health issues, social risk factors, negative experience of childbearing or childbirth, state of marital and family relationships.

psychopathological aspects and mental disorders, risk factors for perinatal mental disorders).

The three standards used to diagnose mental disorders are: the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5), the Mini International Neuropsychiatric Interview (MINI) and the Psychodynamic Diagnostic Manual (PDM). The former provides a clear and systematic description and classification of mental disorders (15). It is intended for mental health professionals and is an international reference. Clinical psychologists and psychiatrists have used this reference to confirm the diagnosis of perinatal mental disorders. The second standard, the MINI, is a short clinical interview structured interview that allows researchers to diagnose psychiatric disorders according to the DSM-IV. The interview was designed for epidemiological studies and multicentre clinical trials (17). When used correctly, it can also be used to make a diagnosis. It measures the absence or presence of an illness, based on rigorous criteria that correspond to those of the Diagnostic and Statistical Manual of Mental Disorders. In this study, we used the French version 5.0.0 only to assess suicidal risk, which is either non-existent, mild, moderate or high. The third reference, the PDM, is the result of an effort to formulate a psychodynamically oriented diagnosis that bridges the gap between clinical complexity and the need for empirical and methodological validity (20, 21). One of the aims of this manual is to complement the DSM and the International Classification of Diseases (ICD). In the context of our research, we used it to make diagnoses of complex psychotrauma and mother-baby relationship disorders (22). All these diagnostic criteria are also those described by the ICD 10: bipolar disorder, depressive episodes with somatic syndrome, neurotic disorders, obsessive-compulsive disorder, reaction to stress factors (adjustment disorder, post-traumatic stress disorder, etc.). Symptoms may have mood-related aspects such as sadness, guilt, self-blame, negative thoughts, etc. Others may express anxiety: irritability, sleep disturbance, panic, etc. Occasionally, mothers may exhibit psychotic signs described in the ICD 10, such as delusions, hallucinations, etc. (23). To sum up, in the light of the above, this approach is a strength, since it relies on several complementary elements to reach a diagnosis. On the other hand, the diagnosis may be limited by the fact that the mothers are still in their teens. The health workers who collected the data did not participate in either the tabulation or the analysis of the data.

Data analysis

The data were analysed using Epidata 3.1 and processed using SPSS 25. Descriptive statistics were first performed. This consisted in highlighting the different frequencies of the modalities of our variables. Next, we calculated the chi-square (X^2), the odds ratio (OR) and the relative risks (RR) for the cross-tabulations. Finally, we performed a linear regression to determine the predictive effect of mental pathologies on suicidal risk factors among teenage mothers.

Results

The general objective was to determine the prevalence of perinatal mental disorders and suicidal risk among adolescent mothers during the perinatal period in Cameroon. To achieve this, we present the sociodemographic characteristics and unmet social needs. We will then use descriptive statistics for prevalence, after collecting data using the DSM-5, PDM and MINI tools. Finally, we will analyse the link and relationship between the different variables using inferential statistics.

Socio-demographic characteristics of teenage mothers

1633 teenage mothers took part in the study. As shown in the Table 2 51.4% were pregnant (prenatal) and 48.5% had a child up to one year old (postnatal). The mean age was 17.91 years and the oldest age group was the age group represented by 18–20 years, i.e., 68.4% of participants. 75% of them were single mothers. In terms of level of education, lower secondary education was the most represented, with 47.8% included. In terms of gestational age, most were between the second and third trimesters, 23.5% and 19.5% respectively. 38% had a single child and 7.8% had 2 children. The average age of the babies was 5.31 months. The majority of these mothers (46.8%) were recruited in health facilities, while 39.1% were recruited door-to-door. When asked what their unmet needs were, 58.7% said money, 55.6% moral support from family and friends, and 47.3% knowledge of how to look after a pregnancy or a baby. Given these characteristics and unmet social needs, one may ask what the prevalence of suicidal risk and perinatal mental disorders is in this population.

Prevalence of suicidal risk and perinatal mental disorders among teenage mothers

Determining the prevalence of suicidal risk and perinatal mental disorders is one of the specific aims of our research. As indicated above, we administered interviews based on the DSM-5, PDM and MINI tools to make diagnoses. 1085/1633 teenage mothers were diagnosed as suffering from at least one mental pathology, as shown in Table 3, a rate of 66.4%. Broken down, the rate was 39.9% for prenatal teenage mothers and 32.6% for postnatal teenage mothers, relative to the total sample. The prevalence of maternal depression was 60.9% (994/1633). 176 suffered from perinatal anxiety (generalised anxiety), a prevalence of 10.7%. With regard to mother-baby relationship disorder, 6.1% were diagnosed as positive. Trauma disorder was also observed, with a prevalence of 7.8% (128/1633). It is distinguished by its two dimensions: post-traumatic stress disorder, 4.9%, and complex traumatic disorder, 2.9%. 4.1% had a behavioural disorder. 1.1% were addicted to substances (alcohol, tobacco and drugs). Among teenage mothers living in dysfunctional families, 411, or 25.2%, were in this category. It was found that 27.4% of teenage mothers were at mild risk of suicide, while 2.7% were at medium risk and 7.3% at high risk.

Unsatisfied social needs, mental disorders and suicide risk

The association between subjects having had at least one mental disorder and those having at least one need was significant

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TABLE 2 Socio-demographic characteristics of teenage mothers.

Characteristics	Frequency	n% (IC=95%)
Perinatal state		
Prenatal	840	51.4 (48.8–53.8)
Postnatal	793	48.5 (46 -50.)
Age (M=17.91; Min=12; Max=20; SD=1.30)		
< 15 years	84	5.1 (4.2–6.4)
15 - 17 years	416	25.5 (23.6–27.9)
18 - 20 years	1117	68.4 (66.8–71.3)
Marital status		
Single	1224	75.0 (73.3–78)
In a cohabiting relationship	274	16.8 (15.2–18.9)
Married	113	6.9 (5.8–8.4
Divorced	1	0.1 (0–0.3)
Widow	1	0.1 (0–0.3)
Level of education		
Out of school	35	2.1 (1.6–3.1)
Primary education	171	10.5 (9.4–12.5)
Lower secondary education	780	47.8 (47.2–52.2)
Upper secondary education	528	32.3 (31.3–36.1)
University level	55	3.4 (2.7–4.5)
Gestational age (M=5.72; Min=1; Max=9; SD=1.98)		
1 - 3 month	126	7.7 (5.7–8.2)
4 - 6 month	384	23.5 (21.4–25.6)
7 - 9 month	318	19.5 (17.6–21.4)
Age of child (M=5.31; Min=1; Max=12; SD=3.54)		
1 - 3 month	301	18.4 (16.5–20.3)
4 - 6 month	200	12.2 (10.6–13.8)
7 - 9 month	132	8.1 (6.7–9.4)
10 - 12 month	127	7.8 (6.4–9.1)
Number of children (M=1.21; Min=1; Max=3; SD=0.45)		
1	621	38.0 (35.6–40.4)
2	128	7.8 (6.4–9.1)
3	15	0.9 (0.4–1.3)
Meeting the teenage mother		
Health Facilities	764	46.8 (44.8–49.7)
Door to door	639	39.1 (37.1–42)
Health worker network	213	13.0 (11.6–14.9)
Unsatisfied social needs		
Money	959	58.7 (56.3–61.1)
Moral support	908	55.6 (53.2–58.0)
Practical support	602	36.9 (34.6–39.2)
Medical care for baby	138	8.5 (7.1–9.8)
Medical care for teenage mothers	163	9.9 (8.4–11.3)
Knowledge about maternity	773	47.3 (44.9–49.7)
Legal assistance	32	2.0 (1.3–2.7)
Training/guidance	477	29.2 (27.0–31.4)
Shelter	48	2.9 (2.1–3.7)
Employment	350	21.4 (19.4–23.4)
School Enrolment	302	18.5 (16.6–20.4)

(Continued)

TABLE 2 Continued

TABLE 3 Prevalence of mental disorders and suicidal risk among teenage mothers in the perinatal period in Cameroon.

Variables		Frequency	n % (IC 95%)
Teenage mothers with at least one mental disorder		1085	66.4 (64.1–68.7)
Prenatal teenage mother		545	33.9 (31.6–36.1)
Postnatal teenage mother		525	32.6 (30.3–34.8)
Depression		994	60.9 (58.5–63.2)
Psychosis		12	0.7 (0.4–1.3)
Traumatic disorder		128	7.8 (6.7–9.3)
Post-traumatic stress disorder		80	4.9 (4.6–5.1)
Complex traumatic disorder		48	2.9 (2.6–3.1)
Substance use disorder		18	1.1 (0.7–1.7)
Generalised Anxiety Disorder		176	10.7 (9.3–12.4)
Disturbance in the mother-baby relationship		101	6.1 (5.1–7.5)
Conduct disorder		67	4.1 (3.2–5.2)
Suicidal risk	Mild	448	27.4 (25.3–29.7)
	Medium	44	2.7 (2–3.6)
	High	120	7.3 (6.1–8.7)
Dysfunctional family		411	25.2 (23.1–27.3)

(p≤0.001), as was the case for those at risk of suicide and having at least one unmet need (p≤0.001). In addition, as presented in Table 4, teenage mothers with at least one unmet social need were 0.17 times more likely to have a mental pathology and 0.28 times more likely to be at risk of suicide during the perinatal period.

In addition, we want to verify the confounding effect or effect modification between having at least one need, in association with

TABLE 4 Correlation between unmet needs, mental disorders and suicide risk.

		Adolescent mother with at least one need		*P-value*	OR
		Yes, n (%; IC)	No, n (%; IC)	<0.001	0.177
Teenage mothers with at least one mental disorder	Yes	1054 (64.5;62.1–66.8)	31 (1.9; 1.2–5.5)		
	No	470 (28.8;26.6–30.9)	78 (4.8;3.7–5.8)		
		Teenage mother with at least one need		<0.001	0.289
Teenage mothers at risk of suicide	Yes	595 (36.4;34–38.7)	17 (1.0;0.5–1.4)		
	No	929 (56.9;54.4–59.3)	92 (5.6;4.4–6.7)		

TABLE 5 Correlation between suicide risk and mental disorders.

	Teenage mothers with at least one mental disorder			
Suicidal Risk	Yes) n (/%; IC)	No) n (/%; IC)	*P-value*	OR (RR)
	552 (33.8;31.5–36.2)	60 (3.7;2.8–4.7)	<0.001	8.423

having at least one pathology and suicidal risk. Indeed, we find that having at least one pathology is an effect modifier (OR1 = 2.223≠ OR2 = 1.283) of the association between having at least one need and having a suicidal risk. Furthermore, we have a quantitative type interaction, because the relationship between having a suicidal risk and having at least one need, go in the same direction, i.e. increasing. It is stronger in subjects with at least one pathology than in those with no pathologies.

Link between mental disorders and suicidal risk

The link between suicidal risk and mental disorders was significant (p≤0.001), as shown in Table 5. In addition, teenage mothers at risk of suicide were 8.4 times more likely to have a mental illness.

Furthermore, the F statistic of 122.536 with a p-value of <0.001 shows that there is a statistically significant relationship between the various mental disorders that have a p-value of less than 0.05 and the fact of haven presented a suicidal risk. This is why these mental disorders explain 31.1% of the total variance in cases of suicidal risk among adolescent mothers. In fact, as presented in Table 6, the regression coefficients for mental disorders with a p<0.05 value are: depression (-0.279), post-partum psychosis (-0.133), trauma disorders (-0.034), generalised anxiety disorder (-0.008) and conduct disorder (-0.020). This implies that, on the whole, these mental disorders have negative and significant effects on the presence of suicidal risk observed in adolescent mothers. In other words, the less an adolescent mother suffers from one of these mental disorders during the perinatal period, the less likely she is to commit suicide.

Discussion

The aim of our study was to determine the prevalence of perinatal mental disorders and suicidal risk among adolescent mothers in Cameroon, and the correlations between these two phenomena. To do this, we identified the field, defined a framework, a sample and collection procedures using the DSM, PMD and MINI tools. A quantitative, descriptive and inferential analysis of the data was carried out and the results obtained.

Our results indicate that 66.4% of teenage mothers in urban areas of Cameroon suffer from at least one mental disorder. This is equivalent to almost 2/3 of teenage mothers in need of treatment. This 66.4% prevalence rate of mental disorders in Cameroon is close to the 72.2% rate of mental health needs identified among adolescent mothers in sub-Saharan Africa from 2013 to 2021 (24). In comparison, our study goes beyond mental health problems and identifies mental disorders using diagnostic instruments. In addition, ours is more precise and focuses on teenage mothers (aged 11–20), whereas in this research, the study populations go beyond the category of teenage mothers and include young mothers (aged 20–24), parents and certain health professionals. The added value of our results is that they go beyond simply presenting the prevalence rate of perinatal depression and the symptoms of perinatal depression in adolescent mothers, as done by other studies in sub-Saharan Africa (Cameroon, Zimbabwe, Nigeria, Ghana, Ethiopia, Tanzania, Uganda, Kenya, Malawi, South Africa) (8). The prevalence of traumatic disorders, generalised anxiety disorders, mother-baby relationship disorders, conduct disorders, substance-related disorders and postpartum psychosis were all highlighted in our research.

With regard to the prevalence of perinatal depression among adolescent mothers in Cameroon, our results show that it is 60.9%. In so-called developed countries, the rate is 48% (3). In sub-Saharan Africa, the rate varies between 8.8% and 94%. The higher rates can be explained by the fact that the populations were exclusively either rape survivors (25) or mothers of premature babies (26). From this point of view, the fact that our study population is more heterogeneous, the rate of 60.9%, seems to us to be closer to the reality of all adolescent mothers. In Central Africa, and Cameroon in particular, an initial study was carried out on the prevalence of depressive symptoms among teenage mothers. The prevalence was 70% (1). Other studies were carried out in Cameroon on a population of adult mothers, and the prevalence of postnatal depressive symptoms was 31.8% and 23.4% (27, 28). The new contribution of our research is that it went further by showing not only the prevalence of diagnosed perinatal depression, but also that of other mental disorders. Our result of 66.4% prevalence of mental disorders in adolescent mothers in urban areas of Cameroon is close to 68.9%, which is the prevalence of mental disorders in a Cameroonian population of children, adolescents and young people in the context of armed conflict and displacement/migration (29).

TABLE 6 Linear regression of suicidal risk and mental disorders.

Summary of models						
Model	R	R-two	Adjusted R-two	Standard error of estimate		
1	.558[a]	.311	.309	.403		
ANOVA[a]						
Model		Sum of squares	ddl	Mean square	F	Sig.
1	Regression	119.144	6	19.857	122.536	.000[b]
	of Student	263.497	1626	.162		
	Total	382.641	1632			

Coefficients[a]					
	Model Non-standardised coefficients		Standardised coefficients		
Model	B	Standard error	Beta	t	Sig.
(Constante)	1.899	.016		116.905	.000
Depression	-.279	.022	-.281	-12.877	.000
Postpartum Psychosis	-.133	.059	-.047	-2.267	.023
Traumatic disorder	-.034	.008	-.094	-4.434	.000
Generalised anxiety disorder	-.008	.004	-.047	-2.251	.024
Conduct disorder	-.020	.005	-.089	-4.292	.000

a=dependent variable (subjects with at least one suicidal ideation); b=predictors or constancy, i.e. the set of variables retained in the model, i.e. depression, postpartum psychosis, traumatic disorder, general anxiety.

