**Systematic Review**

The Relationship between Maternal Perinatal Depression and Offspring Depression: A Meta-Analysis

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Abstract

**Background:** Antepartum depression, with an incidence of 20.7%, is a pressing global public health concern due to its detrimental effects on both the physical and mental health of pregnant women, as well as the potential risk it poses for depression in their offspring. Nevertheless, there is a lack of consensus among existing studies regarding this issue. Here, we systematically evaluated the relationship between maternal perinatal depression and offspring depression by meta-analysis. **Methods:** We conducted a comprehensive search for relevant studies in Pubmed, Embase, The Cochrane Library, CNKI, Wanfang, VIP, and Chinese Biomedical Literature Service System databases. The prospective cohort studies, which were published in English or Chinese, reported the occurrence of maternal antenatal and/or postnatal depression within one year postpartum and assessed the subsequent development of depression in their offspring, were included. Study quality was assessed with the Newcastle-Ottawa Scale. Review Manager 5.4 software was used for meta-analysis. Subgroup analysis was performed. Publication bias was evaluated with a funnel plot. **Results:** Totally, 12 studies were included. The meta-analysis found that maternal perinatal depression increased the risk of offspring depression by 1.64 (95% confidence interval (95% CI): 1.37, 1.96, p < 0.001). Subgroup analysis showed that the risk of offspring depression was significantly increased in the European population with maternal perinatal depression (odds ratio (OR) = 1.90, 95% CI (1.49, 2.42), p < 0.001), but not in the Australian and the American populations. The combined effect sizes of maternal antepartum and postpartum depression were (OR = 1.70, 95% CI (1.27, 2.27), p < 0.001) and (OR = 1.74, 95% CI (1.31, 2.32), p < 0.001), respectively. The combined effect size of the relationship of maternal perinatal depression with offspring depression in childhood and adulthood was (OR = 1.70, 95% CI (1.28, 2.25), p < 0.001) and (OR = 1.60, 95% CI (1.27, 2.02), p < 0.001), respectively. The adjusted and unadjusted combined effect sizes were (OR = 1.44, 95% CI (1.14, 1.82), p < 0.001) and (OR = 1.97, 95% CI (1.49, 2.60), p < 0.001), respectively. There may be some publication bias in the included studies. **Conclusions:** Maternal perinatal depression is associated with an increased risk of depression in offspring. Effective prevention and management of depression in perinatal women is necessary to mitigate the risk of depression in offspring.

Keywords: antenatal; depression; offspring; perinatal depression; postnatal

1. Introduction

Perinatal depression, including antepartum depression and postpartum depression, refers to a mental health condition that occurs during pregnancy and within 12 months postpartum and is characterized by depression, irritability, sensitivity, insomnia, and excessive worry about themselves and their babies. A meta-analysis of 173 studies, encompassing samples from various countries including the United States, Australia, Brazil, and China, showed that the incidence of antepartum depression was as high as 20.7% [1]. The global prevalence of postpartum depression is 17.7% [2]. The incidence of postpartum depression in the United States is approximately 13% [3], and it is estimated to be higher in low- and middle-income countries [4,5]. Postpartum depression is usually closely related to antepartum depression, and 1/3 of pregnant women have depressive symptoms that persist until postpartum [6]. Perinatal depression not only leads to maternal suicide and various psychological diseases [7] but also increases the short- and long-term risk of offspring premature birth and neonatal asphyxia [8]. Additionally, perinatal depression is associated with offspring mental disorders, and behavioral and emotional problems during adolescence and adulthood [9–12].

