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REVIEW – OPEN ACCESS

The Association Between Placenta Previa and Pre-Eclampsia: A Meta-Analysis

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ABSTRACT

There are contradicting results regarding the effect of previa on pre-eclampsia. Therefore, the aim of the present study was to systematically review the relevant literatures and to determine the association between placenta previa and pre-eclampsia in pregnant women. Electronic scientific databases including Scopus, PubMed, and Web of Science were searched to identify relevant published studies. Two independent authors studied the selected studies and extracted data. I^2 statistics was used to assess the variation across studies. The random effects model was used to assess pooled effect sizes. Data were analyzed through Stata software version 12. The results of the present meta-analysis of nine studies indicated a significant relationship between placenta previa and risk of pre-eclampsia. The odds of pre-eclampsia were 0.55 (95% confidence interval (CI) 0.26–0.85) in placenta previa cases compared with the control groups and 0.17 (95% CI 0.07–0.27) in studies with adjustment on confounder variables. Our results showed that placenta previa is associated with a decrease incidence of pre-eclampsia.

Keywords: Placenta previa, pre-eclampsia, pregnancy

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INTRODUCTION

Pre-eclampsia, as a result of hypertension and proteinuria, occurs in pregnant women (1). This complication is distinguished by severe pregnancy complications, such as epigastric pain, impaired liver function, thrombocytopenia, red blood cell breakdown, and impaired kidney function (2). Pre-eclampsia occurs in 2%–8% of all pregnancies (3). As shown in previous studies, it is associated with diabetes mellitus, obesity, overweight, maternal advance age, nulliparity, hypertension, hypothyroidism, angiogenic factors, renal disease, and family history of pre-eclampsia (4–7).

The association between placenta previa and pre-eclampsia was investigated in a previous study (8). In some cases with pre-eclampsia, disruption of blood flow from the uterus to the placenta was observed (9), but in placenta previa, the blood flow is plentiful (10). Therefore, the preventive roles of placenta previa on pre-eclampsia need more investigation. The inconsistent results of this association are more than the consistent results. Hasegawa reported that pre-eclampsia does not occur in pregnant women with placenta previa (11). Some other studies had reported a 50% reduction in pre-eclampsia in these women (12). Jelsema did not find any relationship between placenta previa and the incidence of pre-eclampsia (13). In all mentioned studies, the sample size was small, and therefore designing a meta-analysis study can offer reliable results about the association between placenta previa and pre-eclampsia.

To the best of our knowledge, this is the first meta-analysis that enrolled all of the eligible studies to obtain the acceptable sample to investigate the association between placenta previa and pre-eclampsia in pregnant women.

MATERIALS and METHODS

Data Sources

This meta-analysis was conducted to assess the association between placenta previa and pre-eclampsia in pregnant women. PRISMA statement checklist was used to enhance the quality of reporting (14). We had done search for relevant studies in international databases including Scopus, Web of Science, and PubMed without any restriction in time.

Search Strategy

The main terminologies in the search strategy were ("placenta praevia" [Title] OR "placenta previa" [MeSH terms]) OR ("placenta" [Title] AND "previa" [Title]) OR ("placenta previa" [Title]) AND ("pre-eclampsia" [MeSH terms] OR "pre-eclampsia" [Title] OR "pre-eclampsia" [Title]).

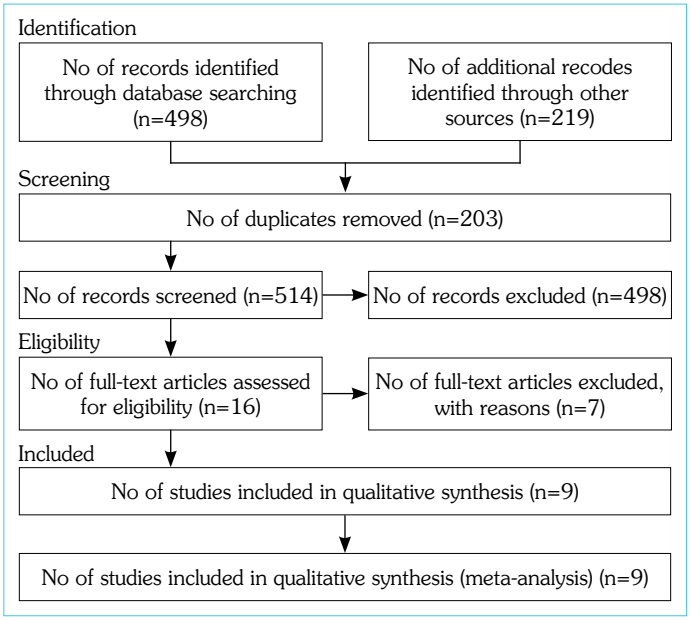

Figure 1. Diagram of studies through the different phases of the systematic review

Inclusion and Exclusion Criteria

By systematic search, all of full texts that reported an association between placenta previa and pre-eclampsia in pregnant women were enrolled in the study. After that, the authors reviewed the full texts and duplicated results from the same population, and low-quality papers that gained low score, <7 points by Newcastle–Ottawa Scale (NOS) assessing, were excluded from the study.