In our work, we found that having an unmet social need had a statistically significant effect on the presence of suicidal risk ($p<0.001$), including mental disorder ($p<0.001$). These results confirm the general trend that the presence of a mental disorder is associated with psychosocial factors (3, 8, 30). In fact, the risk of having a mental illness or being at risk of suicide was slightly higher among teenage mothers with at least one unmet social need (0.28 times and 0.17 times higher).

Our results show a prevalence rate of mild, medium and high suicidal risk of 27.4%, 2.7% and 7.3% respectively. To the best of our knowledge, this is the first study in sub-Saharan Africa to address the phenomenon in terms of the prevalence of suicidal risk among teenage mothers with a significant population (1633). A study carried out in Kenya on suicide instead used a qualitative approach to deal with this suffering among teenage mothers. The aim was to identify themes linked to the risk of suicidal behaviour (9). Another qualitative study in South Africa explored the link between pregnancy, HIV, violence and mental health problems, including suicidal ideation. The population of South Africa's study consisted of pregnant mothers aged 15–24 years (31). We wanted to propose an attempt to explain the presence of suicidal risk. To do this, as described in the results section, we performed multivariate linear regression. The aim was to determine the independent predictors of suicidal risk on the basis of the mental disorders that were significantly associated with suicidal risk in the univariate analyses. This approach differs from those used in the Kenyan and South African studies, which are more qualitative (8, 10, 24, 30). Ours was carried out on a population 6 times larger, with a focus on a single phenomenon, namely mental disorders, in a quantitative and therefore generalisable approach. This is something new in sub-Saharan Africa. In the multivariate linear regression, after various iterations, individual predictors using standardised beta scores were examined. Thus, suffering from depression, psychosis, traumatic disorder, generalised anxiety disorder and conduct disorder explained the greatest variance (31.1%) in the relative burden of suicidal risk among pregnant and breastfeeding adolescents. Adolescent mothers at risk of suicide were 8.4 times (OR=8.423) more likely to suffer from a mental disorder.

Recent research suggests that it is imperative to develop personal identity before sexual orientation and possibly parenthood. Babies and children of teenage mothers are at greater risk of prematurity and low birth weight, followed by developmental delays and behavioural problems. There is also the theory of human birth, which posits that mental illness is a consequence of the disruption of the human relationship immediately after birth during the first year of life (5, 7). On the basis of these postulates and observations, the high prevalence rate of 66.4% of psychological distress among teenage mothers is understandable, on the one hand, and would suggest a significant future increase in mental illness, somatic disease and developmental delays in the Cameroonian population, on the other. The significant presence of risk factors and unmet social needs could also explain the high rate of perinatal mental disorders and suicidal risks among teenage mothers in Cameroon. A further study would shed more light on this hypothesis.

The multifactorial model could also explain this high rate of perinatal mental disorders. These include the young woman's personality, her family history, her personal psychiatric and obstetric history, hormonal changes, the stress of childbirth and the importance of the family and social network (32–34). In view of the difficult histories, the high number of unmet social needs, and the biology of

adolescent mothers who are still growing, we can understand the high prevalence of mental disorders (66.4%.) and suicidal risk (27.4%) in the Cameroonian context. Furthermore, in this perspective, another study (1) that explored risk factors among teenage mothers in Cameroon identified factors linked to depressive symptoms. These were: unwanted or planned pregnancy, being alone or separated, depression or anxiety during pregnancy, experience of abortion, domestic violence. Thus, although epidemiology in psychiatry and health developed somewhat late, we now have the possibility of determining the frequency of mental disorders (descriptive epidemiology) and identifying risk or vulnerability factors (analytical epidemiology). The same applies to perinatal psychiatry (33). It has therefore been possible to apply it in Cameroon to adolescent and adult mothers (1, 35).

In short, we believe that it is important in sub-Saharan and central Africa, and in Cameroon in particular, to know the prevalence of mental disorders and the risk of suicide among teenage mothers. Given that they account for a quarter of adolescent girls in Cameroon, it makes sense to know how widespread these mental disorders are among this population. From a public health planning and surveillance perspective, the prevalence of mental disorders among teenage mothers gives us an idea of the extent of the burden of mental disorders among them (36). The absence of this information in our context (Cameroon) prior to our study proved to be a major shortcoming, given the rate of 66.4%. There are a number of prevention and management solutions available. They involve developing comprehensive, quality reproductive and adolescent health services in schools and health facilities (37).

Limitations and strengths

The first limitation of this study is that the population of teenage mothers was concentrated in an urban area. Teenage mothers living in rural areas and conflict zones in Cameroon were not taken into account. Another weakness is that the latest data collected dates from the end of 2018. In addition, the MINI could also have been used to establish other diagnoses, in addition to that of suicidal risk.

One of the strengths of this research is the method used to recruit teenage mothers, in particular door-to-door canvassing in the community. This approach enabled us to recruit mothers who were unable to visit the health facilities. This seems to us to have contributed to the representativeness of the sample. The large sample of 1633 also seems to us to be a strength.

Conclusion

The prevalence of mental disorders among teenage mothers living in urban areas in Cameroon is 66.4%. The prevalence of suicidal risk is 27.4%. Our hypothesis about the high rate of these phenomena is confirmed. Ultimately, the paucity of research on mental disorders and suicidal risk among adolescent mothers (both quantitative and qualitative), in sub-Saharan, central Africa and Cameroon, constitutes a critical evidence gap. This gap limits evidence-based policy and programmatic responses, as well as national and regional development opportunities, to the negative consequences of perinatal mental disorders. Through this research, we have modestly attempted to contribute to filling these gaps. This research should be multiplied and solutions to combat the mental health problems of teenage mothers developed. And so, a few hypothetical solutions could be proposed, such as monitoring teenagers in schools, more sex education, more sexual information and public health aid centres, psychotherapy for teenagers at school, individual and group psychotherapy for young mothers. And finally, this work suggests future research in Cameroon and Central Africa. It would be interesting to determine the prevalence of disorders among adult mothers in several centres, to contextualise and validate screening and diagnostic tools for perinatal mental disorders, and to identify the most effective treatment approaches for perinatal mental disorders.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by National Ethics Committee for Human Health Research (CNERHH) in Yaoundé. The approval number is: 2014/03/436/L/CNERSH/SP. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

JD: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization. DN: Writing – review & editing, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. BS: Writing – review & editing, Visualization, Project administration, Methodology, Conceptualization. JY: Writing – review & editing, Methodology, Investigation. SV: Writing – review & editing, Visualization, Validation, Methodology, Formal analysis. AM: Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Conceptualization.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The incidence and risk factors of depression across six time points in the perinatal period: a prospective study in China

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Introduction: Perinatal depression (PND) affects approximately 15%–20% of women. This study aimed to determine the incidence of PND and identify risk factors.

Methods: A prospective study was conducted at the Affiliated People's Hospital of Ningbo University. The Edinburgh Postnatal Depression Scale (EPDS) was used to screen for PND. Classification models were constructed using Extreme Gradient Boosting (XGBoost), Logistic Regression (LR), Random Forest (RF), and Support Vector Machine (SVM), and the optimal model was selected.

Results: Between March 2019 and August 2021, a total of 485 participants completed all valid questionnaires. Depression was observed in 75 (15.5%), 47 (9.7%), 25 (5.2%), 94 (19.4%), 85 (17.5%), and 43 (8.9%) cases during the first trimester, the second trimester, the third trimester, 1 week postpartum, 6 months postpartum, and 12 months postpartum, respectively. During the prenatal period, factors such as monthly income, employment status, marital status, and thyroid function significantly impacted depression. Additionally, factors including monthly income, employment status, marital status, parity, and unintended pregnancy were found to affect the likelihood of developing postpartum depression. XGBoost was chosen for its accuracy (0.9097) and precision (0.9005) in predicting prenatal depression, as well as for its accuracy (0.9253) and precision (0.9523) in predicting postpartum depression.

Discussion: In conclusion, the incidence of depression varies throughout the perinatal period, with different factors influencing prenatal and postpartum depression.

KEYWORDS

perinatal depression, incidence, risk factors, six time points, Edinburgh Postnatal Depression Scale

Background

Perinatal depression (PND) encompasses depressive episodes experienced by women during pregnancy and up to 1 year after delivery (1). This clinically relevant disorder affects an estimated 15%–20% of women in China (2). The occurrence of PND varies across different stages of pregnancy. A comprehensive meta-analysis examining depression rates during pregnancy from 21 centers indicated that the incidence of depression in the first trimester ranged from approximately 2.2% to 12.6%, the second trimester exhibited rates between 10.7% and 14.8%, and rates of depression during the third trimester ranged from 7.4% to 12.6% (3). Notably, around 70% of pregnant women experiencing depression reported moderate levels of severity (4).

Maternal depression has been consistently linked to adverse perinatal outcomes. These outcomes encompass an increased likelihood of poor adherence to medical care, compromised nutrition (either insufficient or excessive gestational weight gain), diminished interpersonal and financial resources, as well as heightened risks of smoking and substance abuse and their associated consequences (5, 6). In the postpartum period, persistent depression has been found to impede maternal recovery, impair breast milk production, reduce the intensity of contractions, and increase the risk of postpartum hemorrhage (7).

Women experiencing severe depressive disorder during the perinatal period may exhibit extremely negative thinking patterns and, when subjected to certain triggers, may even develop suicidal tendencies or harm their infants (8). The incidence of suicides resulting from postpartum depressive disorder is alarmingly high in economically underdeveloped countries, reaching up to 20%, while economically developed countries report rates ranging from 5% to 14% (9). This represents a significant cause of maternal mortality worldwide. Furthermore, the effects of maternal depression on newborns include an increased likelihood of preterm birth, low birth weight, higher rates of diarrhea and infectious diseases, and impaired cognitive development (10, 11). Additionally, maternal depression during pregnancy raises the risk of depression in offspring during adulthood, with a risk 4.6 times higher than that in the general population (12). It can also contribute to the development of depression in the spouse (13). Although maternal depression is prevalent and associated with significant social dysfunction, it is only recently that multiple and concurrent risk factors have been identified. Identifying and addressing this issue could potentially reduce the number of suicides among perinatal women experiencing depression, as well as mitigate the adverse effects of untreated maternal depression on the cognitive and behavioral development of their children.

Perinatal depression is a multifaceted condition believed to arise from interactions involving the neuroendocrine hypothalamic-pituitary-adrenal axis, genetics, epigenetics, and environmental and social factors (1). Prior research has identified various risk factors associated with PND. These include race, age, primiparity, unplanned pregnancy, poor physical health, a history of mental illness, low social support within the family, and marital disharmony (14–19). Currently, the diagnosis of PND primarily relies on comprehensive assessments encompassing medical history, psychiatric examination, psychological evaluation, and physical examination, as there are no specific laboratory markers available. Many symptoms of PND lack specificity, such as insomnia, irritability, and self-doubt regarding the adjustment to the role of being a new mother. Consequently, accurately detecting PND can be challenging. Therefore, employing scales and objective indicators to assess the risk of PND, identify influencing factors, and actively intervene to reduce the incidence of PND holds significant importance.

In China, the number of births in 2022 reached 9.56 million. With the recent implementation of the three-child policy, the population of pregnant women is expected to further expand. Consequently, there will likely be a rise in the number of women who are of advanced age and at a higher risk of developing PND, ultimately impacting the incidence of this condition. Thus, the main objective of this study is to determine the incidence of PND and identify its risk factors at various stages of the perinatal period, followed by establishing a model to predict the occurrence of PND.

Materials and methods

Subjects and study setting

The present study was a prospective investigation conducted at the Affiliated People's Hospital of Ningbo University, located in Ningbo, China. The study period spanned from March 2019 to August 2021. Information regarding the study was provided by the attending obstetricians to eligible women with singleton pregnancies who were less than 14 weeks pregnant. Women who expressed interest in participating in the study reached out to the investigators via WeChat or phone, following which an information meeting was arranged. Prior to enrollment, all participants autonomously provided their informed consent by signing the clinical research consent form. The ethical review board of the Affiliated People's Hospital of Ningbo University has granted approval for this study (Approval No. 2017024, Date: 25 July 2017). Based on the research objectives, with an expected incidence rate of 15%, a significance level of 0.05, and a power of 0.80, approximately 196 samples are needed for each of the prenatal and postnatal stages, totaling 392 samples. Considering a 10% loss to follow-up rate, the adjusted minimum sample size is 436.

Characteristics of the participants

The participants in the study attended an initial meeting before reaching gestational week 14, during which they provided various data points, such as age, place of residence, educational background, job, income, and marital status. The inclusion criteria for women participating in this study were as follows: (1) aged 20 years and older, (2) within the first 14 weeks of pregnancy, (3) having a singleton pregnancy, (4) planning to receive prenatal examinations and give birth at the designated research hospital, (5) capable of independently completing the questionnaire, and (6) possessing complete clinical data. The exclusion criteria were as follows: (1) previously diagnosed with a mental illness, (2) this birth resulted in a premature baby, (3) having experienced a stressful incident within the past year, defined as a significant life event that

could affect mental health, such as divorce, loss of a loved one, or serious illness, and (4) refusal to participate in the study.

Procedure

This study identified four common aspects as risk factors for PND, including: (1) sociodemographic factors, such as age, educational background, occupation, place of residence, marital status, and economic status; (2) obstetric factors, such as the number of previous labors, planned pregnancy, gender and health status of the newborns, and pregnancy-related complications; (3) past medical history; and (4) support from social and family members. Apart from the delivery method, postpartum complications, newborn gender, newborn health status, and newborn feeding methods, all other relevant information was obtained during the initial information meeting attended by the participants.

We assessed the participants using the Edinburgh Postnatal Depression Scale (EPDS), which consists of 10 items. Each item is scored on a four-point scale ranging from 0 to 3. Following existing literature, we categorized depression into four types: $\leq$9 as normal, 10–13 as mild depression, 14–20 as moderate depression, and $>$20 as severe depression. The questionnaire survey was conducted at six different time points: during the first trimester (pregnancy $<$ 14 weeks), second trimester (14 weeks $\leq$ pregnancy $<$ 28 weeks), third trimester (pregnancy $\geq$ 28 weeks), 1 week postpartum, 6 months postpartum, and 12 months postpartum.

This study utilized a combination of network and field investigation methods. The questionnaires were assigned unique numbers by the investigators, and all the questionnaire data were thoroughly checked and processed by two researchers. To ensure data quality, a random sampling of 10% of the questionnaire information was independently reviewed by the researchers. The privacy of the participants was strictly safeguarded throughout the entire study.

Statistical analysis

In our analysis of factors related to PND, we took into consideration the distinctions between prenatal and postpartum risk factors. Thus, we categorized our findings into prenatal depression and postpartum depression for a more detailed examination. Prenatal depression was defined as an EPDS score of 10 or higher at any point during pregnancy. Similarly, postpartum depression was characterized by a score of 10 or higher during the postpartum period. All manually processed questionnaires were double-checked for data quality. Firstly, we visually represented the incidence of PND across different demographic groups using bar charts. Subsequently, we constructed classification models using Extreme Gradient Boosting (XGBoost), Logistic Regression (LR), Random Forest (RF), and Support Vector Machine (SVM) to predict the incidence of PND. We compared the accuracy and precision of these models. Accuracy refers to how close a measurement is to the true or actual value. Precision, on the other hand, refers to the consistency or repeatability of measurements.

