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Review

The association between gestational diabetes and postpartum depression: A systematic review and meta-analysis

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ABSTRACT

Aims: Postpartum period is a critical period for mothers, which is often accompanied by increased risk of depression. Many studies have evaluated the relationship between gestational diabetes (GDM) and postpartum depression (PPD), but contradictory results have been reported. Therefore, the present study was conducted to investigate the relationship between GDM and PPD.

Methods: This systematic review and meta-analysis was conducted based on PRISMA Guideline. We searched all the relevant epidemiological studies in international databases of Scopus, PubMed, Science Direct, Embase, Web of Science, CINAHL, Cochrane Library, EBSCO, and Google scholar search engine using the MeSH Keywords in English without time limit until 2018. The heterogeneity of the studies was calculated using the I^2 index and Cochran's Q test. Relative risk (RR) and 95% confidence interval (CI) were extracted from each study. The results of the study were analyzed using the random effects model and Comprehensive Meta-Analysis Software Version 2.

Results: A total of 18 studies with a sample size of 2,370,958 were reviewed. Meta-analysis results showed that GDM significantly increased the risk of PPD, and RR was 1.59 (95% CI: 1.22–2.07, p = 0.001). The RR for 15 cohort studies, 2 cross-sectional studies and 1 case-control study was 1.67 (95% CI: 1.22–2.28), 1.37 (95% CI: 0.91–2.05), and 1.29 (95% CI: 0.98–1.68), respectively.

Conclusions: GDM can be a risk factor for PPD. Therefore, PPD examination in pregnant women with GDM seems to be necessary.

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Contents

1. Introduction

Similar to pregnancy, the postpartum period is accompanied by psychological and physical changes in mothers [1]. Mothers experience a range of mental disorders in this period; from very mild to psychotic [2]. Postpartum depression (PPD) is one of the most common mental postpartum disorders. PPD is a kind of mood disorder associated with childbirth that can affect the mother and child. There may also be symptoms of disorder in sleep and appetite, loss of energy, feelings of worthlessness, or feelings of guilt or suicidal thoughts. It usually starts one week to one month after childbirth [2]. The prevalence of PPD in difference studies in different countries is reported to be 0–60% [3,4]. PPD has a significant negative effect on all aspects of the quality of life of the mother [5–7]. Continued impairment and lack of timely diagnosis of this disease may lead to the ineffective adaptation of the mother to the spouse and family, and consequently, the inability to fulfil maternal and paternal duties, which may finally lead to the tragedy of mother's suicide and infanticide if the disease is exacerbated [8,9]. From etiological point of view, there are various theories about the incidence of PPD that include biological, psychological, and social factors [10,11]. Diagnosis of this complication is a challenge due to common changes that occur in the postpartum period, including changes in sleep patterns, appetite changes, and excessive fatigue. Some studies have found that some of the medical problems in pregnancy predispose a person to PPD. Depression in people with diabetes, hypertension and preeclampsia occurs 5–10 times more [12].

Gestational diabetes mellitus (GDM) is the condition of glucose intolerance, and despite its incompatibility with the body, appears in the body of pregnant women with no history of diabetes. This is a common problem that causes serious problems for the mother and the baby. This disease usually appears between the 24th and 28th weeks of gestation, and at the same time, human placental lactogen is secreted from placenta, which causes insulin insensitivity in the mother [13]. The prevalence of GDM in the United States is estimated to be about 7% [14]. The most common adverse effects of this disorder include macrosomia, damage during childbirth, cesarean section, polyhydramnios, preeclampsia, and neonatal metabolic disorders [15]. The recurrence rate of GDM has been reported to be about 30–69% [16]. It seems that GDM provides a context for PPD through inducing disturbances in the hypothalamic–pitui tary–adrenal axis, inflammatory changes, and disorders in serotonergic regulation. According to the study of Abdollahi et al., there is a significant relationship between GDM and PPD [17], while this relationship was not significant in the study of Miller et al. [18]. Considering the uncertainty regarding the relationship between GDM and PPD and the controversial results, the present study was conducted to

determine the relationship between GDM and PPD in a systematic review and meta-analysis. A meta-analysis consists of specific statistical methods used to summarize the results of independent studies and to find the most accurate form of relationship between the variables under study, which helps to summarize the data of different articles with their different results and methods [19,20].