Data Extraction

Primary search was done by two independent authors (EJ and SK), checking of relevant studies according to title/abstract was performed by all of the authors, and disagreements were resolved by discussion till they reach a consensus. By the three main steps including review of title, abstract, and full text of articles, irrelevant studies were excluded. The data extraction form that contains independent and dependent variables was used to decrease the mistakes in data collection. The data extraction form was filled out for final studies to be enrolled in the meta-analysis. Data in the designed extraction form were years of publications, first author name, country of origin, design of study, study sample size, odds ratio (OR) and 95% confidence interval (CI), adjustment, age (mean or range), and quality of papers.

Quality Assessment

The qualities of papers were assessed by the NOS (15). After scoring, the articles were divided to low-quality papers (scoring <7 points) and high-quality papers (scoring ≥7 points).

Statistical Analysis

Data were analyzed using Stata software, version 12 (Stata Corp., College Station, TX, USA). Heterogeneity in enrolled studies was checked by I^2 statistic. The heterogeneity was in high range (I^2 higher than 75%), and therefore random effects model was used to assess effect sizes. Publication bias test used Begg's and Egger's test in the included studies (16).

RESULTS

Description of Studies

We enrolled 717 records in the initial search based on our predefined search strategy. After removing duplicates, we had determined eligible articles through title, abstract, and full-text evaluation. Overall, nine studies were identified for inclusion in the analysis. The diagram of the included studies is presented in Figure 1.

Three studies were case–control (8, 17, 18), five studies were cohort (13, 19–22), and one study was cross-sectional (23). The total sample size in the present meta-analysis was 752,243 participants. All of the studies were published in English (Table 1).

The potential confounders regarding the association between placenta previa and pre-eclampsia were maternal age, maternal weight, gravidity, previous cesarean section, parity, and gestational age at delivery.

Main Analysis

The association between placenta previa and pre-eclampsia is shown in Figure 2. The present meta-analysis of the eight included studies reported a significant association between placenta previa and pre-eclampsia (OR 0.55, 95% CI 0.26–0.85). The considerable heterogeneity was shown among these studies (I^2=82.8%, p<0.001).

There was symmetry in the funnel plot. Therefore, we did not find

Table 1. Summary results of the included studies

1st aut, year	Country	Design	Sample size	Estimate	Adjustment	Age (mean or range)	Quality
Adam, 2013	Sweden	Case-control	54339	OR	Adjusted	28.7	High
Brenner, 1978	USA	Pros. cohort	31070	OR	Crude	27.1	High
Dawood, 2017	Pakistan	Pros. cohort	374	OR	Crude	27.2	Low
Newton, 1984	USA	Case-control	276	OR	Crude	24.4	High
Raisanen, 2014	Sweden	Cross-sectional	596562	OR	Crude	30.3	High
Ying, 2016	China	Ret. cohort	3174	OR	Adjusted	29.9	High
Jelsema, 1991	USA	Ret. cohort	6576	OR	Adjusted	35.8	High
Harper, 2010	USA	Ret. cohort	59149	OR	Crude	35.5	High
Lucovnik, 2012	Slovenia	Case-control	723	OR	Crude	30.0	High

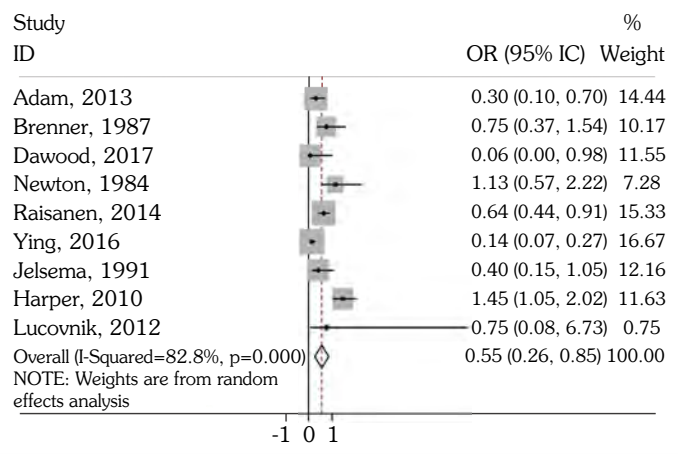

Figure 2. Forest plot of the association between placenta previa and pre-eclampsia