The Global Burden of Disease (GBD) 2019 Disease and Injuries Collaborators shows that depression ranks among the top 25 major burden causes in the world in 2019 [13]. Environmental factors play a crucial role in the occurrence of depression [14]. The fetus and infancy are critical periods of neurodevelopment and are extremely sensitive to adverse environmental stimuli [15]. Perinatal depression is one of the stressful environments to which fetuses and infants are exposed in the early stages, and it can lead to offspring depression by changing hormone levels in offspring [16]. It is reported that the offspring of mothers with postpartum depression are at a higher risk of developing emotional and behavioral problems at the age of 11 to 12 years old [17], and offspring of mothers with antepartum depression are more likely to be depressed at the age of 18 years old [9].
The adverse effects of perinatal depression on offspring have received extensive attention as a major public health problem. There are some studies on the relationship between perinatal depression and offspring depression, however, the results remain inconclusive [9,18]. Tirumalaraju et al. [19] conducted a meta-analysis of relevant studies published before 2019 and confirmed that maternal perinatal depression increased the risk of offspring depression. However, in their analysis, only adolescent and adult offspring were included and offspring younger than 12 years at the time of depression assessment were excluded. Additionally, subgroup analyses based on different cultural backgrounds and different age groups of offspring were not performed, which may introduce certain limitations in the research findings. Therefore, this study systematically evaluated the relationship between maternal perinatal depression and offspring depression by conducting a meta-analysis on prospective cohort studies. Subgroup analyses were performed based on the geographical source of the study population (Europe, Australia, and America), stage of offspring age (childhood and adulthood), and time of maternal depression (antenatal depression and postpartum depression). Our findings may provide evidence for early identification and intervention of offspring depression.

2. Materials and Methods

2.1 Literature Retrieval

Published studies were retrieved from the databases of Pubmed, Embase, The Cochrane Library, CNKI, Wanfang, VIP, and the Chinese Biomedical Literature Service System from the inception of these databases until December 31, 2022. The language was limited to Chinese and English. The search terms included: (postnatal depression OR antenatal depression OR perinatal depression) AND (offspring). Grey literature was not included. This study followed PRISMA guidelines.

2.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) The study design was a prospective cohort study. If multiple studies are reported from the same cohort, the study with the longest follow-up time or the largest sample size was included; (2) The age of the offspring was not restricted; (3) The exposure factor of offspring was the maternal antenatal or/and postnatal depression (within one year postpartum); (4) The outcome was that the offspring suffered from depression or had depressive symptoms, which were clinically diagnosed or evaluated by psychological standards; (5) The odds ratio (OR) and corresponding 95% confidence interval (95% CI) could be obtained or calculated.

Exclusion criteria: (1) The study design was other than a cohort study; (2) Duplicated publications and repeated publications of data; (3) Maternal depression assessment was conducted before pregnancy or more than 1 year postpartum; (4) Mothers were with primary psychiatric disorders; (5) Studies for which effect sizes could not be extracted.

2.3 Literature Screening and Data Extraction

After importing the retrieved literature into Endnote (version X9; Thomson Corporation, Stanford, CA, USA), duplicate publications were excluded. Then, two researchers independently read the titles and abstracts, directly excluding literature unrelated to the topic. For literature that was uncertain whether to include, we reserved it. After reading the full text of 42 articles independently, there were differences in the selection of two articles from the same cohort. After discussion with a third researcher (WS), we decided to include the study [20] with a large sample size that simultaneously analyzed the relationship between prenatal and postpartum depression and offspring depression. The study [9] with a small sample size that only analyzed the relationship between prenatal depression and offspring depression was excluded. The views of the two researchers on the screening and data extraction of the remaining studies showed a basic consensus without any significant differences. The following data were extracted: first author, publication year, study location and inclusion time of the cohort, sample size, sex ratio of offspring, measurement tools and evaluation time, adjusted potential confounding factors, OR value, and 95% CI (if they are adjusted, the adjusted value will be extracted).

2.4 Quality Evaluation

The quality of the included studies was assessed according to the Newcastle-Ottawa Scale (NOS) [21]. NOS has 8 items in 3 dimensions: subject selection (4 items, 4 points), comparability between groups (1 item, 2 points), and outcome measure or exposure factor measurement (3 items, 3 points). The total score of NOS was 9 points. Studies with a score ≤4 points were considered low-quality, those with 5–6 points were considered moderate-quality, and those with ≥7 points were considered high-quality. Low-quality papers with a score ≤4 were excluded to ensure the reliability of the included literature. The quality evaluation was conducted independently by two researchers (QY and WM), and disagreement was resolved by discussion.

