Original Article

Association between circulating concentrations of vitamin D and risk of antenatal, postnatal depression: a meta-analysis

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Received: 31/12/2020 – **Accepted:** 03/03/2021

DOI: 10.15761/0101-60830000000305

ABSTRACT

Background: Previous studies showed consistent results for associations between circulating concentrations of vitamin D and risk of antenatal, postnatal depression.

Methods: Articles published in English before November 2020 were searched in databases as follows: PubMed, EMBASE, Web of Science, Medline, Google Scholar and Cochrane. These articles explored associations between circulating concentrations of vitamin D and risk of antenatal, postnatal depression. The present meta-analysis was conducted using STATA 12.0 software. Odds ratios (ORs) and 95% confidence intervals (CIs) extracted from included studies were computed using a random effects model or a fixed effects model according to heterogeneities between included studies. Q test and I^2 were used to explore heterogeneities between included studies.

Results: 7 cohort studies (including 1567 depression cases and 5254 controls) and 3 case-control studies (including 995 depression cases and 1265 controls) were included in the present study. The study showed that low circulating levels of 25-hydroxy (OH) vitamin D is significantly associated with a higher risk of antenatal and postnatal depression (OR = 1.02, 95% CI 1.01 to 1.04, I^2 = 90.7%, $p < 0.001$).

Conclusion: Our results have shown that the low level of vitamin D may be an adverse factor of antenatal and postnatal depression.

Lin D / Arch Clin Psychiatry. 2021;48(4): 186-190

Keywords: antenatal depression; meta-analysis; postnatal depression; vitamin D; 25-hydroxyvitamin D.

Introductions

Depression is the most common mental illness over the world and leads to the decrease of life quality and the deterioration of clinical outcomes, such as suffering, family disruption, disability, and suicide[1,2]. Pregnancy is a process together with a variety of complicated emotional, psychological and biological changes. These changes such as multiple hormonal changes have been considered as contributing factors of depression[3]. Depression during pregnancy is frequently reported as a severe psychopathological disorder with the risk of suicide and infanticide. In addition, depression during pregnancy is associated with a train of adverse obstetric and neonatal complications, including preterm delivery, preeclampsia, emergent operative delivery, and negative consequences on child neurodevelopment[4,5]. According to recent investigations, the prevalence of depression was 11.9% during the perinatal period[6,7]. Approximately one in four and one in five women experience a major depressive episode during the antenatal and postnatal period, respectively[6,7].

Vitamin D has been recognized as an essential fat-soluble vitamin for bone health and calcium homeostasis. Recent studies have proved that it is related to non-skeletal health, including immunity, cancer, renal disease, and neurological dysfunction[8]. Vitamin D is mainly endogenously produced by skin under the exposure of ultraviolet sunlight, with a small proportion ingesting from food sources[9]. Similarly, vitamin D deficiency has been a global public health problem in all age groups, affecting more than one billion children and adults[10,11].

The available reviews have illustrated the relationship between vitamin D deficiency and depression[12,13]. Several studies also have demonstrated the association between vitamin D deficiency and antenatal, postnatal depression[14,15]. Some studies showed a significant association between circulating concentrations of vitamin D and risk of antenatal, postnatal depression[16,17], whereas some studies showed that no significant association was detected between circulating concentrations of vitamin D and risk of antenatal, postnatal depression[18,19]. Therefore, we conducted the meta-analysis to evaluate available evidence regarding the

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association between circulating concentrations of vitamin D and risk of antenatal, postnatal depression. In addition, the study aimed to provide more reliable guidelines for clinical decision.

Methods

The study was made based on the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guideline[20].

Search strategy

Two independent reviewers (Dan Lin and Mian Pan) used search terms as follows: ('vitamin D' OR 'vitamin D3' OR 'cholecalciferol' OR '25(OH)D' OR '25-hydroxyvitamin D') AND ('perinatal' OR 'antenatal' OR 'postnatal' OR 'peripartum' OR 'antepartum' OR 'postpartum' OR 'pregnancy' OR 'periparturient' OR 'puerperium' OR 'maternal' OR 'puerperal' OR) AND ('depression'). Articles published in English before November 2020 were searched in databases as follows: PubMed, EMBASE, Web of Science, Medline, Google Scholar and Cochrane.