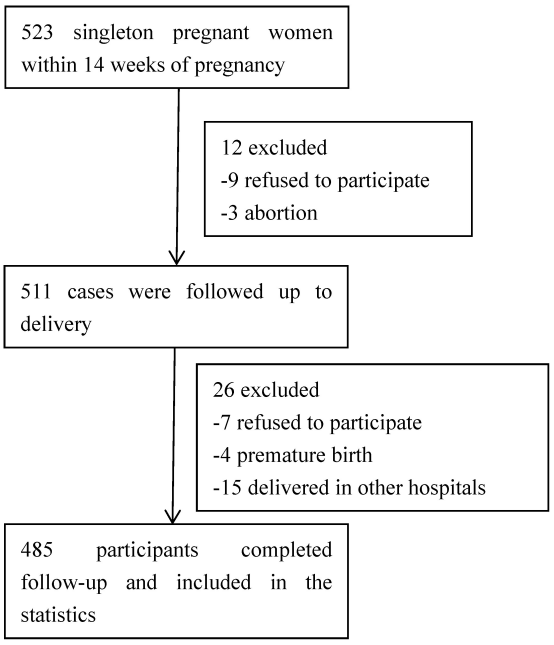

FIGURE 1
Flowchart of participants included in this study.

Considering both accuracy and precision as evaluation metrics, we selected the optimal model for the classification prediction.

Results

Baseline characteristics

A total of 523 pregnant women with singleton pregnancies were initially included in the study. From March 2019 to August 2021, a total of 485 participants successfully completed all valid questionnaires. As illustrated in Figure 1, there were 38 participants who were subsequently excluded from the study. The reasons for exclusion include 16 women who declined to participate, 15 women who delivered in other hospitals, and 7 cases of abortion or premature delivery.

Table 1 provides an overview of the baseline characteristics. The study sample consisted of 485 pregnant women aged between 21 and 47 years, with an average age of 29 $\pm$ 6 years. The majority of participants were under 35 years old (70.52%) and were married (65.57%). A significant proportion had a higher level of education, with 59.80% having achieved a bachelor's degree or above. In terms of residence, 58% reported living in urban or suburban areas. Among all participants, 31.34% identified as housewives, and 50.93% reported a monthly income below 5,000 CNY.

Incidence rate of PND

In the present study, depression was observed in 75 (15.5%), 47 (9.7%), 25 (5.2%), 94 (19.4%), 85 (17.5%), and 43 (8.9%) cases among the total cohort of 485 pregnant women during the first

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TABLE 1 The basic characteristics of the participants and the number of patients with prenatal and postpartum depression.

	N (%)	Prenatal depression *n* (%)*	Postpartum depression *n* (%)*
Age (years)			
<35	342 (70.52)	92 (0.27)	116 (0.34)
≥35	143 (29.48)	33 (0.23)	47 (0.33)
Monthly income (CNY)			
≤5,000	238 (49.07)	74 (0.31)	98 (0.41)
>5,000	247 (50.93)	49 (0.20)	64 (0.26)
Education			
Junior college and below	195 (40.20)	59 (0.30)	64 (0.33)
Bachelor degree	161 (33.20)	32 (0.20)	56 (0.35)
Master degree or above	129 (26.60)	34 (0.26)	43 (0.33)
Employment status			
Housewife	152 (31.34)	64 (0.42)	71 (0.47)
Non-housewife	333 (68.66)	60 (0.18)	93 (0.28)
Place of residence			
Town	282 (58.14)	73 (0.26)	93 (0.33)
Countryside	203 (41.86)	53 (0.26)	69 (0.34)
Marital status			
Unmarried	167 (34.43)	55 (0.33)	68 (0.41)
Married	318 (65.57)	70 (0.22)	95 (0.30)
Cohabitation with spouse			
Yes	249 (51.34)	62 (0.25)	77 (0.31)
No	236 (48.66)	61 (0.26)	85 (0.36)
Parity			
Primipara	205 (42.27)	55 (0.27)	78 (0.38)
Multipara	280 (57.73)	67 (0.24)	87 (0.31)
Planned pregnancy			
Yes	301 (60.06)	75 (0.25)	93 (0.31)
No	184 (37.94)	48 (0.26)	70 (0.38)
Obesity or overweight			
Yes	179 (36.91)	45 (0.25)	57 (0.32)
No	306 (60.09)	80 (0.26)	107 (0.35)
Diabetes			
Yes	152 (31.34)	41 (0.27)	50 (0.33)
No	333 (68.66)	73 (0.22)	117 (0.35)
Thyroid function			
Normal	338 (69.69)	78 (0.23)	122 (0.36)
Dysfunction	147 (30.31)	47 (0.32)	44 (0.30)
Iron deficient anemia			
Yes	75 (15.46)	20 (0.26)	26 (0.34)
No	410 (84.54)	98 (0.24)	131 (0.32)
Mode of delivery			
Spontaneous labor	381 (78.56)	–	133 (0.35)
Cesarean section	104 (21.44)	–	29 (0.28)
Postpartum complications			
Yes	173 (35.67)	–	66 (0.38)
No	312 (64.33)	–	100 (0.32)
Newborn gender			
Boy	275 (56.70)	–	91 (0.33)
Girl	210 (43.30)	–	71 (0.34)
Newborn health status			
Health	359 (74.02)	–	122 (0.34)
Need for medical monitoring	126 (25.98)	–	42 (0.33)
Feeding patterns			
Breast milk	218 (44.95)	–	50 (0.23)
Milk powder	107 (22.06)	–	39 (0.36)
Mixed feeding	160 (32.99)	–	61 (0.38)

n: If diagnosed with depression at any time during first, second, or third trimester, it was classified as prenatal depression; if diagnosed with depression at any time within 1 week, 6 months, or 12 months postpartum, it was classified as postpartum depression. *The proportion of patients with depression within this group.

trimester, second trimester, third trimester, 1 week postpartum, 6 months postpartum, and 12 months postpartum, respectively (Table 2). The incidence rate of prenatal depression in our study was 25.57% (124/485), while the incidence rate of postpartum depression was 33.81% (164/485). Notably, the incidence of depression varied at different time points. The highest proportion of severe depression was observed at 1 week postpartum (20.2%), followed by the first trimester (13.3%). Over the course of the study, the incidence of moderate depression declined gradually, while that of mild depression showed a gradual increase.

Prenatal depression related factors

In the analysis of prenatal depression related factors, we included age, monthly income, education, employment status, place of residence, marital status, cohabitation with spouse, parity, planned pregnancy, obesity or overweight, diabetes, thyroid function, and iron deficient anemia. If diagnosed with depression at any time during the first, second, or third trimester, it was classified as prenatal depression. The number of patients was shown in Table 1. We presented the proportions of individuals with prenatal depression across different demographic groups using a bar chart (Figure 2A). The chart reveals that factors such as monthly income, employment status, marital status, and thyroid function have a significant impact on the likelihood of developing prenatal depression.

TABLE 2 The incidence rate of PND at six different time points.

	Total depression *N* (%)	Mild depression *N* (%)*	Moderate depression *N* (%)*	Severe depression *N* (%)*
First trimester	75 (15.5)	30 (40.0)	35 (46.7)	10 (13.3)
Second trimester	47 (9.7)	24 (51.1)	20 (42.6)	3 (6.4)
Third trimester	25 (5.2)	13 (52.0)	10 (40.0)	2 (8.0)
1 week postpartum	94 (19.4)	44 (46.8)	31 (33.0)	19 (20.2)
6 months postpartum	85 (17.5)	51 (60.0)	27 (31.8)	7 (8.2)
12 months postpartum	43 (8.9)	32 (74.4)	9 (20.9)	2 (4.7)

*The proportion of patients with different levels of depression among all depression patients within this time period.

For construction of the classification models, we employed XGBoost, LR, RF, and SVM. The comparison of accuracy (Figure 2B) and precision (Figure 2C) is depicted in the chart below. Notably, the XGBoost model demonstrated the highest accuracy and precision, with scores of 0.9097 and 0.9005, respectively. Considering both accuracy and precision as evaluation metrics, we selected the XGBoost model for the classification prediction. The visualization of feature weights is displayed in Figure 2D. Among all the factors, employment status exhibited the highest influence on PND, followed by monthly income.

Postpartum PND related factors

During the analysis of postpartum risk factors, we expanded the scope of our investigation compared to the prenatal phase by incorporating additional factors. These include mode of delivery, postpartum complications, infant gender, infant health status, and infant feeding methods. If diagnosed with depression at any time within 1 week, 6 months, or 12 months postpartum, it was classified as postpartum depression. The number of patients was shown in Table 1. To illustrate the distribution of postpartum depression across various demographic groups, we depicted the proportions of individuals affected in each group using a bar chart (Figure 3A). The chart explicitly demonstrates the significant impact that factors such as monthly income, employment status, marital status, parity, and unintended pregnancy have on the likelihood of developing postpartum depression.

We conducted a comparative study of four modeling methods, namely XGBoost, LR, RF, and SVM, and found that the XGBoost model outperformed the others in terms of accuracy (Figure 3B) and precision (Figure 3C). When employing the XGBoost model for our analysis, we discovered that employment status had the most significant impact on postpartum depression, followed by iron deficient anemia, monthly income, parity, obesity, and unintended pregnancy (Figure 3D).

Discussion

Our study yields three key findings. Firstly, we observed variations in the incidence of depression across the six time points of perinatal period. And, the rate of PND is significantly higher postpartum compared to antepartum, reaching its peak in the first week after delivery. Secondly, there are differences in the related factors of prenatal and postpartum depression. Thirdly, work status emerged as a significant determinant in the occurrence of PND throughout the entire perinatal period.

Our study revealed a decline in the incidence of prenatal depression. The incidence rates of depression were approximately 15.5%, 9.7%, and 5.2% during the first, second, and third trimesters, respectively. Furthermore, the incidence of postpartum depression was observed to be 19.4%, 17.5%, and 8.9% at 1 week, 6 months, and 12 months postpartum. This could be attributed to female patients gradually adapting to their current circumstances. Therefore, greater attention should be paid to the mental health status of patients during early pregnancy and the postpartum period. In our study, the incidence rate of postpartum depression was observed to be 33.81%, surpassing the incidence rate of prenatal depression, which was 25.57%. This finding contradicts the research results of Gelaye et al. (20) who conducted a comprehensive analysis of 51 articles on antepartum depression and 53 articles on postpartum depression. They concluded that in low- and middle-income countries, the incidence of antepartum and postpartum depression was estimated at 25.8% (95% CI, 22.8%–29.0%) and 19.7% (95% CI, 16.9%–22.8%) respectively (20). However, it is important to acknowledge that these rates may vary based on geographical and socioeconomic factors.

Our study identified several significant predictors of prenatal depression, including being a housewife, a monthly income less than 5,000 CNY, being unmarried and thyroid dysfunction. Low household income has been identified as an important factor influencing prenatal depression. Previous research has shown that both hypo- and hyperthyroidism can lead to mood disorders, with clinical hypothyroidism being present in 1%–4% of patients with affective disorders (21). It is worth noting that abnormal thyroid function not only increases the risk of depression in the mother during pregnancy but also in their offspring (22). The underlying pathophysiology explaining the emotional and behavioral disorders in patients with hypothyroidism remains uncertain. However, it has been observed that nuclear receptors for triiodothyronine are present in the brain, particularly in regions such as the amygdala and hippocampus, which play a significant role in emotion regulation (22). Therefore, monitoring thyroid function during pregnancy is crucial. Previous study had shown that women with unintended pregnancies had higher odds of experiencing current stress, current depressive symptoms, and initiating prenatal care after the first trimester compared to women with intended pregnancies (23). However, in our research, there was no significant relationship between unintended pregnancies and prenatal depression. Furthermore,

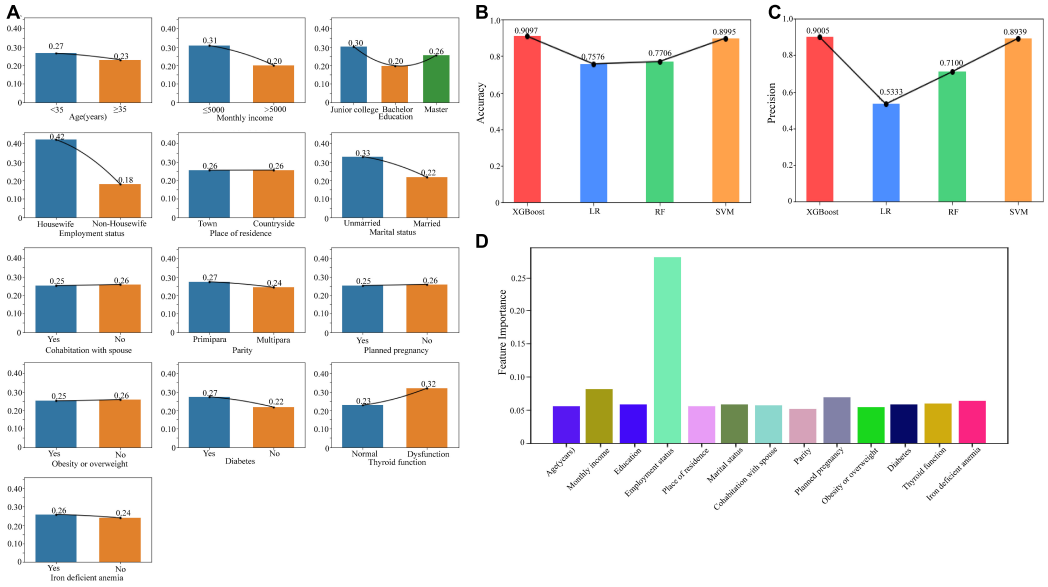

FIGURE 2
Risk factors related to prenatal depression. **(A)** The bar chart showed the proportions of individuals with prenatal depression across different demographic groups. **(B)** The accuracy of the models including XGBoost, LR, RF, and SVM. **(C)** The precision of the models including XGBoost, LR, RF, and SVM. **(D)** The feature weights of each risk factor based on the XGBoost model. XGBoost, Extreme Gradient Boosting; LR, Logistic Regression; RF, Random Forest; SVM, Support Vector Machine.

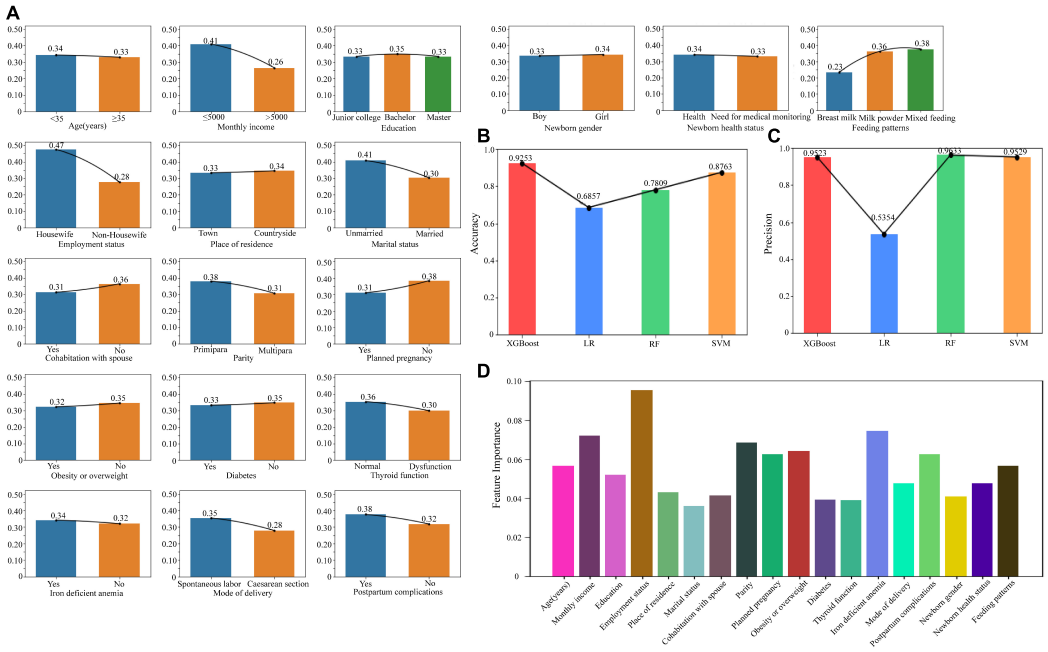

FIGURE 3
Risk factors related to postpartum depression. **(A)** The bar chart showed the proportions of individuals with postpartum depression across different demographic groups. **(B)** The accuracy of the models including XGBoost, LR, RF, and SVM. **(C)** The precision of the models including XGBoost, LR, RF, and SVM. **(D)** The feature weights of each risk factor based on the XGBoost model. XGBoost, Extreme Gradient Boosting; LR, Logistic Regression; RF, Random Forest; SVM, Support Vector Machine.

several studies have reported associations between gestational diabetes mellitus (GDM) and prenatal depression (24–26). Conversely, depression identified in early pregnancy may increase the risk of subsequent GDM development (26). However, in Lara-Cinisomo et al.'s (27) study, no significant association between prenatal depression and diabetes status was found. The same result was observed in our study.