2.5 Statistical Analysis

Review Manager (version5.4; Cochrane Collaboration, Oxford, UK) was used for meta-analysis. Cochran Q test and I² test were used for the heterogeneity test. If there is no statistical heterogeneity among studies (p > 0.10 and I² < 50%), a fixed-effects model was used. If p ≤ 0.10 or I² > 50%, there is heterogeneity among studies (p < 0.10 or I² > 50%), a random-effects model was used. Subgroup analysis was performed based on the following factors: the geographic source of the study population (Europe, Austr-
<table>
<thead>
<tr>
<th>Included studies</th>
<th>Study region</th>
<th>Number of participants</th>
<th>Offspring sex (Male/Female)</th>
<th>Maternal measure (tools/time)</th>
<th>Offspring measure (tools/time)</th>
<th>Adjusted potential confounding factors</th>
<th>Quality evaluation score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quarini et al. [20] (2016)</td>
<td>United Kingdom (1991–1992)</td>
<td>7959</td>
<td>4099/3860</td>
<td>EPDS Antepartum: 18, 32 weeks gestation Postpartum: 2 months postpartum, 8 months postpartum</td>
<td>CIS-R and ICD-10 criteria for diagnosis</td>
<td>Maternal education, maternal age, parity, and other timing depression (prenatal depression adjusted for postnatal depression and postnatal depression adjusted for prenatal depression)</td>
<td>9</td>
</tr>
<tr>
<td>Plant et al. [25] (2015)</td>
<td>United Kingdom (1986)</td>
<td>103</td>
<td>49/54</td>
<td>CIS Antepartum: 20 and 36 weeks gestation Postpartum: 3 months postpartum, 12 months postpartum</td>
<td>DSM-IV</td>
<td>None</td>
<td>8</td>
</tr>
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Table 1. Continued.

<table>
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<tr>
<th>Included studies</th>
<th>Study region</th>
<th>Number of participants (Male/Female)</th>
<th>Offspring sex (Male/Female)</th>
<th>Maternal measure (tools/time)</th>
<th>Offspring measure (tools/time)</th>
<th>Adjusted potential confounding factors</th>
<th>Quality evaluation score</th>
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<tbody>
<tr>
<td>Antepartum: first, second, and third trimesters of gestation Postpartum: 8 months postpartum</td>
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<tr>
<td>Murray et al. [28] (2011) United Kingdom</td>
<td>93</td>
<td>45/48</td>
<td>EPDS, SPI</td>
<td>KSADS</td>
<td>None</td>
<td>16 years</td>
<td>7</td>
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<tr>
<td>Postpartum: 6 weeks postpartum, 8 weeks postpartum</td>
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<tr>
<td>Pawlby et al. [29] (2009) United Kingdom</td>
<td>127</td>
<td>Unknown</td>
<td>Interviews and diagnostic assessments</td>
<td>Computer-generated information obtained from the Child and Adolescent Psychiatric Assessment.</td>
<td>None</td>
<td>16 years</td>
<td>6</td>
</tr>
<tr>
<td>Antepartum: 20 and 36 weeks of gestation Postpartum: 3 months postpartum, 12 months postpartum</td>
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DSM, Diagnostic and Statistical Manual of Mental Disorders; EPDS, Edinburgh Postnatal Depression Scale; DSSI, Depression Subscale of Delusions-Symptoms-States Inventory; CIS, Clinical Interview Schedule; CES-D, Radloff’s Centre for Epidemiological Studies Depression Scale; SPI, Standardized Psychiatric Interview; PAPA, Preschool Age Psychiatric Assessment; SCID, Structured Clinical Interview for DSM; BDI, Beck Depression Inventory; ICD, The International Statistical Classification of Diseases and Related Health Problems; DIS, Computerized Diagnostic Interview Schedule; KSADS, Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version.
al, and America), time of offspring depression (childhood and adulthood), time of maternal depression (antepartum depression and postpartum depression), and whether the effect size is adjusted. A funnel plot was used to test for publication bias. Sensitivity was assessed by omitting one study at a time.