2. Methods

2.1. Study protocol

This study was conducted on the basis of PRISMA guideline for systematic review and meta-analyses [21]. All steps were carried out independently by two researchers. Investigation of the agreement between the results and cases of disagreement were resolved by the third researcher.

2.2. Search strategy

The primary epidemiologic studies published until 2018 without time limits were searched in Scopus, PubMed/Medline, Science Direct, Embase, Web of Science (ISI), CINAHL, Cochrane Library, EBSCO databases and the Google Scholar search engine using Medical Subject Heading (MeSH): (pregnancy OR postpartum period OR pregnant OR postnatal OR post-natal OR antenatal), (depression OR depressive disorder, major OR major depression OR depression, postpartum OR puerperal depression OR major depressive disorder OR MDD OR postnatal depression), (gestational OR insulin dependent diabetes OR non-insulin dependent diabetes OR pregnancy diabetes mellitus).

2.3. Inclusion and exclusion criteria

Inclusion criteria according to PICO (related to Evidence-Based Medicine) [22]: (1) Population: cross-sectional, case control or cohort studies that investigated the association between GDM and PPD; (2) Intervention: Serological test for confirmed GDM and self-reported questionnaire or ICD-10 for confirmed PPD; (3) Comparison: Studies that show the incidence rate of PPD in GDM patients compared to non-GDM patients; (4) Outcome: Studies that estimate the incidence of PPD in GDM patients.

Exclusion criteria:

(1) Studies with sample size with any mental illness in the 1-year period
(2) Studies in which data for women with GDM and PPD were combined with data for women with other conditions
(3) Studies that reported PPD based on measuring anxiety or bipolar disorder
(4) Studies that only reported fetal or newborn outcomes (*i.e.*, no maternal outcomes)
(5) Maternal outcomes other than PPD
(6) Letters to the editor without original data, review and case report or studies with non-human samples
(7) Duplicate studies.

2.4. Qualitative assessment

The modified Newcastle Ottawa Scale (NOS) checklist for non-randomized studies [23] was used. The quality of the studies was divided into three categories: low (less than 5 points), moderate (5–6 points) and high (7–8 points). In case of disagreement, group discussion was conducted. The minimum score for entering the meta-analysis process was 5.

2.5. Data extraction

Data extraction was done based on pre-prepared checklist, which included: study design, publication year, country, sample size, patient characteristics, definition or measures of PPD and GDM, and relative risk (RR) or odds ratio (OR) with 95% confidence interval (CI).

2.6. Exposure measurement

GDM is defined as the intolerance of different carbohydrates that are initiated during pregnancy or are the initial diagnosis during pregnancy [13].

2.7. Outcome measurement

PPD, also called postnatal depression, is a type of mood disorder associated with childbirth, which can affect both genders [10].

2.8. Statistical analysis

The results of the study were analyzed using Comprehensive Meta-Analysis Software Version 2. In analyzing the effect of GDM on PPD, RR or OR with 95% CI were used. Heterogeneity among studies was determined using Cochran's Q test and I^2 index. There are three classifications in this regard (less than 25%: low heterogeneity, 25–75%: moderate heterogeneity, and above 75%: high heterogeneity); therefore, the random effects model was used in cases of moderate and high heterogeneity. Subgroup analysis was done based on study type, study design, continent type and time of measuring PPD to find the cause of heterogeneity. Sensitivity analysis was also done by omitting a study at a time. The Egger and Begg's tests were used to evaluate the publication bias. The significance level of the test was considered to be P-value < 0.05.

3. Results

3.1. Search results

In this meta-analysis, 320 articles were identified by two researchers, and 160 duplicate articles were deleted. Finally, 18 articles entered the meta-analysis process (Table 1 and Fig. 1).

Table 1 – Summary of the included studies.