In our study, several factors were found to significantly predict postpartum depression, including housewife status, monthly income less than 5,000 CNY, unmarried status, primipara, and

unintended pregnancy. These findings are consistent with previous research that has identified various risk factors for postpartum depression, such as a history of mental illness, high living burden, poor socioeconomic status, adverse delivery outcomes, and postpartum sleep disturbances (20, 28). Notably, our study also revealed that unintended pregnancy was an important risk factor for postpartum depression, which is supported by Gastaldon et al.'s (29) study indicating a 50% increased risk of postpartum depression in women with unintended pregnancies. However, contrary to expectations, thyroid dysfunction was not found to be statistically significant in predicting postpartum depression, which aligns with the conclusions drawn by Keshavarzi et al. (30). Additionally, Tachibana et al.'s (19) study highlighted that antenatal risk factors, including "a perceived lack of family cohesion," being a primipara, and receiving treatment for physical or psychiatric illness during pregnancy, could be utilized as indicators for predicting postpartum depression at 20 weeks. Furthermore, clinical studies have demonstrated that experiencing perinatal pain is associated with an increased risk of postpartum depression, while the use of epidural analgesia can potentially reduce this risk (31). Regrettably, these aspects were not included in our study.

In our study, being a housewife emerged as a significant factor influencing depression throughout the entire perinatal period. Across all six time points, the incidence of depression among housewives consistently exceeded that of non-housewives. This finding might be attributed to the demanding responsibilities of childcare that housewives undertake after childbirth. However, in another study by Tachibana et al. (19), "leaving or losing one's job" was identified as a marginally significant predictor of postnatal depression among Japanese women. This discrepancy could potentially be attributed to differences in social contexts. In China, being a housewife often signifies long-term unemployment, lack of financial resources, limited social support, and lower family status.

In summary, each period of the perinatal period is associated with specific risk factors for depression. It is crucial to focus on different high-risk factors based on the patient's gestational week and postpartum period to timely identify postnatal depression. This highlights the significance of our research.

However, our study has several limitations. Firstly, as mentioned earlier, we selected all eligible pregnant women from a single hospital, which may not fully represent the current situation in Ningbo, Zhejiang province, China. Additionally, we did not include various factors such as twins, premature infants, perinatal pain, laboratory examinations, and genetic factors. Women with a history of mental health problems are also a major limitation that compromises the generalization of the results. Previous research has confirmed that perinatal genes play a role as risk factors for postpartum depression (31). For example, one study identified DNA methylation in antenatal TTC9B and HP1BP3 genes, which can predict with 80% accuracy whether a woman will develop depression in the postpartum period (32, 33). Therefore, future research should encompass a comprehensive exploration of the risk factors of depression, incorporating symptoms, signs, laboratory tests, and relevant biological markers. Specifically, studies should aim to integrate genetic data, clinical information, and environmental factors to construct a more holistic understanding of the etiology of postpartum depression. By adopting a multi-faceted approach, future research has the potential to identify more accurate predictors of depression and develop targeted interventions to improve the mental health of mothers during the perinatal period.

Conclusion

In summary, depression incidence varies across the perinatal period, with distinct factors affecting prenatal and postpartum depression. Employment status significantly influences PND rates. Our XGBoost model effectively predicts PND, offering a valuable tool for early detection and targeted intervention.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the corresponding author, without undue reservation.

Ethics statement

The studies involving humans were approved by The People's Hospital Affiliated to Ningbo University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

JuZ: Data curation, Investigation, Writing – original draft. YY: Resources, Investigation, Writing – original draft. XL: Software, Validation, Writing – original draft. YC: Data curation, Investigation, Writing – original draft. LC: Data curation, Investigation, Writing – original draft. YL: Resources, Investigation, Writing – original draft. QW: Project administration, Writing – review & editing. JiZ: Resources, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Postpartum depression and autoimmune disease: a bidirectional Mendelian randomization study

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Purpose: The rising prevalence of postpartum depression (PPD) is harmful to women and families. While there is a growing body of evidence suggesting an association between PPD and autoimmune diseases (ADs), the direction of causality remains uncertain. Therefore, Mendelian randomization (MR) study was employed to investigate the potential causal relationship between the two.

Methods: This study utilized large-scale genome-wide association study genetic pooled data from two major databases: the IEU OpenGWAS project and the FinnGen databases. The causal analysis methods used inverse variance weighting (IVW). The weighted median, MR-Egger method, MR-PRESSO test, and the leave-one-out sensitivity test have been used to examine the results' robustness, heterogeneity, and horizontal pleiotropy.

Results: A total of 23 ADs were investigated in this study. In the IVW model, the MR study showed that PPD increased the risk of type 1 diabetes (OR , = 1.15 (1.05–1.26),p<0.01),Hashimoto's thyroiditis((OR) = 1.21 (1.09–1.34),p<0.0001), encephalitis((OR) = 1.66 (1.06–2.60),p<0.05). Reverse analysis showed that ADs could not genetically PPD. There was no significant heterogeneity or horizontal pleiotropy bias in this result.

Conclusion: Our study suggests that PPD is a risk factor for type 1 diabetes, Hashimoto's thyroiditis, and encephalitis from a gene perspective, while ADs are not a risk factor for PPD. This finding may provide new insights into prevention and intervention strategies for ADs according to PPD patients.

KEYWORDS

postpartum depression, autoimmune disease, Mendelian randomization, genetic cause, etiology

1 Introduction

Postpartum depression (PPD), a prevalent major depressive following childbirth, affects 17.22% women worldwide with a higher prevalence in developing countries compared to developed countries (1). PPD is characterized by symptoms such as depression, emotional instability, feelings of guilt, loss of appetite, low self-esteem, and sleep disturbances, along with a 20% increase in suicidal ideation (2–4). Not only does PPD affect the women themselves, but may also increase the risk of depression in partners and mental retardation in children, increasing the economic burden on families (5–7). Life circumstances (8), social and psychological stress (9), postpartum grief (10), prenatal depression (11), lifestyle (12), vaginal delivery (13), hormonal changes (14), and marital or partner dissatisfaction (11) have been shown to be the common risk factors for PPD. Notably, the correlation between autoimmune diseases (ADs) and PPD has been underexplored in existing studies.

Recent research has highlighted the complex interplay between ADs and PPD. ADs are disease states caused by an immune response of the body's immune system against its own components due to the fact that it is impossible to distinguish between self and non-self (15). A recent nationwide sibling comparison study demonstrated a bidirectional association between PPD and ADs (16). Although several observational studies have shown that women with ADs are at higher risk for postpartum depression, studies on MS are conflicting (17–21). Notably, preliminary evidence suggests a potential risk of subsequent ADs development in individuals with PPD (22, 23). Despite these insights, the genetic underpinnings of the relationship between PPD and ADs remain poorly understood, with a gap in research elucidating this aspect.

The objective of this study was to examine the causal relationship between PPD and autoimmune diseases (ADs) using bi-directional Mendelian randomization (MR) analysis. MR is a robust method that utilizes genetic variation as instrumental variables to establish causal relationships between risk factors and diseases (24). This method can play a critical role in addressing issues related to confounding factors and reverse causality in observational studies (25). Bi-directional MR analysis can effectively investigate the impact of ADs on the risk of postpartum depression (PPD), as well as the risk of ADs following PPD.

2 Methods

2.1 Study overview

In this study, we investigated the causal relationship between ADs and PPD using a bi-directional Mendelian randomization (MR) approach. We selected 23 subtypes of autoimmune disease diagnoses and obtained their Genome-Wide Association Study (GWAS) summary statistics data from publicly accessible databases. The initial research received ethical approval and informed consent. The study's flow chart is depicted in Figure 1.

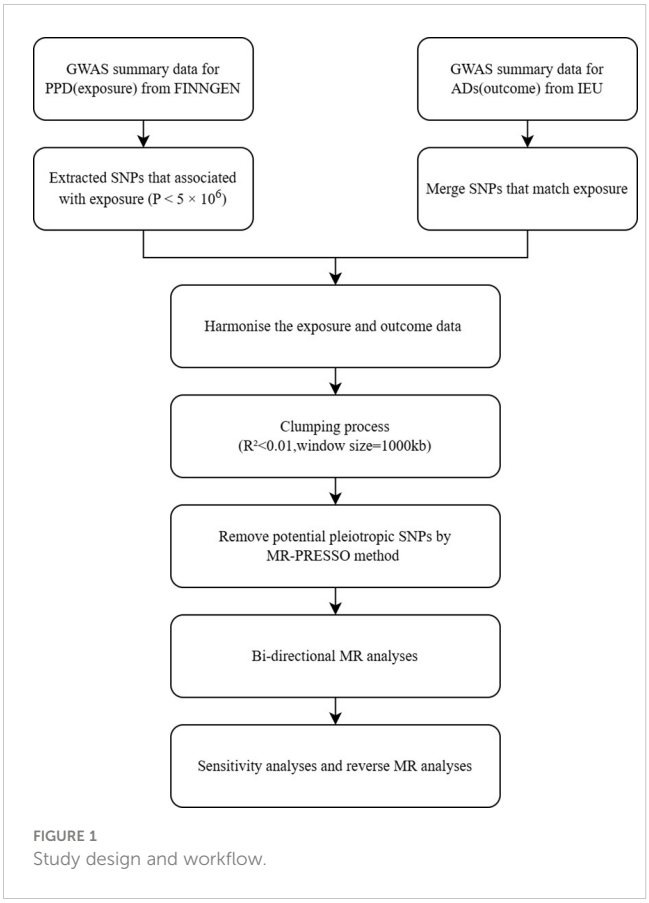

FIGURE 1
Study design and workflow.

2.2 Data sources

Genome-wide association study (GWASs) summary statistics data for PPD from FinnGen R8, survey of 14,116 European women (prevalence 7.11%, mean age 41.03 years) (26). The diagnostic criteria for PPD are delivery status and International Classification of Diseases, Tenth Edition (ICD-10) codes F32, F33 and F53.0.

GWAS data for ADS were obtained from the IEU Open GWAS project (https://gwas.mrcieu.ac.uk/), which includes data from the UK Biobank (27), FINNGEN (26), and the International Multiple Sclerosis Genetics Consortium (28). The study includes the following ADs: Type 1 diabetes (29), Graves' disease (30), Hashimoto thyroiditis (30), Rheumatoid arthritis (30), Ankylosing spondylitis (26), Giant cell arteritis with polymyalgia rheumatica (26), Polyarteritis nodosa and related conditions (26), Allergic purpura (26), Behcet's disease (30), and Systemic lupus erythematosus (30), Psoriasis vulgaris (30), vitiligo (26), alopecia areata (26), idiopathic thrombocytopenic purpura (30), multiple sclerosis (28), myasthenia gravis (31), encephalitis (26), Guillain-Barre syndrome (26), ulcerative colitis (26), Crohn's disease (32), coeliac disease (26), IgA nephropathy (30), and sarcoidosis (30). Detailed information on the ADs data is in Supplementary Table 1.

2.3 Instrumental variable selection

In magnetic resonance analyses of PPDs with ADs, the following three conditions were employed in order to select the optimal instrumental variable (IV) in order to ensure that the results were true and accurate: (I) the IV was closely related to PPDs, (II) the IV was not related to confounders and (III) the IV was not related to ADs (33). We selected SNPs that were significantly associated with PPD as IVs,

choosing only those that were smaller than the genome-wide statistical significance threshold (5×10^{-6}). To ensure independence between IVs, SNPs with linkage disequilibrium were filtered using a clump window of 10,000 kb and r2 > 0.001. F-statistics were calculated for all independent variables (IV) to ensure that the F-statistics for the SNPs used in the analyses were all greater than 10. SNPs significantly associated with the results ($p < 10^{-8}$) were also excluded. To prevent any distortion of strand orientation or allele coding, we removed palindromic SNPs (e.g. A/T or G/C alleles).

2.4 MR analysis

The inverse-variance weighted (IVW) MR method was applied as the primary method to identify potential associations between ADs and PPD (24). To evaluate the stability of the IVW results, we also used MR-PRESSO weighted median, heterogeneity test, MR-Egger regression heterogeneity test, Cochrane's Q test, and weighted median (34, 35). The Cochrane Q test was used to assess the heterogeneity of the SNPs, and heterogeneity was present if P < 0.05 (36). Directed pleiotropy of genetic tools was tested using MR-Egger regression (37). To exclude SNPs whose abnormalities would affect our results, we also performed a leave-one-out sensitivity test (36). By analyzing the same trends in IVW and weighted median and MR-Egger analyses, the relationship between exposure and outcome was confirmed.

Analysis was performed using R 4.3.2 and the TwoSampleMR package.

3 Results

3.1 IVs selection

After rigorous screening, a total of 28 SNPs strongly associated with PPD ($p<10^{-6}$) were used in this study. Detailed snps information can be found in Supplementary Table 2.

3.2 MR analysis of PPD for ADs

MR analysis revealed that PPD had a significant causal relationship($p<0.05$) with three out of the 23 autoimmune diseases. Women who suffer from PPD are at a higher risk of developing type 1 diabetes (odds ratio (OR) = 1.15 (1.05–1.26), $p<0.01$), Hashimoto's thyroiditis [(OR) = 1.21 (1.09–1.34], $p<0.0001$), and encephalitis [(OR) = 1.66 (1.06–2.60),$p<0.05$] (Figure 2). No significant causal association was found between PPD and the other 20 subtypes of ADs. Complete results are available in Supplementary Table 3.

3.3 Sensitivity analysis of MR

The scatterplot shows that MR-Egger, weighted median, weighted mode, and simple mode results all follow the same trend as IVW:A for Hashimoto's thyroiditis, B for type 1 diabetes, C for encephalitis (Figure 3). The test for heterogeneity was conducted using Cochrane's Q-statistics, and no heterogeneity ($p>0.05$) was found for any of the three outcomes (Table 1). Tests of pleiotropy indicated no horizontal pleiotropy for type 1 diabetes (p=0.84), Hashimoto's thyroiditis (p=0.13), and encephalitis (p=0.33).

4 Discussion

In this study we further validated the causal relationship between PPD and ADs using MR in a European population. Our findings provide robust support for the involvement of PPD in the risk of Type 1 diabetes, Hashimoto's thyroiditis, and Encephalitis. Sensitivity analyses also confirmed the reliability of our results, indicating that MR analyses of PPD are trustworthy. However, no association was observed between PPD and the remaining 20 ADs ($p>0.05$).