3. Results

3.1 The Basic Characteristics of the Studies

A total of 1049 studies were obtained after database searching. The study flowchart is shown in Fig. 1. After excluding duplicate publications, publications of irrelevant topics, publications of other study types than cohort study, publications of irrelevant outcome, data from the same cohort, and repeated publication of data, 12 English studies were finally included in this meta-analysis [10,18,20,22–30]. The basic characteristics and quality of all studies are shown in Table 1. The study populations were from 6 countries including the United Kingdom, Australia, Finland, Germany, Canada, and the United States. Two studies [20,25] reported the relationship between maternal antepartum/postpartum depression and offspring depression, with each extracting two effect sizes. Thus, a total of 14 independent effect sizes were extracted and included in the meta-analysis. Of note, six studies [20,22–24,27,30] and seven effect sizes reported using multivariate ordered logistic regression and other methods to adjust for covariates such as offspring gender, life events experienced by the offspring, and maternal depression status at the time of offspring depression assessment. Table 1 (Ref. [10,18,20,22–30]) presents the basic characteristics of the included studies (author, publication date, sample size, distribution of offspring gender, and location) as well as key variables (assessment time for maternal depression, age of offspring depression assessment, assessment tools, and adjusted potential confounding factors). Additionally, there were 11 high-quality studies included in this analysis, while one study was of moderate quality. No studies of low quality were identified.

3.2 Meta-Analysis Results

There were 12 studies [10,18,20,22–30] (including 14 independent samples) that reported the relationship between maternal perinatal depression and offspring depression. The fixed-effects model (p = 0.20, I^2 = 24%) showed that the combined OR of the relationship between maternal perinatal depression and offspring depression was 1.64 (95% CI: 1.37–1.96, p < 0.001) (Fig. 2 (Ref. [10,18,20,22–30])), suggesting that relative to the non-exposed group, the risk of depression in offspring of mothers with perinatal depression increased by 64%.

3.3 Subgroup Analysis Results

First, subgroup analysis was conducted according to the geographical origin of the study population, and the results showed that the maternal perinatal depression of the European population significantly increased the risk of depression in the offspring (OR = 1.90, 95% CI (1.49, 2.42), p < 0.001). However, no such increased risk was observed in the Australian (OR = 1.50, 95% CI (0.98, 2.31), p = 0.06) and the American populations (OR = 1.29, 95% CI (0.91, 1.81), p = 0.15) (Table 2).

Second, subgroup analysis was carried out based on the time of maternal depression. One study [26] was not included in the subgroup analysis because its effect size could not distinguish between antepartum and postpartum depression. The combined effect sizes of maternal antepartum and postpartum depression were (OR = 1.70, 95% CI (1.27, 2.27), p < 0.001) and (OR = 1.74, 95% CI (1.31, 2.32), p < 0.001), respectively (Table 2), suggesting that both maternal antepartum depression and postpartum depression could increase the risk of depression in offspring.

Third, subgroup analysis was performed according to the time of offspring depression. As shown in Table 2, the combined effect sizes of offspring depression in childhood and adulthood were respectively (OR = 1.70, 95% CI (1.28, 2.25), p < 0.001) and (OR = 1.60, 95% CI (1.27, 2.02), p < 0.001), suggesting that maternal perinatal depression could significantly increase the risk of depression in offspring in childhood and adulthood.

Fourth, subgroup analysis was performed according to whether the effect size is adjusted or not. The adjusted and unadjusted combined effect sizes were (OR = 1.44, 95% CI (1.14, 1.82), p < 0.001) and (OR = 1.97, 95% CI (1.49, 2.60), p < 0.001), respectively, indicating that the maternal perinatal depression can significantly increase the risk of depression in offspring (Table 2).
3.4 Publication Bias Analysis

A funnel plot was used to analyze the publication bias of the included studies. As shown in Fig. 3, the included studies were not completely symmetrical, indicating that there may be some publication bias.

3.5 Sensitivity Analysis

The method of omitting each study one by one was used to observe the effect of a single study on the total combined effect. After omitting a study, there was no significant change in the results, indicating that the results of the meta-analysis were relatively stable.