First author, publication years	Type of study	Definition/measures of depression	Timing of depression measures	Country	Continent	Sample size	RR (95%CI)	P-Value
Abdollah et a., 2014 [17]	Cohort prospective	Edinburgh Postnatal Depression Scale (EPDS) ≥ 12	Within 12 week after delivery	Iran	Asia	1449	2.93 (1.46–5.88)	0.0002
Berger et al., 2014 [24]	Cohort retrospective	EPDS ≥ 13 or did not answer "No" to self-harm question	Within 4 d after delivery	Pennsylvania	USA	322	12.1 (1.90–77.8)	–
Burgut et al., 2013 [25]	Cross-sectional	EPDS ≥ 12	Within 6 Month of delivery	Qatari	Asia	837	1.65 (1.02–2.69)	–
Burgut et al., 2013 [25]	Cross-sectional	EPDS ≥ 12	Within 6 Month of delivery	Arab	Asia	542	1.09 (0.63–1.91)	–
Dalfra et al., 2012 [26]	Cohort prospective	CES-D ≥ 16	Within 8 week after delivery	Italian	Europe	245	5.7 (4.2–7.3)	–
Katon et al., 2014 [27]	Cohort retrospective	Patient Health Questionnaire-9 (PHQ-9)	Within 6 week after delivery	Washington	USA	1423	0.68 (0.40–1.13)	–
Kim et al., 2005 [28]	Cohort prospective	Center for Epidemiologic Studies Depression Scale (CES-D) (cutoff NR)	Within 8–12 week after delivery	San Fran	USA	1445	1.22 (0.54–2.77)	–
Liu et al., 2012 [29]	Cohort prospective	Survey asking if diagnosed or discussed with Healthcare Provider (HCP)	Within 36 week after delivery	New York	USA	3748	0.80 (0.40–1.60)	–
Räisänen et al., 2013 [30]	Case-control retrospective	International Classification of Disease (ICD) 10 codes F31.3, F31.5, F32-34	Within 6 week after delivery	Finland	Europe	511,422	1.29 (0.99–1.69)	–
Sundaram et al., 2014 [31]	Cohort retrospective	survey of symptoms based on PHQ-2	N/A	Florida	USA	61,733	0.96 (0.64–1.52)	0.890
Walmer et al., 2015 [32]	Cohort prospective	ICD-9 codes 296.2, 296.3, 309.0, 309.1, 311, 300.4	N/A	Massac Hu	USA	18,888	1.46 (1.16–1.83)	–
Whiteman et al., 2015 [33]	Cohort retrospective	ICD-9-CM codes 293.83, 296.2, 296.3, 300.4, 301.12, 309.0, 309.1, 311	N/A	Florida	USA	1,057,647	1.44 (1.26–1.65)	–
Nahbandi et al., 2015 [34]	Cohort prospective	EPDS ≥ 12	Within 5wk after delivery	Iran	Asia	262	1.79 (1.37–2.20)	–
Hinkle et al., 2016 [35]	Cohort prospective	EPDS ≥10 or antidepressant medicine use after delivery	Within 6 week after delivery	US	USA	2802	4.62 (1.26–16.98)	–
Miller et al., 2016 [18]	Cohort prospective	PHQ-9	N/A	Chicago	USA	305	0.74 (0.33–1.66)	–
Silverma et al., 2017 [36]	Cohort prospective	ICD-10	N/A	Sweden	Europe	707,701	1.70 (1.36–2.13)	–
Zwolinska et al., 2017 [37]	Cohort prospective	(ICD-10) and Hospital Anxiety and Depression Scale (HADS)	Within 6 week after delivery	Poland	Europe	70	1.33 (0.56–3.19)	0.512
Varela et al., 2017 [38]	Cohort prospective	dEPDS ≥ 12	N/A	Greece	Europe	117	4.69 (1.07–20.64)	–