Table 2. Results of subgroup analysis of placenta previa on pre-eclampsia

Subgroups	Studies		
	No. of studies	OR (95% CI)	I^2
Crude	6	0.78 (0.35, 1.20)	70.7%
Adjust	3	0.17 (0.07, 0.27)	2.4%

OR: Odd ratios; CI: Confidence interval

publication bias. The p values for Begg's and Egger's regression were 0.533 and 0.252, respectively.

Subgroup Analysis

The subgroup analysis was performed based on how to deal with confounders (crude/adjusted) in retrieved studies. The pooled results in crude and adjusted studies were 0.78 (95% CI 0.35–1.20) and 0.17 (95% CI 0.07–0.27), respectively. A significant correlation in adjusted studies was found. There was no heterogeneity in the subgroup-adjusted studies (Table 2).

Quality of the studies

Except for one study, all other observational studies had high-quality according to the NOS (Table 1).

DISCUSSION

In this meta-analysis, for the first time, we assessed the association between placenta previa and pre-eclampsia in nine individual studies. Findings of the study revealed that there is a significant negative association between placenta previa and pre-eclampsia. Pooled estimate of the included studies showed that the overall odds of pre-eclampsia were 0.55 (95% CI 0.25–0.85) in placenta previa cases compared with the control groups and 0.17 (95% CI 0.07–0.27) in studies with adjustment on potential confounders.

Symptomatic placenta previa (bleeding) is related to a threefold increase in neonatal mortality rate compared with normal placenta (24). In addition, the volume of blood vessels of the placenta villi is considerably higher in placenta previa than in normal placenta (25). Weiner et al. in 2019 reported symptomatic placenta previa in relation to increased placenta malperfusion lesions, proposing a relationship of maternal malperfusion with abnormal placenta separation. The simultaneous finding of retro-placenta hemorrhage with symptomatic placenta previa can be shown as an indicator for more severe placenta separation, suggesting a relationship with adverse fetal outcomes (26).

The effect of placenta previa on the reduction risk of pre-eclampsia has not yet been well proven. A possible pathophysiologic mechanism for the protective effect of placenta previa is that the placenta implantation at or over the cervical os gains a greater reserve of oxygen and blood than normal placenta. Therefore, hypoxemia, because of the shallow implantation of the placenta, can be decreased, and vascular repair can be eased (27). In addition to the altered placenta perfusion role in pregnant women with placenta previa, the trophoblasts attached in the lower uterine segment and infiltrated the helicine arteries more easily (12).

Consistent with the literatures (28–30), our results showed that pregnancy with placenta previa is associated with low occurrences of pre-eclampsia and low maternal blood pressure. Evidences show that in pregnant women with placenta previa, women with pre-eclampsia had no higher incidence of fetal growth restriction than women without pre-eclampsia. These findings may be due to increased placenta blood supply in pregnant women with placenta previa (22).

The placental location (fundal and lateral) except previa is associated with adverse outcomes in mothers and neonates. Granfors et al. in 2019 reported that the fundal and lateral placenta locations compared with the posterior placenta are associated with adverse outcomes during pregnancy and delivery for mother and child. Furthermore, lateral placental location was related to pre-eclampsia and severe postpartum hemorrhage (31).

However, our study has some limitations. First, the majority of studies were conducted at more advance countries, so that from eight included study, four of them were conducted in the USA and two in Sweden; therefore, the generalizability of findings to all other settings is doubtful. Second, only in three studies adjustment had been made on confounders, so our overall estimated OR is susceptible to the effect of confounders. Finally, the provided data by the included studies to the meta-analysis were not adequate to implement some subgroup analyses to handle the effects of confounding variables.

CONCLUSION

In summary, our results showed that placenta previa is associated with a decline in incidence of pre-eclampsia.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – EJ, SK; Design – EJ, YV; Supervision – EJ; Data Collection and/or Processing – EJ, YV; Analysis and/or Interpretation – EJ, SK; Literature Search – YV, EJ, SK; Writing – EJ, SK, YV; Critical Reviews – EJ, SK, YV.

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