The association between PPDs and ADs is a topic of complexity and controversy. An observational study in Sweden

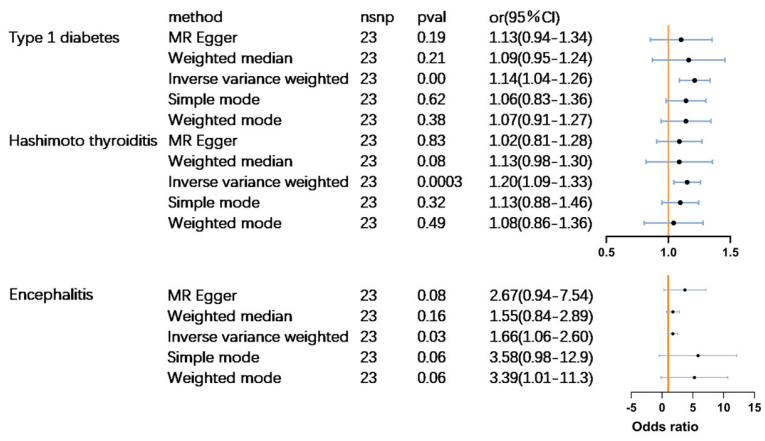

FIGURE 2
Main Mendelian randomisation results and forest plots.

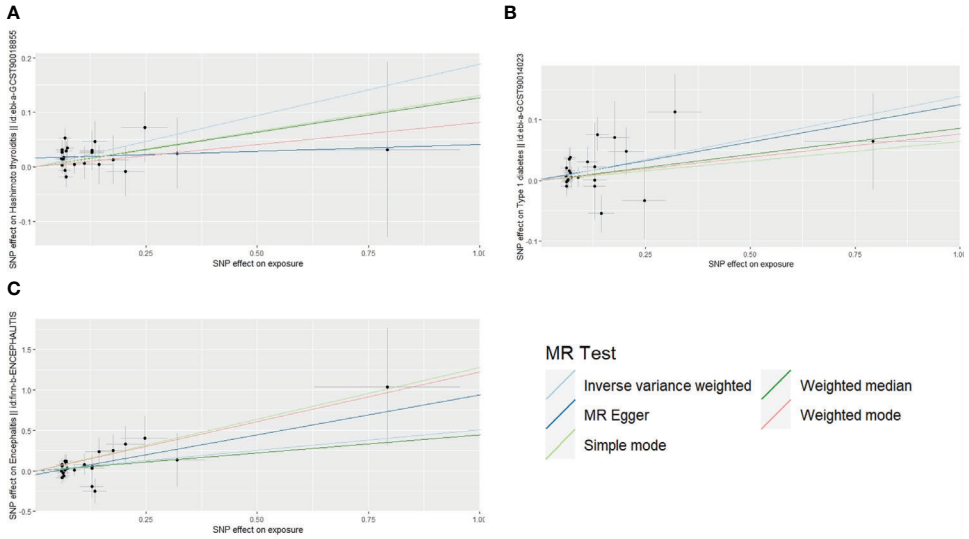

FIGURE 3
Scatterplot of main results.

found a bidirectional association between certain ADs (such as autoimmune thyroid disease, psoriasis, multiple sclerosis, ulcerative colitis, and celiac disease) and perinatal depression among unaffected sisters, independent of psychiatric comorbidity (16). However, previous studies have produced conflicting results (21, 38–41). Additionally, various studies have shown that inflammatory bowel disease, rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, and psoriasis can increase the risk of PPD (18–20, 22, 40). However, the focus of most previous studies has been on investigating the risk of PPD following ADs, with limited research on the risk of subsequent ADs associated with PPD. A survey from Canada indicated that women with perinatal psychiatric disorders were at a higher risk of developing ADs, though not significantly different from women with non-perinatal psychiatric disorders (17). These findings were mainly based on observational studies that were unable to consider all potential mediators influencing the results, leading to controversies. Factors such as small sample sizes, confounding variables, reverse causation, and differences in study designs may contribute to the inconsistencies in the literature.

TABLE 1 Heterogeneity testing using the Cochrane Q statistic.

outcome	method	Q	Q df	Q pval
Type 1 diabetes	MR Egger	23.43	21	0.32
	Inverse variance weighted	23.48	22	0.37
Hashimoto thyroiditis	MR Egger	15.20	21	0.81
	Inverse variance weighted	17.69	22	0.72
Encephalitis	MR Egger	20.11	21	0.51
	Inverse variance weighted	21.11	22	0.51

In this study, evidence was found suggesting a potential association between Postpartum Depression (PPD) and Type 1 diabetes, Hashimoto's thyroiditis, and Encephalitis. Type 1 diabetes is a chronic autoimmune disease typically occurring in childhood, although the American Diabetes Association (ADA) has classified latent autoimmune diabetes in adults as T1DM as well (42, 43). This form of diabetes is thought to stem from a combination of genetic and environmental factors, presenting as heterogeneous at different stages (44). The progression of the disease may be exacerbated by psychological factors and obesity, leading to pancreatic beta cell exhaustion and autoimmune destruction (45). Moreover, latent autoimmune diabetes in adults and PPD are commonly linked to obesity, physical inactivity, and lifestyle factors (46, 47). Physiologically, PPD may be associated with type 1 diabetes through thalamic damage and HbA1c levels, indicating a potential pathway connecting the two conditions (48–50).

Hashimoto's thyroiditis, an autoimmune thyroid disorder, is predominantly observed in women and results from a blend of genetic and environmental factors (51). Hormonal fluctuations during the perinatal phase and heightened stress in the postpartum period are believed to heighten the vulnerability of women with postpartum depression (PPD) to developing Hashimoto's thyroiditis (52, 53). The occurrence of pregnancy leads to notable modifications in thyroid function, with variations in hormone levels such as human chorionic gonadotropin, estrogen, and progesterone being associated with the initiation and progression of Hashimoto's thyroiditis (22, 52). It is crucial to closely monitor thyroxine levels in women with PPD to forestall autoimmune thyroid disease. Research findings suggest that individuals with chronic mental disorders have a low likelihood of acquiring autoimmune encephalitis (54). There is a proposition

that individuals enduring postpartum psychosis may exhibit higher susceptibility to encephalitis (55). Our study's outcomes reveal that postpartum depression is linked to an elevated risk of encephalitis, as indicated by a higher odds ratio (OR=1.6). Our results suggest that patients with PPD have an increased risk of type 1 diabetes, Hashimoto's thyroiditis, and encephalitis associated with their genetic susceptibility.

The use of genetic variation consistent with Mendel's law of random assignment as an instrumental variable allows for the exclusion of confounding factors in MR analysis (24). This method addresses the issue of reduced confidence in previous observational studies on the relationship between PPD and ADs, which was attributed to the presence of confounding factors and reverse causality that were difficult to avoid. Furthermore, since these single nucleotide polymorphisms (SNPs) are strongly associated with disease and exist before the onset of disease, reverse causation is no longer a concern (56). The GWAS summary data selected for this study were derived from research with large sample sizes, enhancing the reliability of the results.

Several limitations need to be considered in our study. Firstly, the analysis was confined to GWAS studies conducted in Europe, thus it would be advantageous to incorporate data from other regions. Moreover, the study population consisted solely of females; however, it is worth mentioning that most studies utilizing GWAS data for autoimmune diseases did not differentiate between genders.

This is the first study to employ MR to investigate the potential causal relationship between ADs and PPD. The findings indicate that PPD is associated with an increased risk of developing Type 1 diabetes, Hashimoto's thyroiditis, and Encephalitis. Further experimental and mechanistic studies are required to validate the results obtained.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding authors.

Author contributions

WY: Writing – original draft, Writing – review & editing, Data curation, Methodology, Project administration. BS: Data curation, Formal analysis, Project administration, Writing – original draft, Writing – review & editing. CW: Conceptualization, Methodology, Supervision, Validation, Writing – review & editing. QX: Investigation, Software, Supervision, Writing – review & editing. YS: Data curation, Investigation, Project administration, Software, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2024.1425623/full#supplementary-material

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TYPE Systematic Review
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The effects of exercise on antenatal depression: a systematic review and meta-analysis

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Objective: The aim of this study was to conduct a systematic evaluation of exercise interventions' effectiveness on antenatal depressive symptoms in pregnant women and to investigate the impact of different intervention factors on the relationship between exercise and antenatal depressive symptoms.

Methods: We conducted comprehensive searches in several databases, including PubMed, Embase, Web of Science, Cochrane Library, and others. The search period covered from database inception to May 2023. After thorough screening, a total of 7 papers with 524 subjects were included in the analysis.

Results: The meta-analysis revealed that the overall effect size of exercise intervention on antenatal depressive symptoms in pregnant women was SMD = -0.41, with a 95% confidence interval of [-0.78, -0.05], and P = 0.03, indicating a significant improvement in depressive symptoms due to exercise intervention during the antenatal period. However, some degree of heterogeneity was observed among the studies, with I^2 = 74%, P = 0.0007.

Conclusion: The results indicate that exercise interventions significantly contribute to the improvement of antenatal depressive symptoms in pregnant women, as inferred from the combined findings of the studies. Notably, static exercise intervention showed better results than dynamic exercise intervention. Moreover, interventions conducted before 20 weeks' gestation had superior outcomes compared to those conducted after 20 weeks' gestation, and interventions lasting longer than the trimester duration exhibited more favorable effects than shorter interventions. However, to validate these findings and optimise exercise intervention protocols for better antenatal maternal depressive symptom management, larger sample sizes and more comprehensive studies are required, given the observed heterogeneity and potential limitations in the present study.

Systematic review registration: https://www.crd.york.ac.uk/prospero/ PROSPERO, identifier (CRD42023422315).

KEYWORDS

depression, antenatal, exercise, systematic review, meta-analysis

1 Background

The antenatal period marks a pivotal phase in a woman's life, profoundly influencing her physical and mental well-being, and consequently impacting the trajectory of her child's life. Nevertheless, approximately 20 per cent of women globally experience depression during this critical period of pregnancy (WHO 2017). The symptoms of antenatal depression share similarities with general depression, but it is distinct from postpartum depression. Antenatal depression exerts detrimental effects on both the maternal health and the developing foetus, heightening the risks of preterm birth and low birth weight. Symptoms of antenatal depression encompass a spectrum that includes mood swings, anxiety, sleep disturbances, and cognitive impairments, alongside negative perceptions of pregnancy. Notably, individuals may also suffer from persistent fatigue and bodily pain, coupled with diminished emotional attachment to their unborn child. These manifestations underscore the distinct clinical profile of antenatal depression, highlighting its complex interplay with both psychological and physical health parameters (1). Additionally, it may exert enduring impacts on the child's behavioral and cognitive development (2, 3).

Numerous investigations have explored various antenatal interventions for depressed pregnant women, including antidepressants, psychotherapy, complementary and alternative medicine (CAM), and physical activity (4, 5). Antidepressant medications, encompassing selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCA), and serotonin-norepinephrine reuptake inhibitors (SNRIs), have demonstrated their efficacy in alleviating depressive symptoms and ameliorating the psychological well-being of antenatal depression patients. However, concerns have arisen regarding the potential risks to foetal development and birth defects associated with regular antidepressant use during pregnancy, prompting some women to discontinue treatment (6). Furthermore, individual differences may result in adverse effects such as dizziness, nausea, and insomnia in certain pregnant women taking antidepressants (7).

Psychotherapy, acknowledged for providing emotional support to individuals with antenatal depression, fostering feelings of empathy and care, has emerged as a viable option. Psychotherapy represents a pivotal treatment modality for antenatal depression, serving to bolster emotional support while fostering empathy and nurturing care. Various psychotherapeutic approaches, including cognitive behavioural therapy (CBT), interpersonal therapy (IPT), and psychodynamic therapy, have been rigorously evaluated and applied in this context. CBT targets maladaptive cognitive processes and behaviours, aiming to enhance mood regulation and resilience (8). IPT, on the other hand, concentrates on enhancing interpersonal relations and bolstering social support networks to address and ameliorate relational conflicts (9). Psychodynamic therapy delves into the deeper realms of the unconscious mind and the echoes of early developmental experiences, seeking to uncover and resolve the underlying psychological roots of distress (10). Each of these therapies offers distinct mechanisms through which the complex emotional challenges of antenatal depression can be addressed, reflecting the multifaceted nature of this condition. Nonetheless, its time and cost implications can hinder access to treatment for many pregnant women (11). Additionally, studies investigating the effectiveness of elements such as probiotics, vitamins, and minerals for antenatal depression in pregnant women are currently lacking sufficient scientific evidence to substantiate their efficacy and safety (12).

Exercise is increasingly recognised as a viable non-pharmacological therapy, augmenting traditional psychotherapy and pharmacotherapy in managing prenatal depression. The simplicity and accessibility of physical activity, coupled with its broad spectrum of benefits to both physical and mental health, underscore its importance. Empirical evidence reveals that regular exercise substantially elevates beta-endorphin levels within the body. This naturally occurring peptide not only mitigates pain but also enhances positive emotions by mimicking opioid effects. The mental health benefits of exercise are mediated through several key physiological mechanisms. Notably, physical activity boosts the production of neurotrophic factors such as brain-derived neurotrophic factor (BDNF), which plays a crucial role in neuronal growth, development, and repair, thereby enhancing overall brain functionality and cognitive control. Additionally, exercise stimulates the release of pivotal neurotransmitters, including serotonin, dopamine, and norepinephrine, which are integral to mood regulation and emotional stability (13). From a psychological standpoint, engaging in physical exercise fosters an individual's sense of control and agency, attributes reinforced through the achievement of measurable fitness goals and enhanced physical self-efficacy (14). Group exercise sessions also provide valuable social interaction, reducing feelings of isolation and strengthening interpersonal connections, which are essential for mitigating prenatal depression. Moreover, mindfulness-based physical practices such as yoga and tai chi not only involve physical exertion but also incorporate meditation and mindfulness exercises. These activities enhance present-moment awareness and emotional regulation capabilities, which are crucial for managing symptoms of antenatal depression (15). Thus, exercise emerges as a multifaceted therapy with profound implications for both preventing and alleviating prenatal depression.

In the domain of antenatal care, meticulously designed exercise interventions, customised to suit the unique characteristics and physical conditions of each expectant mother, are increasingly recognised for their potential to enhance maternal health during pregnancy. The selection of appropriate exercise modalities—such as aerobics, yoga, and Pilates—and the maintenance of moderate intensity are critical to ensuring both safety and effectiveness. Moreover, continuous engagement with healthcare providers is essential to ascertain the safety and efficacy of these exercise programs. These measures not only contribute to the alleviation of symptoms associated with antenatal depression but also hold promise for the prevention of postnatal depression, underscoring their significant role in comprehensive prenatal health strategies (16).

The reverberating benefits extend even further. The amelioration of postpartum depressive symptoms not only contributes to improved infant growth, development, and behaviour but also holds the potential for enduring positive

effects (17). Consequently, by addressing mood disruptions, including anxiety, sleep disturbances, and appetite fluctuations, judicious exercise emerges as a practical, non-pharmacological avenue devoid of side effects in the prevention and treatment of maternal depression.

Numerous systematic reviews have focused on exercise interventions as a valuable means of postpartum depression recovery (18–20). However, limited attention has been given to investigating the relationship between exercise and antenatal depression. Although some studies suggest the potential efficacy of exercise in addressing depression during pregnancy, their conclusions are drawn from a restricted number of trials, which exhibit considerable heterogeneity and wide confidence intervals (21–24). Additionally, these findings are predicated on a limited pool of low- and moderate-quality trials, further contributing to the heterogeneity in sample size, experimental design, and intervention approaches (21, 23).