Selection criteria

Two independent reviewers (Dan Lin and Mian Pan) read the titles, abstracts and full texts to include studies according to selection criteria. Inclusion criteria were showed as follows: 1) Included studies explored the association between circulating concentrations of vitamin D and risk of antenatal, postnatal depression; 2) Included studies should be cohort and case-control studies. We excluded studies according to the following criteria: 1) secondary processing articles (meta-analyses and reviews); 2) case reports; 3) Studies did not provide sufficient information to obtain odds ratios (ORs) and 95% confidence intervals (CI) regarding association between circulating concentrations of vitamin D and antenatal, postnatal depression.

Data extraction

Two independent reviewers (Dan Lin and Mian Pan) independently used an Excel file to abstract data as follows: Author, publication year, study type, study location, sample size, mean age of included participants, subgroups, time and method of depression diagnosis, depression cases, adjusted variables and results.

Meta-analysis

The present meta-analysis was conducted using STATA 12.0 software. ORs and 95% CIs extracted from included studies were computed using a random effects model or a fixed effects model according to heterogeneities between included studies. Q test and I^2 were used to explore heterogeneities between included studies. With high heterogeneity (p value for Q test ≤ 0.05 and $I^2 \geq 50\%$), a random effects model was used to compute all the ORs and 95% CIs; Inversely, with low heterogeneity (p value for Q test > 0.05 and $I^2 < 50\%$), a fixed effects model was used to compute all the ORs and 95% CIs. Subgroup studies (for different types of studies, different ethnic groups, antenatal or postnatal depression) were conducted to explore source of the heterogeneity. In addition, sensitivity analysis was performed to assess the stabilization of the meta-analysis. Moreover, we used Begg's test, Egger's test and funnel plot to assess publication bias.

Results

Study characteristics

Supplementary Figure 1 showed the process of including studies. Supplementary Table 1 showed data extracted from included studies. Finally, 7 cohort studies[1,16-18,21-23] (including 1567 depression cases and 5254 controls) and 3 case-control studies[14,15,19] (including 995 depression cases and 1265 controls) were included in the present study.

Results of meta-analysis

The study showed that low circulating levels of 25-hydroxy (OH) vitamin D is significantly associated with a higher risk of antenatal and postnatal depression (OR = 1.02, 95% CI 1.01 to 1.04, I^2 = 90.7%, p < 0.001, Figure 1). Subgroup studies showed that low circulating levels of 25(OH) vitamin D is significantly associated with a higher risk of antenatal and postnatal depression in both cohort and case-control studies (cohort studies: OR = 1.02, 95% CI 1.01 to 1.04; case-control studies: OR = 1.94, 95% CI 1.40 to 2.70; figure 2). In addition, subgroup study showed a significantly negative association between circulating levels of 25(OH) vitamin

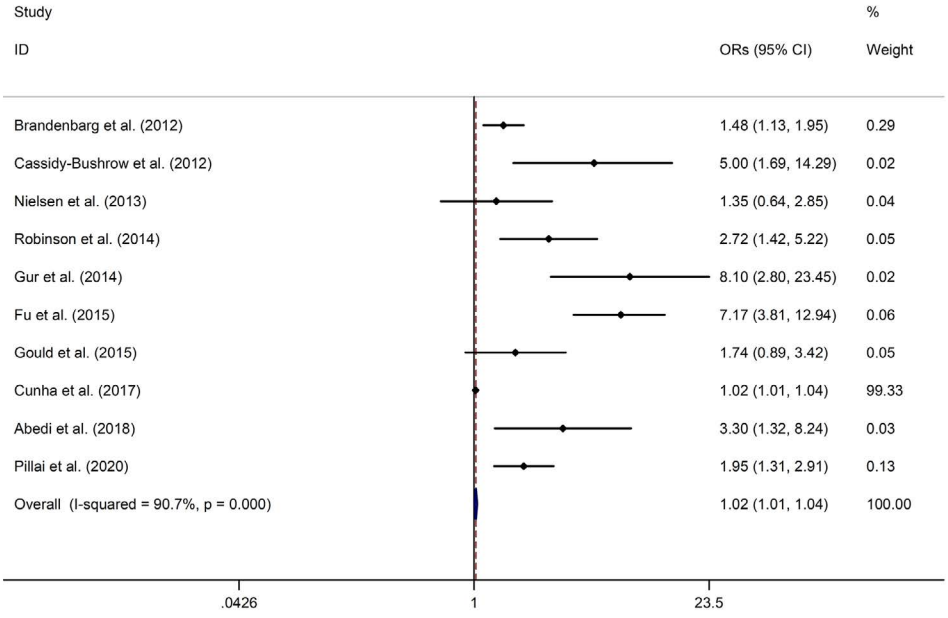

Figure 1. Forest plot regarding associations between circulating levels of 25-hydroxy (OH) vitamin D and risk of antenatal and postnatal depression.