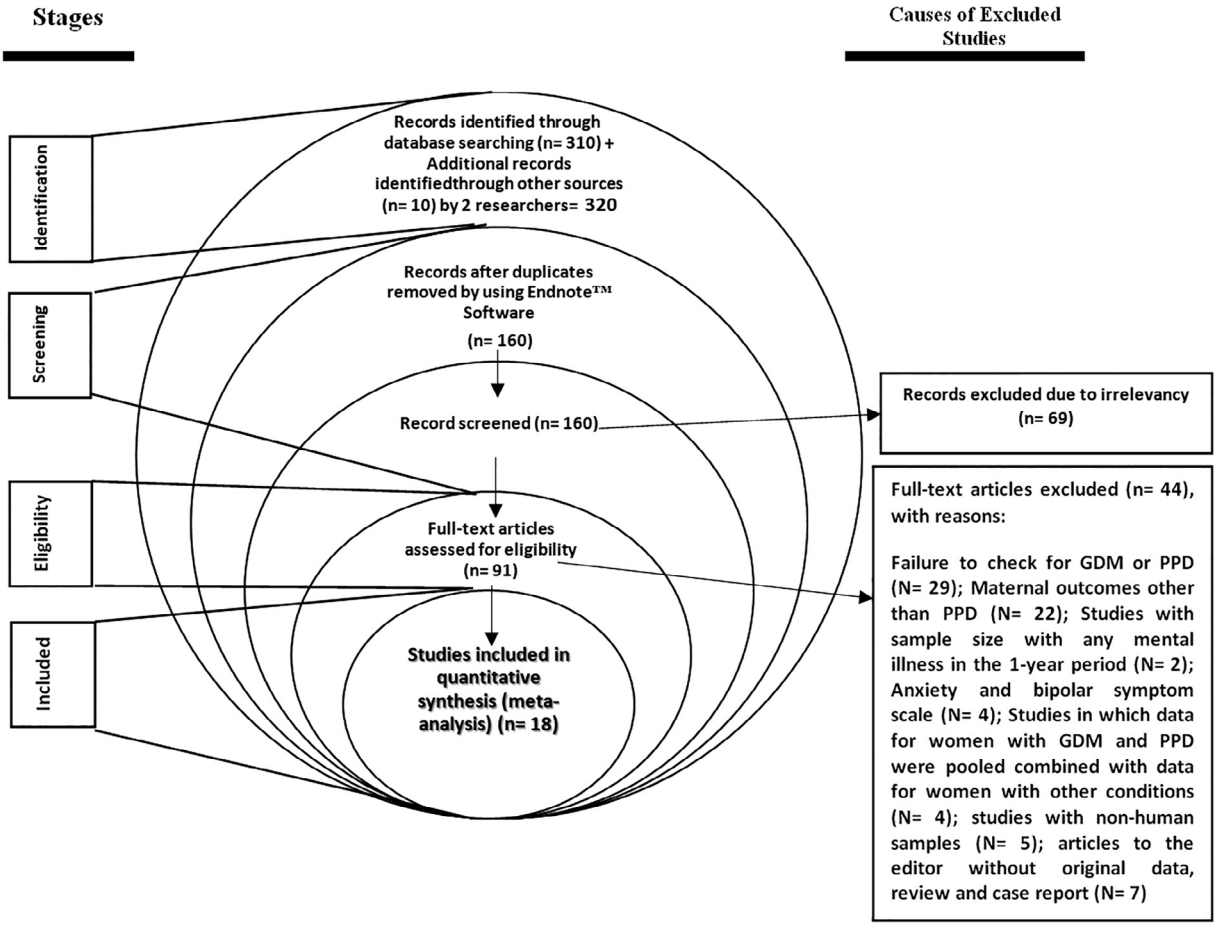

Fig. 1 – The flowchart of the literature search for the systematic review of studies.