Current reviews predominantly center their attention on dissecting the causal disparities in the impacts of antenatal versus postnatal exercise on postpartum depression, delving into the underlying rationales found within the original literature. However, they tend to provide scant specific discourse regarding the formulation of exercise regimens. Likewise, extant meta-analyses primarily fixate on assessing the quantifiable extent of exercise interventions on maternal depression, gauging the effect size. Regrettably, these endeavours often overlook pivotal moderating variables' determination, encompassing the nature and intensity of exercises, along with their nexus to maternal depression within the context of exercise programs (20).

Conspicuously absent in the literature is an exploration of the interplay between the constituents, intensity, and other pivotal variables underpinning exercise interventions and their nexus with maternal depression. This dearth of research has resulted in a conspicuous deficiency in practical guidance and recommendations pertinent to the construction of daily exercise intervention programs tailored for maternal depression. It is worth underscoring that the crux of enhancing the efficacy of exercise intervention for maternal depression hinges on the judicious selection of exercise type, intensity, duration, and frequency. These determinants hold sway over both the effectiveness of exercise and the safety of expectant mothers.

Regrettably, there is a paucity of international exercise guidelines tailored explicitly for maternal depression. The profound divergence in individuals' physical capacities and health statuses underscores the paramount importance of discerning the optimal exercise modality for each individual, thereby ensuring the safe engagement of pregnant women devoid of undue physical strain.

Moreover, it is imperative to factor in the multitude of physiological and metabolic transformations that transpire within a pregnant woman's body during gestation. These encompass shifts within the cardiovascular system, hormonal profiles, body weight, and center of gravity. Therefore, the selection of exercise modality must adroitly navigate these changes to safeguard the comfort and well-being of pregnant women.

The timing of exercise assumes critical significance in the prevention of antenatal depression (25). Ideally, commencing exercise prior to conception proves most advantageous, affording the opportunity to cultivate a robust state of physical and mental well-being. However, even in cases where exercise commences during pregnancy, it is incumbent upon expectant mothers to seek professional counsel and supervision from a healthcare provider. Additionally, vigilance must be exercised with regard to the duration and frequency of exercise, as pregnant women possess distinct characteristics warranting prudent consideration. Excessive or frequent exercise can precipitate fatigue, physical discomfort, and potentially elevate the risk of injury. Hence, exercise regimens should be characterised by a gradual, progressive approach, permitting expectant mothers to incrementally acclimatise and amplify both the duration and intensity of their exercise routines. It merits acknowledgment that different modes of physical activity exert distinct effects on the body and mind (26). Static exercises, for instance, may prove beneficial in fostering relaxation and enhancing posture, while dynamic exercises may be more instrumental in fortifying cardiorespiratory function and metabolism. By juxtaposing these two modalities, it becomes conceivable to delineate which type of exercise aligns more harmoniously with the prevention and treatment of antenatal depression, tailored to individual proclivities and requisites.

To date, a comprehensive assessment of the overall effects of exercise in alleviating antenatal depression remains lacking, as there is a scarcity of systematic reviews and meta-analyses encompassing all pertinent studies. Therefore, the need arises to synthesise existing research to comprehensively evaluate the potential effectiveness of exercise in mitigating antenatal depression. Such an analysis holds the promise of providing novel insights and methodologies to enhance maternal mental health during this critical period.

2 Methods

This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement (27) and the Cochrane Collaboration Handbook. The protocol was registered on PROSPERO (CRD42023422315).

2.1 Data sources and searches

The systematic search was conducted by two independent reviewers (ZZ and LJY) in four databases: the Cochrane Library, Embase, PubMed and Web of Science, and was designed to retrieve articles up to May 2023, with disagreements resolved by consensus and by a third reviewer (SL) in case of disagreement. Terms from the Medical Subject Headings (MeSH) and words from the text were used as follows: ("Pregnant" OR "antenatal" OR "ante-natal" OR "ante-partum" OR "prenatal" OR "pre-natal" OR "prepartum" OR "pre-partum" OR "mother" OR "maternal" OR "perinatal" OR "peri-natal" OR "peripartum" OR "peri-partum") AND ("Depression" OR "Depressive Symptoms" OR "Depressive

Symptom" OR "Symptom, Depressive" OR "Emotional Depression" OR "Depression, Emotional") AND ("Exercise" OR "Exercises" OR "Physical Activity" OR "Activities, Physical" OR "Activity, Physical" OR "Physical Activities" OR "Exercise, Physical" OR "Exercises, Physical" OR "Physical Exercise" OR "Physical Exercises" OR "Acute Exercise" OR "Acute Exercises" OR "Exercise, Acute" OR "Exercises, Acute" OR "Exercise, Isometric" OR "Exercises, Isometric" OR "Isometric Exercises" OR "Isometric Exercise" OR "Exercise, Aerobic" OR "Aerobic Exercise" OR "Aerobic Exercises" OR "Exercises, Aerobic" OR "Exercise Training" OR "Exercise Trainings" OR "Training, Exercise" OR "Trainings, Exercise"), Specific details of the search algorithms for each database are provided in Supplementary Material 1.

2.2 Inclusion and exclusion

The study's inclusion criteria were meticulously determined based on the PICOS principles, a rigorous evaluation framework used in Cochrane systematic appraisals. Participants (P) Healthy pregnant women with no contraindications to exercise or other major medical conditions (I) multifactorial exercise interventions with different content, intensity, duration, frequency and periodicity (28) (C), routine care or other standard antenatal activities were taken into account. The primary subject of observation (O) centred around antenatal depression, with the main indicators of depression outcomes derived from various depression rating scales. The study design (S) predominantly focused on randomised controlled trials (RCTs), which are widely recognised as the gold standard for clinical effectiveness research, ensuring a robust and reliable foundation for analysis. To maintain the study's precision and rigor, specific literature exclusion criteria were employed. Pregnant women with depression arising from other medical conditions were excluded, as were those with alcohol and cigarette abuse. Additionally, comprehensive interventions were not considered, and studies lacking complete data or not published in English were excluded. Non-RCT studies were also not included in the analysis, further ensuring the study's consistency and validity.

2.3 Assessment of risks of bias

Two reviewers (ZZ and LJY) independently conducted risk of bias assessments for the included studies, adhering to the Cochrane Collaboration guidelines. This widely accepted and comprehensive tool allowed us to evaluate the methodological quality of each eligible study in a standardised manner. The Cochrane Collaboration network provides a detailed description of risk assessment for each item, with specific criteria classified as low, high, or unclear risk.

The following key areas were evaluated to assess the risk of bias for each study: randomisation, allocation concealment, blinding of participants and researchers, incomplete outcome data, selective reporting, and other biases. Due to ethical reasons, blinding of participants can often be challenging. Each study was independently assessed by two reviewers (ZZ and LJY), and any discrepancies were resolved through discussion or consultation with a third reviewer (SL) if necessary.

The results of the risk of bias assessment, providing a transparent and comprehensive overview of the methodological quality of each included study, are summarised in Supplementary Material 2 in a risk of bias table. When interpreting the results of the META analyses and drawing conclusions about the effectiveness of preconception exercise interventions in reducing the risk of antenatal depression, we carefully considered the outcomes of this assessment.

By adhering to the Cochrane Collaboration guidelines and employing a rigorous risk of bias assessment process, we ensured the reliability and validity of our meta-analysis. This robust evaluation of each study's methodological quality further enhances the credibility and significance of our study's findings and conclusions.

2.4 Data extraction

With a standardised form, two reviewers (ZZ and LJY) independently extracted the pertinent data from each included study, encompassing essential details such as author names, year of publication, gestational weeks, sample size of the intervention and control groups, age group characteristics of both intervention and control groups, type of intervention, intervention length, frequency, and duration, type of control group, and outcome measures.

The utilisation of a standardised form ensured consistency and accuracy in data extraction across all studies, minimising the risk of errors and enhancing the reliability of the collected information. Each reviewer diligently recorded the required data elements from the eligible studies, and any discrepancies or uncertainties were resolved through discussion or consultation with a third reviewer (SL) if necessary.

By employing this rigorous and systematic data extraction approach, we obtained comprehensive and reliable information from the included studies, forming the foundation for our comprehensive META analysis. The detailed data extracted from each study are presented in the Supplementary Materials, providing transparency and facilitating a thorough understanding of the primary characteristics of the studies included in our research.

2.5 Assessment of overall effect size

Statistical analyses were conducted using Review Manager V.5.3, and overall effect sizes were calculated based on the statistical analyses of the results from the measurement scale tests of the seven included articles. Hedge's g standardised effect sizes were utilised for each included study to measure the intervention's effect size, with effect sizes of 0.2, 0.4, and 0.8 indicating small, medium, and large effects, respectively. To ensure consistency and that all effect sizes were in the expected direction of the intervention, $p<0.05$ was considered significant.

Given the different measures of the effect of exercise on antenatal maternal depression, the standardised mean difference (SMD) was chosen as it reflects the overall intervention effect size. To synthesise the effect of physical activity on antenatal depression scores in the meta-analysis, the standardised mean difference (SMD) was calculated using the Practical Meta-Analysis Effect Size Calculator (Wilson) along with its corresponding 95% confidence intervals. A heterogeneity test was also conducted to assess the extent of differences between the included studies in describing the overall effect sizes. Heterogeneity was assessed using methods such as the Q statistic and the I2 indicator. I2 values quantitatively assessed heterogeneity, where 0% indicated no heterogeneity, ≥25% indicated low heterogeneity, ≥50% indicated moderate heterogeneity, and ≥75% indicated high heterogeneity. When I2 values indicated moderate to high heterogeneity, a random-effects model was used for data combination, and conversely, a fixed-effects model was utilised (29).

Finally, potential publication bias in the results of the meta-analysis was considered, as studies without significant results are less likely to be published than those with significant results. Due to the limited number of studies (seven) included in this meta-analysis, publication bias was manually checked using assessment criteria from the Cochrane Collaboration Guidelines (CCG) for each study. The assessment covered aspects such as randomisation, masked allocation, blinding, incomplete outcome data, selective reporting, etc. The results of the bias assessment for each study were recorded in a table or form, and two assessors (ZZ and LJY) conducted the assessment independently. In case of any inconsistencies in the assessment results, a third assessor (SL) could arbitrate through discussion, if needed, to resolve any assessment disputes.

2.6 Subgroup analysis of exercise intervention programmes

Subgroup analyses were performed to investigate potential sources of heterogeneity and to examine whether the effect of physical activity on antenatal depression differed between subgroups, considering different characteristics of the included studies. Specifically, we conducted subgroup analyses based on three groups: the gestational age at which the exercise intervention started, the type of physical activity (classified as static and dynamic physical activity), and the duration of the exercise intervention.

Conducting subgroup analyses of this nature empowers researchers to garner deeper insights into the multifaceted effects of exercise on antenatal depression across varying contexts. Furthermore, this approach avails the opportunity to tailor clinical recommendations to align with the distinctive needs and characteristics of diverse pregnant women. This nuanced research paradigm not only enhances comprehension of exercise interventions' impacts on antenatal depression but also fosters the formulation of finely targeted intervention strategies.

For each subgroup, effect sizes (Hedge's g) and their corresponding 95% confidence intervals were calculated using Review Manager V.5.3. The statistical significance of the effect sizes in each subgroup was assessed at a significance level of $p<0.05$. Heterogeneity tests were employed to determine whether there were significant differences between subgroups.

3 Results

3.1 Search process

We searched 4 databases for 608 studies. After removing duplicates, META analyses and systematic reviews were excluded from the remaining 421 studies, leaving 353 studies that were screened for titles and abstracts, resulting in 84 studies that needed to be read in full. Of these, 77 studies were excluded for reasons including researching postnatal depression, noncompliance with the intervention, and inappropriate subjects. Finally, our meta-analysis included data from 7 studies. The detailed process used to search for these is shown in Figure 1 Flowchart and selection of studies.

3.2 Characteristics of the included studies and participants

The characteristics of the seven trials that were included in this META analysis are shown in Table 1. The publication dates of the seven studies varied from 2012 to 2022; the sample sizes of each included study varied from 19 to 167; the duration of exercise for antenatal depression in each study varied from 9 to 28 weeks' gestation; the mean ages of the intervention and control groups are shown in Table 1; the types of exercise used varied from dynamic to static, the type of exercise used was a combination of aerobic exercise and a high-intensity interval training programme, the type of static exercise was yoga, and the control group was routine care and usual antenatal education. The types of exercise interventions were dynamic and static, combined aerobic exercise and high-intensity interval training for dynamic exercise, yoga for static exercise, and usual care and normal antenatal education for the control group. The duration of the exercise intervention ranged from 1 to 6 months, and the frequency of the intervention ranged from once a week to three times a week. Depression Inventory II (n=1); Centre for Epidemiological Studies Depression Scale (n=3); Hospital Anxiety Depression Scale (n=1); Profile of Mood States Questionnaire (n=1); Edinburgh Postnatal Depression Scale (n=1).

3.3 Risks of bias

Among the seven included papers, random sequence generation was assessed as low risk in all seven studies. Five studies had a low risk of bias due to allocation concealment, while two studies had an unknown risk due to underreporting. Participant blinding was assessed as high risk in six studies and unknown risk due to underreporting in one study. Assessor blinding was rated as low risk in five studies and unknown risk in two studies. Similarly,

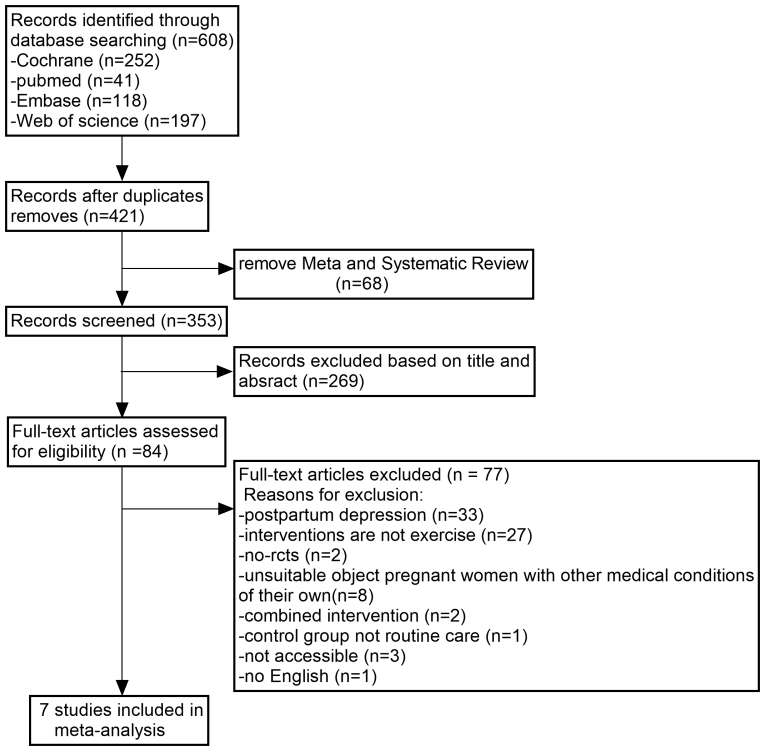

FIGURE 1
Flowchart and selection of studies.

TABLE 1 Characteristics of the included studies and participants.