D and the risk of antenatal, postnatal depression in both Caucasian and Asian populations (Caucasian: OR = 1.02, 95% CI 1.01 to 1.04; Asian: OR = 2.93, 95% CI 2.14 to 4.01; Figure 3). Subgroup study also showed that low circulating levels of 25(OH) vitamin D is significantly associated with a higher risk of both antenatal and postnatal depression (antenatal depression: OR = 1.02, 95% CI 1.01 to 1.04; Asian: OR = 2.64, 95% CI 2.07 to 3.35; Figure 4). The present sensitivity analysis indicated that no changes in the direction of effect happened when any study was excluded from the meta-analysis (Supplementary figure 2). Begg's test, Egger's test and funnel plots showed a significant risk of publication bias (Begg's test: $p = 0.721$; Egger's test: $p < 0.001$; supplementary figure 3).

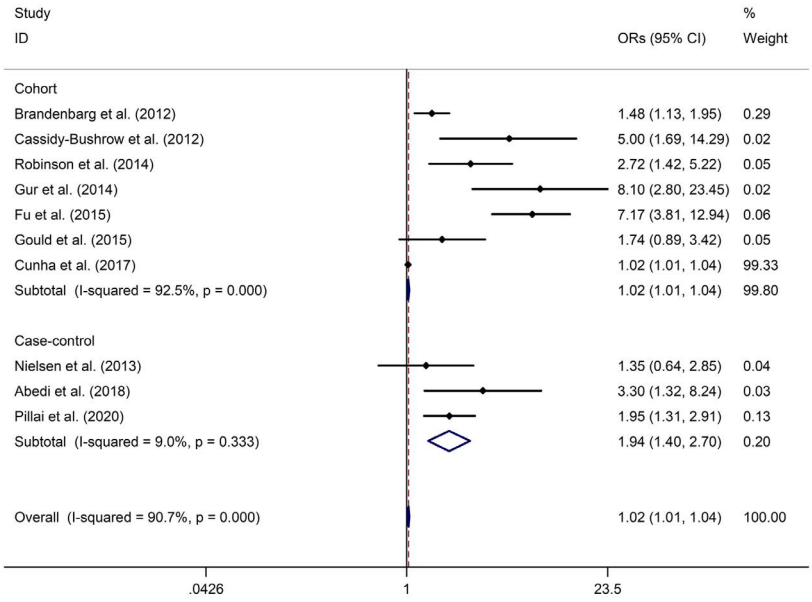

Figure 2. Subgroup studies regarding associations between circulating levels of 25-hydroxy (OH) vitamin D and risk of antenatal and postnatal depression in different types of studies.

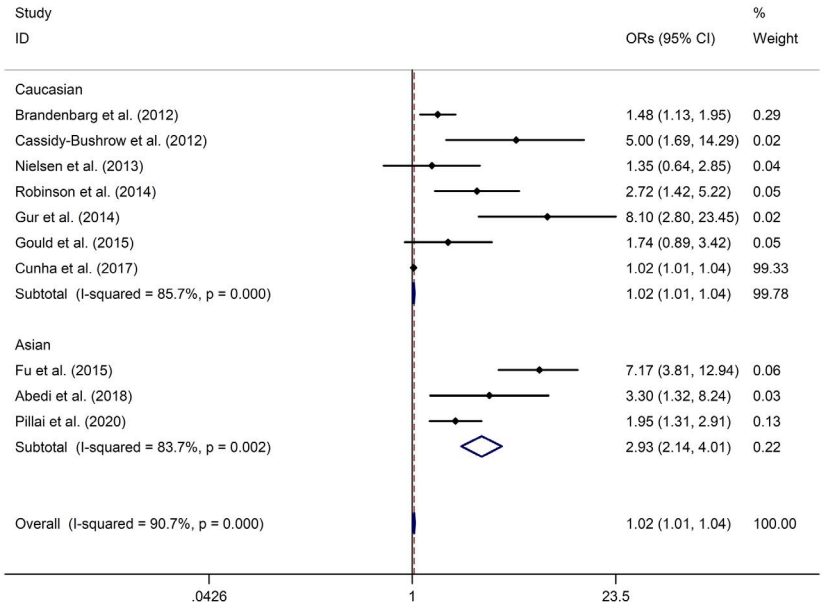

Figure 3. Subgroup studies regarding associations between circulating levels of 25-hydroxy (OH) vitamin D and risk of antenatal and postnatal depression in different ethnic groups.