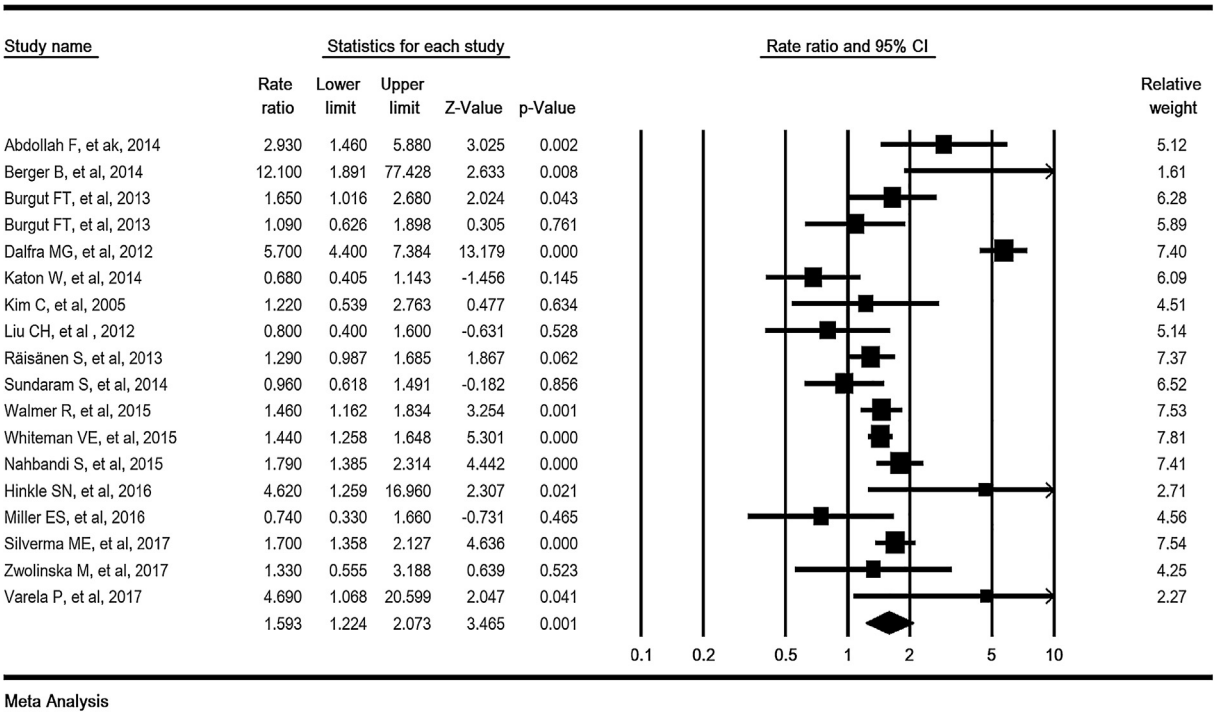

Fig. 2 – Relationship between gestational diabetes mellitus and postpartum depression. CI: Confidence interval

Table 2 – Relationship between gestational diabetes mellitus and postpartum depression by subgroups.

Variable		Studies (N[a])	Heterogeneity		RR[b]	95% CI[c]
			I^2	P-Value		
Type of Study	Cohort	15	89.25	0.001	1.67	1.22–2.28
	Case-control	1	0.000	0.062	1.29	0.98–1.68
	Cross-sectional	2	17.82	0.125	1.37	0.91–2.05
Test for subgroup differences: Q = 1.56, df(Q) = 2, P-value = 0.457						
Study design	prospective	11	89.08	0.002	1.87	1.25–2.79
	retrospective	5	73.90	0.285	1.19	0.86–1.64
	momentary	2	17.8	0.125	1.37	0.91–2.05
Test for subgroup differences: Q = 2.98, df(Q) = 2, P-value = 0.224						
Type of continent	USA	9	65.97	0.192	1.19	0.91–1.56
	Europe	5	94.63	0.022	2.28	1.12–4.62
	Asia	4	39.58	0.0001	1.70	1.26–2.29
Test for subgroup differences: Q = 4.6, df(Q) = 2, P-value = 0.096						
Time of measuring postpartum depression	≤10	7	92.30	0.031	2.20	1.07–4.54
	>10	4	63.62	0.154	1.42	0.87–2.33
	N/A	7	45.79	0.0001	1.40	1.20–1.63
Test for subgroup differences: Q = 1.47, df(Q) = 2, P-value = 0.479						

[a] Number.
[b] Relative risk.
[c] Confidence interval.