Studies	Sample Size (IG/CG)	Age Range (IG/CG)	Gestational weeks	IG Type	CG Type	Frequency/ duration	outcome measures
Dominika Wilczyńska (2022) (30)	34/20	31 ± 4/32 ± 4	22 ± 4	HIIT	EDU group	8-week/three 60-min training sessions a week	BDI-II
Marina Vargas-Terrones (2020) (31)	36/25	32.5 ± 3.3/ 32.6 ± 4.7	12–16	10-min-warm-up, 25-min-aerobic, 10-min-muscle strengthening, 5-min-coordination and balance, 5-min-pelvic-floor exercises, 5–10-min-relaxation.	usual care	three sessions per week from 12–16 gestational weeks to the end of the third trimester (weeks 38–40)	CES-D
M. Satyapriya (2013) (32)	51/45	26.41 ± 3.01/ 24.96 ± 2.58	18–20	Yoga	standard antenatal exercises	2 h/day (3 days/week) for one month	HADS
M. Perales (2014) (33)	90/77	31.08 ± 3.39/ 31.66 ± 3.86	9–12	5–8-min-warm-up, 25-min- muscle strengthening, 10-min-balancing exercises, 10-min-pelvic-floor exercises, 5–8-min-relaxation.	usual care	three times per week between 9 and 12 weeks of gestation and continued Weeks 39 and 40	CES-D
Angelo Fernando Robledo-Colonia (2012) (34)	37/37	21 ± 3/ 21 ± 3	16–20	10-min-walking, 30-min-aerobic exercise, 10-min-stretching, 10-min-relaxation.	usual care	three 60-min exercise classes per week for 3 months	CES-D

(Continued)

TABLE 1 Continued

Studies	Sample Size (IG/CG)	Age Range (IG/CG)	Gestational weeks	IG Type	CG Type	Frequency/ duration	outcome measures
Cathryn Duchette (2021) (35)	10/9	27.1 ± 2.88/ 30.11 ± 4.10	20.94 ± 4.69	Yoga	usual care	at least one prenatal yoga class each week for 10 weeks	POMS
Kyle Davis (2015) (36)	20/19	29.74 ± 5.40/ 30.57 ± 4.46	>28	Yoga	usual care	yoga intervention consisted of eight consecutive 75-min weekly group classes.	EPDS

IG, Intervention group; CG, Control group; HIIT , high intensity interval training program; EDU group , educational program; BDI-II, Beck depression inventory-II; CES-D, Center for Epidemiological Studies-Depression Scale; HADS, Hospital Anxiety Depression Scale; POMS, Profile of Mood States Questionnaire; EPDS, Edinburgh Postnatal Depression Scale.

blinding of outcome assessment was considered low risk in five studies and unknown risk due to underreporting in two studies. Regarding "incomplete outcome data," two studies were deemed to have a low risk, while five studies were rated as unknown risk due to underreporting. Additionally, for selective reporting of study results, three studies were assessed as having low risk, and four studies were considered to have an unknown risk. Lastly, all studies were assessed as having an unclear risk of other bias due to a lack of necessary information. The comprehensive assessment of the risk of bias for each study is provided in Supplementary Material 2.

3.4 Meta-analysis result

In this study, we employed various scales, namely BDI II, CES-D, HADS, POMS, and EPDS, due to their diverse measurement tools. To address this variability, the standardised mean difference (SMD) was selected for the analysis. The overall evaluation of the seven papers yielded a heterogeneity test result with df = 6 (p = 0.0007) and I^2 = 74%, indicating moderate heterogeneity. Consequently, we applied the random effects model to the analysis, as depicted in Figure 2.

The combined intervention effect size was reported as [SMD = -0.41, 95% CI -0.78 to -0.05, Z = 2.20, p = 0.03], signifying a statistically significant overall combined effect. These findings suggest that antenatal exercise can effectively alleviate depression in pregnant women. Notably, all seven papers utilised screening tools with higher scores associated with deeper depression. An effect size represented by a negative value indicates that exercise has a beneficial effect in reducing symptoms of antenatal depression in pregnant women. The SMD of -0.41 corresponds to a medium effect size, indicating that exercise can significantly improve the symptoms of antenatal depression in pregnant women.

To explore potential sources of heterogeneity in the study results, we conducted an exclusion-by-exclusion sensitivity analysis. Through this process, we systematically removed selected research literature and observed the effects on heterogeneity indicators. Interestingly, during this analysis, we observed the deletion of one study (Dominika Wilczyńska, 2022) that investigated HIIT training interventions for maternal depression. Surprisingly, the removal of this literature resulted in a significant reduction in overall heterogeneity, with a p-value of 0.08 and I^2 of 49%. Although the p-value did not reach the conventional significance level of 0.05, this sensitivity analysis implies that this particular literature may play an important role in contributing to the observed heterogeneity. Therefore, we have made the decision to retain this literature for further exploration and discussion, as it explores HIIT training as an intervention for maternal depression within the context of our research questions, and was published in a peer-reviewed journal (30–36).

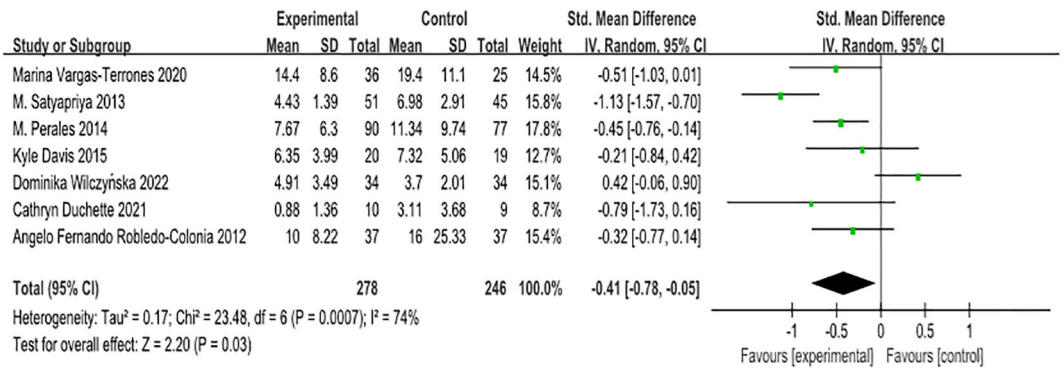

FIGURE 2
Forest plot of the effect of exercise intervention on antenatal maternal depression.

3.5 Subgroup analysis of moderating variables for exercise intervention programmes

In this study, we established subgroups to examine three elements of the exercise and exercise program: the type of exercise intervention, the duration of continuous intervention, and the timing of the intervention during pregnancy (see Table 2). The type of exercise intervention was categorised into static exercise, represented by yoga, and dynamic exercise, represented by aerobics and HIIT. Due to the limited number of included studies and the relatively small sample size, Intervention duration is bifurcated at the threshold of three months, thereby segregating participants into two distinct groups: those with intervention durations less than or equal to three months, and those with intervention durations exceeding three months. Simultaneously, with respect to the initiation of exercise intervention, the demarcation is delineated as the commencement of pregnancy at the 20-week mark. This partitions the subjects into two categorical cohorts: those commencing intervention prior to or at 20 weeks of gestation, and those who embark on intervention after 20 weeks into pregnancy.

Following this categorisation, we performed analyses within these subgroups to explore potential variations in the intervention effects. The subgroups allowed us to better understand how different exercise types, intervention durations, and timings during pregnancy may influence the outcomes. The results of these subgroup analyses are presented in the subsequent sections, shedding light on the specific effects of exercise interventions on antenatal depression in pregnant women.

3.5.1 Type of exercise intervention

In this study, we conducted a subgroup analysis on seven papers, classifying them according to the type of exercise intervention. The included studies encompassed three main types of exercise: yoga, categorised as static exercise, and aerobic exercise and HIIT, categorised as dynamic exercise. Our aim was to investigate the effects of these exercise interventions on depressive symptoms in pregnant women.

The results revealed that both static and dynamic exercise had a significant impact on reducing depressive symptoms in pregnant women. Effect sizes in both groups exhibited moderate heterogeneity, with a standardised mean difference (SMD) of -0.73 (95% confidence interval [-1.35, -0.11]) for static exercise and SMD of -0.23 (95% confidence interval [-0.62, 0.17]) for dynamic exercise. The results of the heterogeneity test demonstrated that the difference between the two subgroups was not statistically significant (p = 0.18). The index of heterogeneity (I^2) was calculated at 45.3%, indicating a moderate level of heterogeneity within the studies in each subgroup. For detailed findings and graphical representation, please refer to Figure 3.

3.5.2 Duration of continuous intervention

Subgroup analyses were conducted based on the duration of the ongoing intervention. The research literature was divided into two groups, using three months as the cut-off point. Trials lasting less than or equal to three months exhibited a standardised mean difference (SMD) of -0.39 (95% confidence interval [-0.98, 0.20]), while trials lasting more than three months demonstrated an SMD of -0.47 (95% confidence interval [-0.73, -0.20]).

The results of the heterogeneity analysis indicated no statistically significant difference between these two subgroups (P = 0.81). The index of heterogeneity (I^2) was calculated at 0%, suggesting no heterogeneity of results within each subgroup. However, given the limited number of studies included, it is essential to interpret these results with caution. To validate these findings and gain a more comprehensive understanding of the effect of exercise intervention duration on outcomes of interest, further studies with larger and more diverse study populations are warranted. For detailed graphical representation, please refer to Figure 4.

3.5.3 Timing of intervention during pregnancy

Subgroup analyses were conducted based on the timing of the intervention during pregnancy, and the research literature was divided into two groups using 20 weeks' gestation as the cut-off point. Trials conducted before 20 weeks of pregnancy showed a standardised mean difference (SMD) of -0.60 (95% confidence interval [-0.95, -0.25]), whereas trials conducted after 20 weeks of pregnancy displayed an SMD of -0.10 (95% confidence interval [-0.76, 0.56]).

The results of the heterogeneity analysis showed no statistically significant difference between these two subgroups (P = 0.19). The index of heterogeneity (I^2) was calculated at 42.3%, indicating

TABLE 2 Subgroup analysis of exercise intervention for depressive symptoms in antenatal pregnant women.

Adjustment variables	Subgroup	Heterogeneity test		Sample size	SMD [95%CI]
		P	I^2(%)		
Type of Exercise Intervention	Static exercise	0.18	45.3%	154	-0.73[-1.35-0.11]
	Dynamic exercise			270	-0.23[-0.62,0.17]
Duration of Continuous Intervention	≤ 3 months	0.81	0%	296	-0.39[-0.98,0.20]
	> 3 months			228	-0.47[-0.73,-0.20]
Timing of Intervention during Pregnancy	Before 20 weeks	0.19	42.3%	402	-0.60[-0.95,-0.25]
	After 20 weeks			126	-0.10[-0.76,0.56]

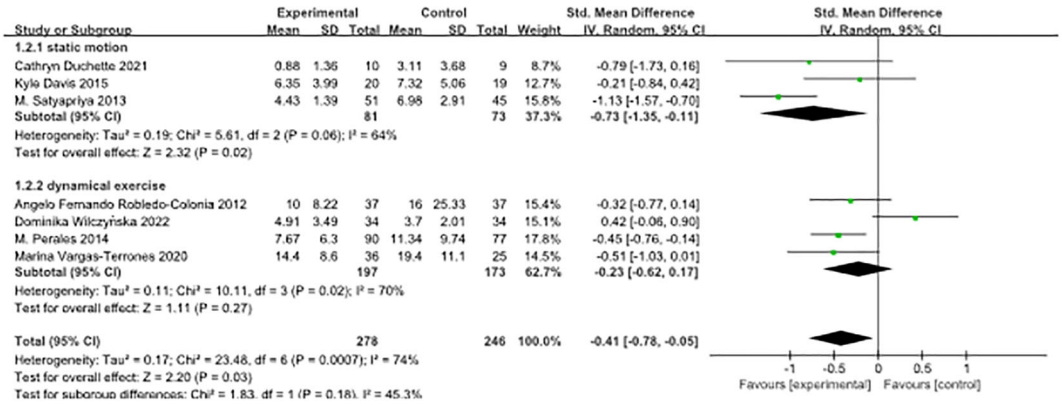

FIGURE 3
Forest plot of subgroup analyses of pre-pregnancy depression by type of exercise intervention.

moderate heterogeneity of results within each subgroup. These results underscore the potential effectiveness of interventions at different stages of pregnancy in improving the outcomes of interest. However, it is crucial to interpret these findings with caution due to the limited number of included studies. To validate these results and gain a more comprehensive understanding of the effect of the timing of interventions during pregnancy on the outcomes of interest, further studies with larger sample sizes and more diverse study populations are needed, as illustrated in Figure 5.

3.6 Publication bias test

A funnel plot was meticulously crafted to scrutinise the presence of publication bias within the realm of exercise interventions for antenatal depression. A perusal of the publication bias funnel plot, as depicted in Figure 6 Funnel plot of publication bias tests for included studies, reveals a harmonious symmetry exhibited across all seven studies. This symmetry, coupled with the absence of conspicuous asymmetrical distortions, signifies a low prevalence of publication bias within the dataset. Additionally, the overall high quality of these studies further reinforces their suitability for inclusion in the ensuing meta-analysis.

4 Discussion

4.1 Main findings

The meta-analysis clearly showed that exercise intervention had a significant overall effect on reducing antenatal depression symptoms. The standardised mean difference (SMD) of -0.41, 95% confidence interval of -0.78 to -0.05 and p-value of 0.03 confirms the benefit of physical activity in controlling antenatal depression. This result is important because it highlights the potential of exercise as a viable non-pharmacological intervention to alleviate depressive symptoms in pregnant women.

In the context of exercise interventions targeting the amelioration of antenatal depression, the results indicated a notable reduction in depressive symptoms attributable to both types of exercise interventions. Intriguingly, it was observed that static exercise displayed a relatively more substantial effect size, although it did not attain statistical significance (P = 0.18). These

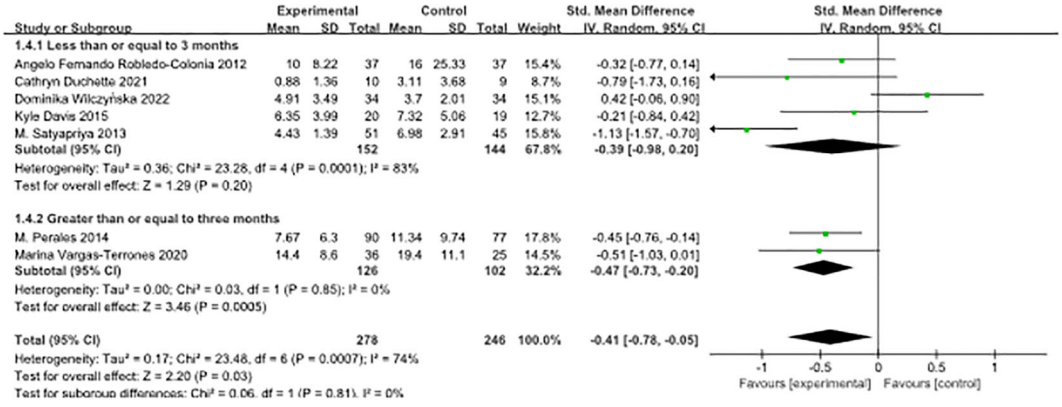

FIGURE 4
Forest plot of subgroup analyses of pre-pregnancy depression by duration of continuous intervention.