4. Discussion

Depression is one of the common mental health problems, and affects about 300 million people worldwide [31], bringing a heavy psychological and economic burden to patients and their families [32]. Unfavorable maternal environment and family adversity during pregnancy are high-risk factors for depression in children and adults [33]. A large body of evidence indicates that maternal perinatal depression and anxiety are closely related to offspring behavioral developmental abnormalities, anxiety, and depression [19,34]. The results of this meta-analysis showed that offspring of mothers with perinatal depression had a 64% increased risk of depression compared with non-depressed...
mothers. The diathesis-stress theory of depression is a classic theory to explore the causes of depression, which emphasizes that the formation of depression is the result of the interaction between inner quality and external environmental events [35]. On the one hand, based on genetic factors, the offspring of depressed mothers are susceptible to depression [36]. The effect of genetic susceptibility on female offspring is higher than that on male offspring [37]. The long-term stable effect may eventually lead to depression in adulthood [38], and even increase the risk of antepartum depression in female offspring [39]. On the other hand, the offspring of depressed mothers may experience more childhood trauma, which may lead to an increased risk of offspring depression to a certain extent [33]. Furthermore, exposure of offspring to the stressful environment of maternal depression in the early phase can lead to depression by changing the hormone levels of offspring [15]. It is shown that the hypothalamic-pituitary-adrenal axis is dysfunctional after stress failure [40], and corticotropin-releasing hormone reactivity is increased. Under this condition, the secretion of adrenal-corticotrophin-hormone and glucocorticoid increases, which leads to depression [41]. In addition, individual stress failure can also affect the growth of emotional function neurons through the brain derived neurotrophic factor-tropomyosin related kinase B (BDNF-TrkB) signaling pathway, which plays a crucial role in the emergence of depressive behaviors [42,43].

Subgroup analysis of the study region in this study showed that maternal perinatal depression in the European population, but not the Australian and American populations, significantly increased the risk of depression in their offspring. On the one hand, there may be publication bias due to the inclusion of only 2 studies from Australia and America. On the other hand, this difference may be caused by different tools used for depression assessment. The main assessment tool for perinatal depression in the European population included in this study was the Edinburgh Postnatal Depression Scale (EPDS), while other tools such as the Center for Epidemiological Studies Depression Scale (CES-D) were used in the Americas and Australia. EPDS has a higher detection accuracy for perinatal minor depressive disorder or major depressive disorder than CES-D [44].

Moreover, we conducted a subgroup analysis on the time of maternal depression and found that antepartum and postpartum depression both increase the risk of depression in offspring, which is consistent with previous results [35]. In addition, subgroup analysis on time of offspring depression showed that the risk of depression in childhood and adulthood increased by 70% and 60% in offspring of mothers with perinatal depression, respectively, suggesting that the risk of depression in offspring may be higher in childhood than in adulthood. Maternal antepartum depression has a significant predictive effect on offspring’s childhood mental state and depression in adulthood [45]. Wu et al. [46] found through behavioral experiments that the incidence of depression-like behavior in the offspring of postpartum depression mice was higher than that in the non-depressed group. However, there was no significant difference in the depressive-like behaviors of the adult offspring, which to a certain extent suggested that the offspring of mothers with perinatal depression were more likely to develop depression in childhood. Different from adult depression, the innate factors (genes) and acquired factors (environment) play different roles in the causes of depression in children at different ages [47], and the role of environmental factors in children’s depression is more important [48]. Offspring exposed to the maternal depressive environment may experience more childhood physical abuse, sexual abuse, and severe discipline, all of which will increase the possibility of childhood depression in the offspring to a certain extent [33]. Additionally, we found that the adjusted and unadjusted combined effect sizes both suggested that maternal perinatal depression could significantly increase the risk of depression in offspring, which was consistent with the results by Najman et al. [24].

This study has some limitations. First, studies published in languages other than Chinese and English and non-cohort studies were excluded. Although the sensitivity analysis showed that the results of our study were relatively stable, the funnel plot was not completely symmetrical. These all indicate that there may be some publication bias. Secondly, there were differences in the evaluation criteria for maternal perinatal depression and offspring depression, which may have a certain impact on the results. Future research with more high-quality studies is warranted.

5. Conclusions

In conclusion, this meta-analysis provides evidence that maternal perinatal depression may increase the risk of depression in offspring, especially childhood depression. It is worth noting that the effects of maternal perinatal depression on offspring depression in different populations are inconsistent, which may be related to the different depression evaluation standards in different regions. Our findings underscore the importance of addressing the mental health of women during the antepartum and postpartum periods. Prompt intervention for perinatal depression can foster an environment conducive to child development and hinder potential pathways for offspring depression. Due to the limitations of the included studies, these conclusions should be further validated by additional high-quality research.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

QY designed the research study. QY and WM performed the research. QY collected the funds. FS analyzed
the data. QY and FS interpreted the data. WS prepared the study. QY wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate
Not applicable.

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Conflict of Interest
Not applicable.

Supplementary Material
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References