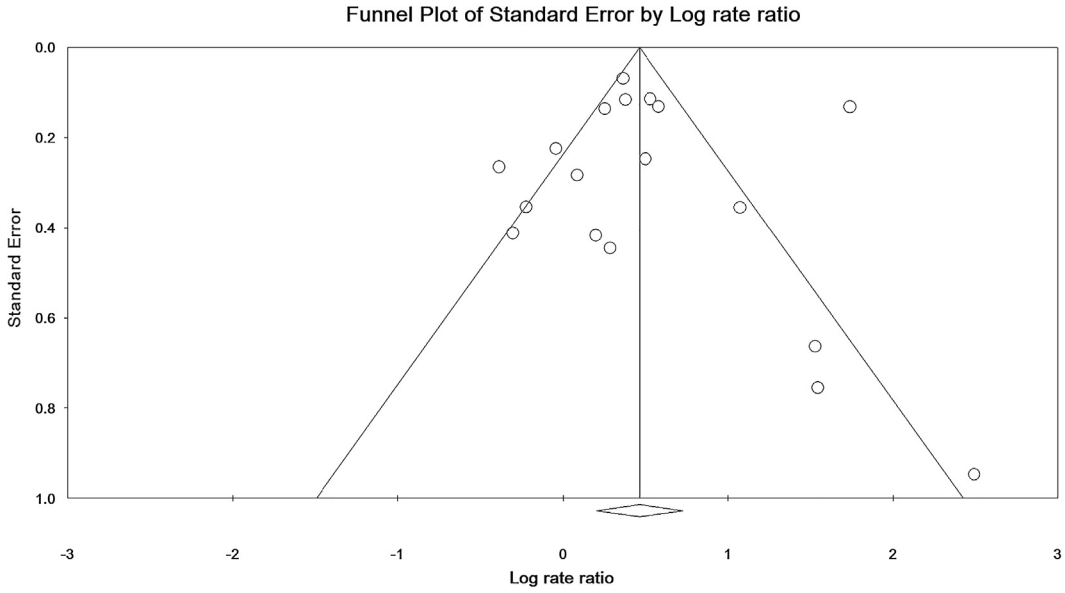

Fig. 3 – Funnel plot for detection of publication bias for the relationship between gestational diabetes and postpartum depression.

3.2. *The association between GDM and PPD*

In a review of 18 studies with a sample size of 2,370,958, the meta-analysis results showed that GDM significantly increased the risk of PPD with (RR = 1.59 [95% CI: 1.22–2.07, p = 0.001]) (Fig. 2). In addition, heterogeneity rate was significant (Heterogeneity test: P = 0.001, I^2 = 87.50%).

3.3. *Relationship between GDM and PPD by subgroups*

3.3.1. *Based on the type of study*

A total of 15 cohort studies, 2 cross-sectional studies and one case-control study were found with (RR = 1.67 [95% CI: 1.22–2.28, p = 0.001]), (RR = 1.37 [95% CI: 0.91–2.05, p = 0.125]), and (RR = 1.29 [95% CI: 0.98–1.68, p = 0.062]) respectively. That

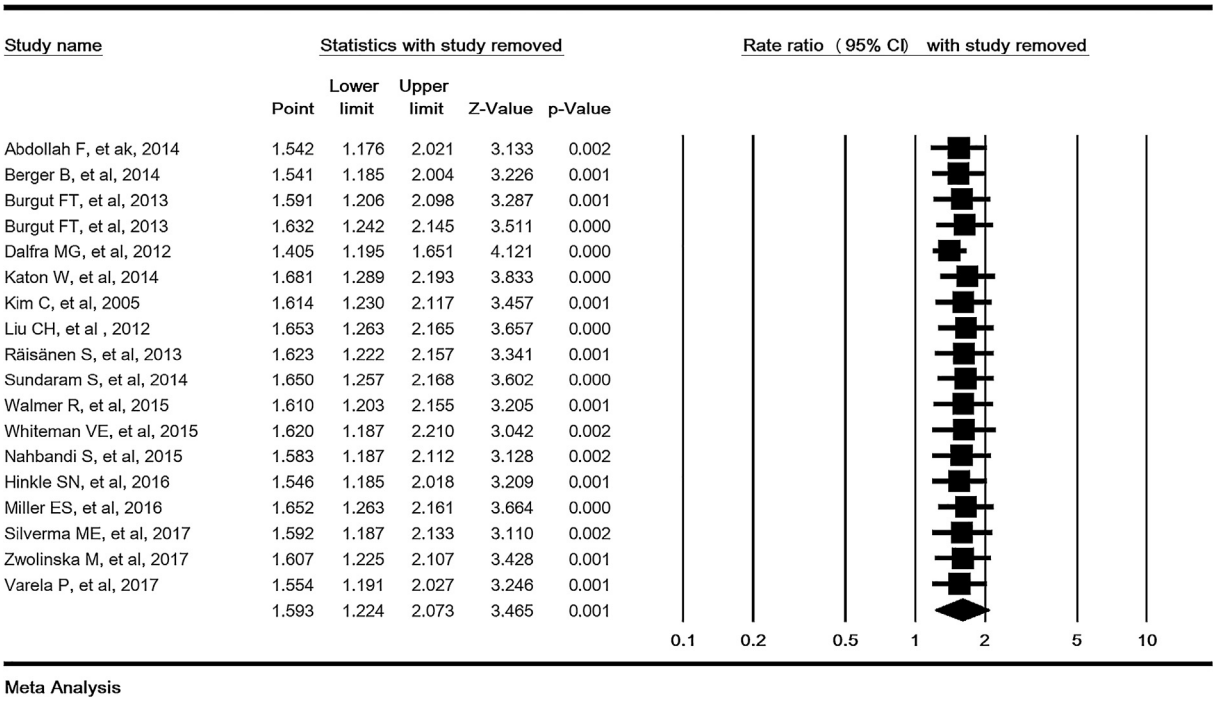

Fig. 4 – Sensitivity analysis for the relationship between gestational diabetes and postpartum depression. CI: Confidence interval

result showed the relationship between GDM and PPD was significant only in cohort studies (Table 2).