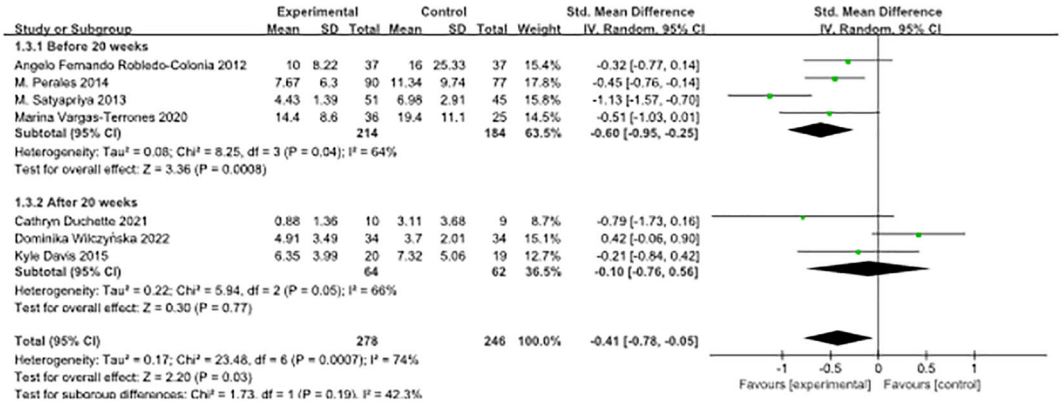

FIGURE 5
Forest plot of subgroup analyses of pre-pregnancy depression by timing of intervention during pregnancy.

findings offer a tantalising suggestion that static exercise may exert a more pronounced influence on moderating outcomes as compared to its dynamic counterpart. It was challenging to directly compare the effects of aerobic exercise and high-intensity interval training (HIIT) interventions due to the limited inclusion of only one article on HIIT. From a physiological perspective, both static and dynamic exercise interventions impact maternal depressive symptoms through endocrine regulatory mechanisms, such as increasing levels of neurotrophic factors, promoting the production of relevant adipocytokines, regulating neurotransmitter expression, enhancing mitochondrial function, and influencing melatonin secretion levels. Furthermore, exercise interventions also influence inflammatory pathways and mediate microRNA expression (37).

However, yoga stands out as a particularly effective intervention due to its emphasis on the mind-body connection and the continuous adjustment and balancing of postures and breathing. These features contribute to restoring mind-body balance, which is crucial in managing antenatal depression. Pregnant women often experience hormonal changes and physical discomfort, and yoga can help them adapt to these physiological and psychological changes. While aerobic exercise and HIIT also offer mental health benefits, certain pregnant women may be unable to engage in high-intensity aerobic exercises due to their physical condition or pregnancy limitations. The gentle movements of yoga are better suited to the physical characteristics of pregnant women, minimising the risk of overexertion that could contribute to antenatal depression. In addressing antenatal depression, the significance of yoga and aerobic exercises extends beyond their biological impacts to include key psychological mechanisms such as emotional regulation, mindfulness, and self-efficacy, which are crucial for the psychological well-being of pregnant women (38). Regular engagement in these activities has been shown to significantly improve mood and reduce stress by increasing the production of mood-enhancing neurotransmitters like endorphins and serotonin, and through practices like controlled breathing in yoga, which amplifies parasympathetic activity and lowers cortisol

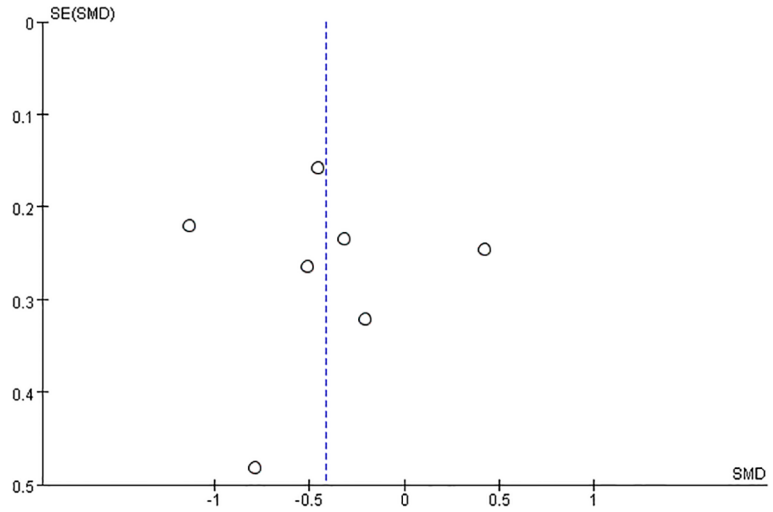

FIGURE 6
Funnel plot of publication bias tests for included studies.

levels (39). Moreover, yoga's unique mindfulness practices enhance present awareness and help participants detach from negative thought patterns, reducing depressive symptoms by limiting rumination and anxiety (40). Additionally, achieving fitness goals through yoga and aerobic exercises boosts self-efficacy, providing pregnant women with a sense of mastery over their physical health and better management of mental health challenges This comprehensive approach not only addresses the symptoms of depression but also enhances overall psychological resilience during pregnancy (32).

Ensuring exercise is carried out correctly is vital to prevent any negative effects on antenatal depression. A scientific and well-designed exercise intervention program that prioritizes stimulating the mother's subjective motivation is essential. It should also avoid high-intensity exercise that may have negative physical and mental impacts on the mother, as well as passive exercises that could add unnecessary pressure. In conclusion, exercise during pregnancy holds promise as an effective intervention for managing antenatal depression. While both static and dynamic exercise interventions offer benefits, the unique features of yoga make it particularly valuable in restoring mind-body balance and addressing the physiological and psychological changes associated with antenatal depression. Selecting appropriate exercise interventions and fostering mothers' motivation in a carefully designed program are vital for ensuring a positive impact on antenatal depression. Further research and comprehensive studies are needed to delve deeper into the specific effects and mechanisms of various exercise interventions on maternal mental health during pregnancy.

Concerning the temporal dimension of interventions throughout pregnancy aimed at enhancing antenatal depression, the trial outcomes, as unveiled through subgroup analyses, provided insights into the impact of intervention timing. It is worth noting that these interventions, when administered at various points during pregnancy, did indeed manifest an influence on the trial outcomes. Nevertheless, an intriguing observation emerged, with interventions administered prior to the 20th week of gestation exhibiting a comparatively larger effect size, albeit lacking statistical significance ($p = 0.19$), when juxtaposed with interventions implemented after the 20th week of gestation. This finding implies the possibility of a more conspicuous moderating effect of interventions on the overall outcomes. The presence of moderate heterogeneity within these subgroups may be attributed to variances in the design of the encompassed studies, participant characteristics, or the intricacies of the intervention protocols. The first 20 weeks of gestation represent the early stage of pregnancy, characterised by more pronounced psychological adjustments and mood fluctuations in pregnant women. During this period, the pregnant woman's body is adapting to hormonal changes and physiological adjustments. Implementing exercise interventions at this stage can effectively help pregnant women cope with psychological stress and mood fluctuations throughout pregnancy, leading to a reduction in symptoms of antenatal depression. Conversely, exercise interventions during the latter half of pregnancy (after 20 weeks of gestation) may be less effective due to increased physical burden and discomfort associated with advancing pregnancy. At this stage, the focus shifts more towards preparing for childbirth, and pregnant women may find it more challenging to actively engage in exercise interventions, potentially reducing the antidepressant effects of such interventions (41).

The outcomes stemming from the subgroup analysis investigating the duration of exercise interventions in the context of antenatal depression treatment shed light on a significant impact evident in both short-term (≤ 3 months) and long-term (> 3 months) interventions. Notably, although both of these categories exhibited substantial effects on the outcomes of interest, the disparity between them failed to attain statistical significance within this subgroup analysis ($P = 0.81$). More precisely, it was apparent that both short-term and long-term exercise interventions were correlated with enhanced outcomes. These findings may hold substantial implications for the formulation of exercise programs tailored to pregnant women grappling with depressive symptoms, given the observable significant effects on the outcomes of interest for both short-term (≤ 3 months) and long-term (> 3 months) interventions.

In light of the outcomes derived from the three distinct subgroup analyses, it is crucial to acknowledge that these analyses did not yield statistically significant differences. Despite our meticulous examination from various angles, the p-values consistently exceeded the 0.05 threshold, rendering them insufficient to establish the statistical significance of these analyses within the scope of our study. This particular result may be attributed to a confluence of factors, including variances in sample characteristics, the sensitivity of measurement instruments, and methodological heterogeneity. These intricacies may have collectively contributed to our inability to discern noteworthy disparities. It is imperative to recognise that our study possesses certain limitations, encompassing aspects such as data quality, heterogeneity in the criteria for study selection, and the potential influence of publication bias. These limitations bear relevance to our results, necessitating caution in the interpretation of our findings. In light of these constraints, future investigations could embark on a more comprehensive exploration of this domain, delving deeper into potential discrepancies between subgroups. Augmented sample sizes, thorough data collection, and intricate methodological analyses have the potential to furnish a more holistic comprehension of this intricate issue. In summation, our findings underscore the imperative for further inquiries aimed at elucidating the impacts of exercise-based interventions, encompassing exercise type, duration, and timing, on antenatal depression, thereby endeavouring to bridge extant knowledge gaps. The transparency and rigor characteristic of such findings can serve as a compass guiding the trajectory of future research efforts.

These findings have significant implications for healthcare professionals and policymakers in designing exercise intervention programs for pregnant women with antenatal depression. Early and consistent exercise interventions during the first 20 weeks of pregnancy may offer substantial benefits in terms of mental health support and depression management. However, it is essential to recognise the individual differences and preferences of pregnant women when recommending exercise interventions and

to ensure that the programs are tailored to meet their specific needs and circumstances.

4.2 Strengths and limitations

Our review exhibits several notable strengths. Firstly, the exercise interventions analysed are highly feasible and accessible, as they can be conducted at home or any other convenient location under the guidance of medical professionals, making them practical for pregnant women and their families. Secondly, the inclusion of randomised controlled trials (RCTs) in our review enhances the reliability of our results, as RCTs are considered robust study designs for assessing the efficacy of interventions.

However, certain limitations should be acknowledged in this study. Firstly, the small sample sizes of the groups may limit the generalizability of our results, and thus, the findings should be interpreted with caution. The limited sample size may have reduced the statistical power and precision of our estimates.

Secondly, the lack of blinding in most of the included studies introduces the potential for biases in outcome assessment, which could influence the reliability of the results. Although the issue of blinding in exercise intervention studies remains controversial, it remains an important consideration in the interpretation of the findings.

Thirdly, due to the limited data available, our meta-analysis may not be able to make strong recommendations about the optimal exercise intervention program. The scarcity of comprehensive data in the field of exercise interventions during pregnancy may limit the scope of our analysis and the extent to which we can draw definitive conclusions.

Fourthly, the majority of the included literature primarily focused on analysing depression in the exercise intervention group and the non-intervention group. This narrow focus may have overlooked the potential influence of other factors, such as participants' physical fitness levels and lifestyle choices, which could confound the inclusion of relevant literature and impact the overall conclusions.

Lastly, the literature reviewed herein predominantly utilised depression measures such as the Beck Depression Inventory II (BDI-II), which were not originally tailored for the perinatal period. This highlights a critical concern: the extent to which these instruments have been modified to accurately reflect the unique psychological and physiological conditions inherent to the perinatal phase. During pregnancy and postpartum, significant changes in a woman's mental and physical state necessitate specialised assessment tools to ensure precise evaluation and diagnosis of depression. Consequently, there is an imperative need for the development and validation of assessment tools that are specifically designed for the perinatal period. Addressing this gap not only enhances the accuracy of research but also improves clinical outcomes for pregnant and postpartum women, marking a crucial direction for future investigations in perinatal mental health research.

In conclusion, while our review provides valuable insights into the potential benefits of exercise interventions for antenatal depression, it is crucial to recognise the limitations that stem from small sample sizes, lack of blinding, and insufficient data. To build a more robust evidence base and provide comprehensive recommendations, future research should strive to address these limitations by conducting larger-scale and well-designed studies, exploring various aspects of exercise interventions, and taking into account additional influencing factors. By doing so, we can advance our understanding of the role of exercise in managing antenatal depression and optimise its implementation for the overall well-being of pregnant women.

5 Conclusion

The main conclusions of this study can be summarised as follows: For the investigation of the intervention effect, we found that exercise has a moderate effect on depression symptoms in pregnant women. The type of exercise intervention, the starting time of the exercise intervention, and the duration of exercise in the exercise intervention programme are the important factors influencing the effect of exercise intervention on antenatal depression; Among the different types of exercise interventions, we found that static exercise, especially yoga, had a significantly better effect on improving antenatal depression than dynamic exercise. Among the different types of exercise interventions, we found that static exercise, especially yoga, had a significantly better effect on improving antenatal depression than dynamic exercise; in terms of the timing of interventions during pregnancy, we found that exercise interventions before 20 weeks' gestation were significantly more effective than those after 20 weeks' gestation; and that long-term interventions were slightly more effective than short-term interventions.

It is imperative to underscore the importance of exercising a greater degree of caution in our interpretation of the results, especially when none of the three subgroup analyses have demonstrated statistical significance. We must refrain from making definitive claims regarding the existence of clear associations between specific intervention characteristics and their corresponding outcomes. Instead, we find ourselves compelled to acknowledge the presence of certain limitations within the scope of this study. These limitations encompass a range of factors, including variances in sample characteristics, the sensitivity of measurement tools, variations in study design, and the presence of methodological heterogeneity. It is plausible that these multifaceted elements have played a role in elucidating why the subgroup analyses failed to yield statistical significance. In light of these circumstances, it becomes evident that there is a compelling need for a more comprehensive investigation into the effects of exercise type, duration, and timing on antenatal depression, thereby aiding in the process of bridging the existing gaps in our knowledge. To acquire a more nuanced understanding of the intricate nature of this issue, we extend our encouragement to future research endeavours to consider a broader spectrum of potential influencing factors. This conclusion, framed within the paradigm of cautious and transparent research, not only acts as a guidepost but also propels the trajectory of future research initiatives.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Author contributions

ZZ: Conceptualization, Investigation, Writing – original draft. YL: Data curation, Formal analysis, Methodology, Writing – original draft. LS: Conceptualization, Data curation, Investigation, Writing – review & editing. X-DZ: Conceptualization, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2024.1290418/full#supplementary-material

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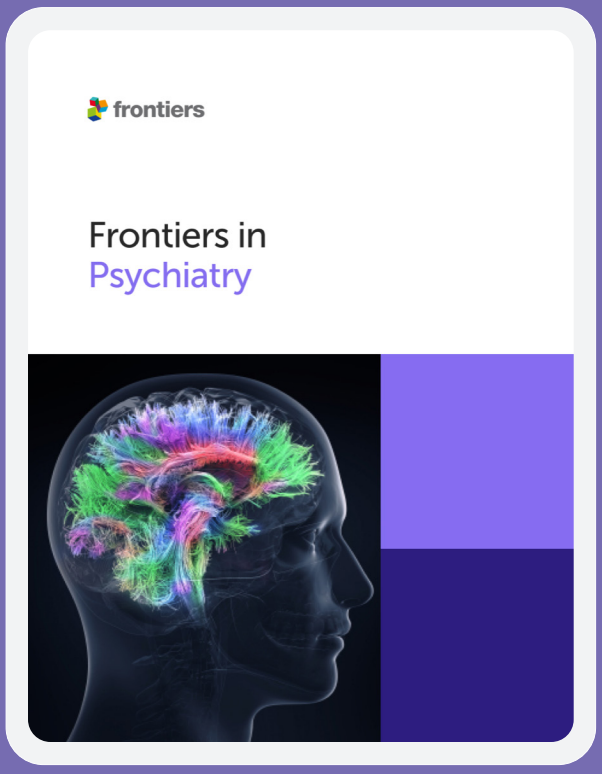

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