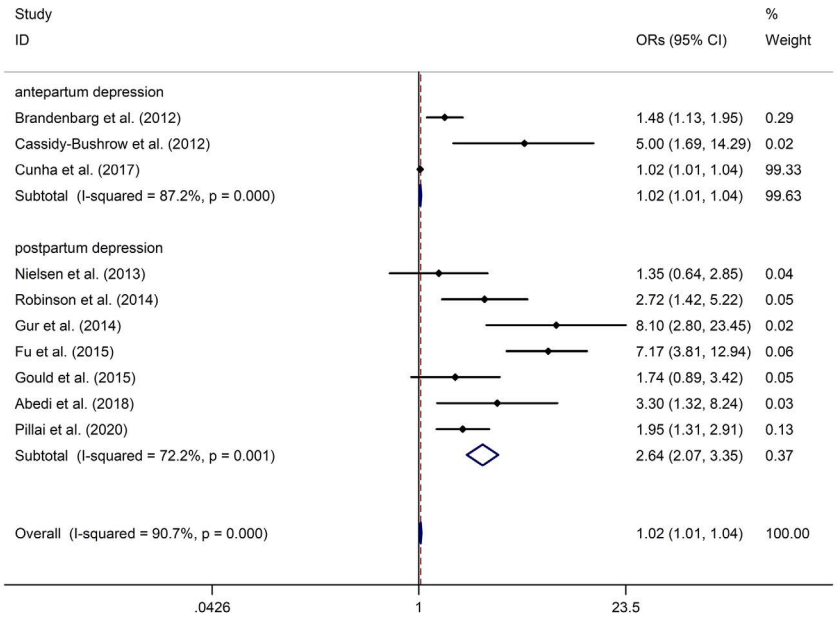

Figure 4. Subgroup studies regarding associations between circulating levels of 25-hydroxy (OH) vitamin D and risk of antenatal and postnatal depression.

Discussion

Our meta-analysis included 3 case-control studies and 7 cohort studies investigating the relationship between vitamin D deficiency and perinatal depression. Our results showed that there were strong associations between vitamin D deficiency and risk of antenatal and postnatal depression (OR = 1.02, 95% CI 1.01 to 1.04). And subgroup analysis also showed that compared with antenatal depression, there was a more significant positive association between vitamin D deficiency and postnatal depression (antenatal depression: OR = 1.02, 95% CI 1.01 to 1.04; postnatal depression: OR = 2.64, 95% CI 2.07 to 3.35). Our results were in line with a previous article published in 2018[24]. However, we just compared the different effects of high and low levels of serum 25-hydroxy (OH) vitamin D on the onset of depressive symptoms, and did not determine the accurate cut-off value of vitamin D deficiency.

The potential mechanism of high risk of perinatal depression in pregnant women with vitamin D deficiency are still unclear. A study published in 2018 showed that serum 25-hydroxy (OH) vitamin D levels were positively associated with peripheral grey matter volume. In addition, the dysmaturation of grey matter may partly explain the abnormalities of neural development[25]. One of the main functions of vitamin D is contributing to the calcium homeostasis. The vitamin D deficiency may lead to persistent increase in calcium, resulting in the onset of depression[26,27]. Another important function of vitamin D is regulating the synthesis of serotonin. In addition, depression is associated with the reduction of serotonin[28,29]. The hypothalamic-pituitary-gonadal (HPG) axis participate in the regulation of female reproductive cycle and sex hormone levels. Following a sudden estrogen drop after delivery, the reduction of maternal calcium deposits can affect gonadotropin-releasing hormone (GnRH), which played a role in fertility cycle and postpartum depression[30]. Several clinical studies have also demonstrated that vitamin D supplement can reduce depressive symptoms[31].

There were still some limitations in our study. First, the classification criteria of vitamin D is different in all included studies. We just compared the effects of highest and lowest levels of vitamin D on depression. Second, Begg's test, Egger's test and funnel plots showed a significant risk of publication bias, which may suggest that our results have been exaggerated. This may be because of lack of unpublished studies.

Conclusions

Our results have shown that the low level of vitamin D may be an adverse factor of antenatal and postnatal depression. However, whether pregnant women with vitamin D deficiency need extra supplement should be treated with caution. There remains a need for more randomized controlled trials and empirical studies to evaluate the role of vitamin D in the antenatal and postnatal depression.

Funding

No funding.

Conflicts of Interest

No conflicts of interests.

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