3.3.2. *Based on study design*

A total of 11 prospective studies, 5 retrospective studies, and 2 momentary studies were found, in which 95%CI and RR were as follows to respectively: (RR = 1.87 [95% CI: 1.25–2.79, p = 0.002]), (RR = 1.19 [95% CI: 0.86–1.64, p = 0.285]), and (RR = 1.37 [95% CI: 0.91–2.05, p = 0.125]). That results showed the relationship GDM and PPD were significant only in prospective studies (Table 2).

3.3.3. *Based on continent*

A total of 9 studies were conducted in the USA, 5 studies in Europe and 4 studies in Asia, whit RR and 95% CI were as follows to respectively: (RR = 1.19 [95% CI: 0.91–1.56, p = 0.192]), (RR = 2.28 [95% CI: 1.12–4.62, p = 0.022]), and (RR = 1.70 [95% CI: 1.26–2.29, p = 0.0001]). And results showed that the association between GDM and PPD was significant in the Asian and European studies (Table 2).

3.3.4. *Based on the time of measuring PPD*

PPD was measured before the tenth week in 7 studies, it was measured after the tenth week in 4 studies and the time of measurement was unclear in 7 studies, with RR and 95% CI were as follows to respectively: (RR = 2.20 [95% CI: 1.07–4.54 , p = 0.031]) (RR = 1.42 [95% CI: 0.87–2.33, p = 0.154]), and (RR = 1.40 [95% CI: 1.20–1.63, p = 0.001]). The results showed that the association between GDM and PPD was significant in studies in which PPD was measured before the tenth week and studies in which the time of measurement was unclear (Table 2).

3.4. *Publication bias*

The Egger's test has more power to detect the publication bias, and the p-values in the Begg's test and Egger's test were p = 0.197 and p = 0.978, respectively, suggesting that there was no publication bias (Fig. 3).

3.5. *Sensitivity analysis*

Sensitivity analysis by omitting a study at a time showed that omission of one study has no effect on the pooled estimate (Fig. 4).

4. Discussion

The present study is the first systematic review and meta-analysis on the relationship between GDM and PPD. There were no significant relationships between GDM and PPD in a number of studies [18,27–31,37], while in some studies, this relationship was significant [17,24–26,32–36,38]. The present study showed that GDM increases the risk of PPD with relative risk and confidence intervals of 1.59 (95%CI: 1.22–2.07). Although there are some preliminary studies in this area, no final decision has been made on the association between GDM and PPD. In this study, considering the systematic review of all documents and their combination through meta-analysis, this relationship was investigated, and the existence of such relationship was indicated. Moreover, the possible mechanisms that justify the association between GDM and PPD can be the disturbance of the hypothalamic–p ituitary–adrenal axis, inflammatory changes, disorders in serotonergic regulation, the effects of hyperinsulinemia on

the thyroid and the mental stress caused by the treatment of chronic disease [19,39].

P-value of publication bias for GDM and PPD according to Begg and Egger's tests were p = 0.197 and p = 0.978, respectively, and publication bias did not affect the results of studies. It is assumed that the observed differences are due to different sampling and also the difference in the measured parameters in different societies.

One of the strengths of this study is that the majority of studies that entered the meta-analysis process were of prospective cohort type, and evaluation of the mimicking symptoms of depression, such as thyroid disorders and anemia was done. Regarding the limitations of the study, it can be noted that a number of studies on PPD only used self-reporting tools, inability of national databases to search for a combination of keywords. Some studies, such as medical theses and studies with inadequate data, were excluded from the study due to poor quality. Several studies were also omitted due to lack of reporting articles of the same nature and publication bias.

5. Conclusion

GDM can be a risk factor for PPD. Therefore, PPD testing in pregnant women with GDM seems to be necessary.

Conflict of interest

There is no conflict of interest.

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