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Original Paper

Previous Cesarean Section and the Risk of Preeclampsia: A Meta-analysis

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ABSTRACT

Introduction: Preeclampsia is a common pregnancy complication with the multisystem variable disorder. Yet, the literature has not been systematically reviewed for the relationship between previous cesarean section and the risk of preeclampsia.

Objective: This study aimed to identify the relationship between previous cesarean delivery and the risk of preeclampsia.

Materials and Methods: This study was a systematic review and meta-analysis. PubMed, Scopus, ProQuest, and Web of Sciences were searched to identify eligible observational studies until May 25, 2019. The odds ratio (OR) and 95% confidence intervals (CI) were calculated as random effect estimates of association among studies. The quality of the included studies was examined based on the Newcastle-Ottawa scale.

Results: This study included 7 eligible articles (2 studies with a case-control design, 4 with a cohort design, and 1 with a cross-sectional design). The meta-analysis results showed an increased risk of preeclampsia in the women with previous cesarean section compared to women without cesarean section (OR=1.28, 95% CI, 1.15%-1.41%, P=0.001), I^2=37.2%. The quality of all studies except one study was high based on the Newcastle-Ottawa scale. The subgroup analysis was conducted based on the adjusted form of studies. The crude and adjusted studies were 1.29 (95% CI, 0.13%-2.46%, P=0.2) and 1.29 (95% CI, 1.22%-1.36%, P=0.001), respectively.

Conclusion: These findings showed that previous cesarean section is a risk factor for preeclampsia. Therefore, education programs and interventions should be considered to reduce elective cesarean section on maternal requests.

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Highlights

- Preeclampsia is a common complication of pregnancy with the multisystem variable disorder.
- Preeclampsia can cause maternal and fetal morbidity and death by affecting multiple organ systems.
- The results of studies have shown the relationship between previous cesarean delivery and the risk of preeclampsia.
- This meta-analysis determined the association between previous cesarean section and preeclampsia.

Plain Language Summary

Preeclampsia is a common pregnancy complication characterized by new-onset hypertension, edema, and proteinuria during pregnancy or immediately after delivery. Preeclampsia can cause maternal and fetal morbidity and death by affecting multiple organ systems. Cesarean-induced scar in the uterus can affect placenta implantation in a subsequent pregnancy. Abnormal uteroplacental blood flow and unusual trophoblastic invasion due to uterine changes in previous cesarean section may result in preeclampsia in subsequent pregnancies. This study aimed to identify the relationship between previous cesarean delivery and the risk of preeclampsia. We searched terms in PubMed, Scopus, ProQuest, Web of Sciences, and Google Scholar databases to identify eligible studies until May 25, 2019. This meta-analysis study showed an association between previous cesarean section and preeclampsia. These findings indicated that previous cesarean section is a risk factor for preeclampsia. We found a 28% increased risk for preeclampsia in women with previous cesarean section. This issue should be considered, especially for pregnant women who undergo cesarean delivery based on their request without any maternal or fetal indication.

Introduction

Preeclampsia is a common pregnancy complication with the multisystem variable disorder, characterized by new-onset hypertension, edema, and proteinuria during pregnancy or immediately postpartum [1-4]. It affects about 2% to 8% of pregnancies, and in the second half of pregnancy, it is responsible for over 70000 maternal deaths and 500000 fetal deaths worldwide every year [4]. A blood pressure measurement greater than 140/90 mm Hg on two separate loads and urinary protein excretion exceeding 300 mg/d are clinical signs of clinical diagnosis [5]. The etiology of preeclampsia is complicated, and factors of the maternal and fetal and or paternal genetic determinants have the main role [6].

Preeclampsia can cause maternal and fetal morbidity and death by affecting multiple organ systems [7-9]. The risk of preeclampsia is increased in women with a previous history of preeclampsia, chronic and gestational diabetes, parity, multiple pregnancies, nulliparity, family history, body mass index before pregnancy, maternal age ≥40 years, autoimmune disease, renal disease, chronic hypertension, and angiogenic factors [7, 10, 11].

Delivery can reduce most signs and symptoms of preeclampsia. In addition, preeclampsia can persist after delivery and develop during the postpartum period. In the peripartum period, preeclampsia is related to an increased risk of peripartum cardiomyopathy that can progress to chronic heart failure, cardiac transplantation, or death [12].

Evidence suggests that previous uterine scars can lead to placental-related complications such as abnormal placental abruption, preeclampsia, and preterm delivery [13-15]. It also appears that the initial pathology in preeclampsia is associated with maternal-fetal problems [16]. It is acknowledged that cesarean delivery is the most common surgery in obstetrics, and its rate continues to rise worldwide [17, 18]. Cesarean-induced scar in the uterus can affect placenta implantation in a subsequent pregnancy [19]. Abnormal uteroplacental blood flow and unusual trophoblastic invasion due to uterine changes in previous cesarean section may result in preeclampsia in subsequent pregnancies [20]. The results of studies have shown the relationship between previous cesarean delivery and the risk of preeclampsia [14, 20, 21].

Yet, the literature has not been systematically reviewed the relationship between previous cesarean section and the risk of preeclampsia. Therefore, the present meta-analysis study was designed to identify the relationship between previous cesarean delivery and the risk of preeclampsia.

Materials and Methods

This study was a systematic review and meta-analysis. We utilized a modified form of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist as a guide to enhance the quality reporting of the review. The literature search was conducted by the following keywords: (Previous cesarean section OR prior cesarean section OR previous cesarean OR prior cesarean) AND (preeclampsia OR preeclampsia OR pregnancy toxemia OR edema-proteinuria-hypertension gestosis) and based on MeSH database. The major international databases PubMed, Scopus, ProQuest, Web of Sciences, and Google Scholar search engine were searched to identify eligible studies from 1987 until May 24, 2022. We also searched gray literature, conferences, and references in the retrieved studies to find studies.

All studies that determined the association between previous cesarean section and the risk of preeclampsia were considered for inclusion in the present meta-analysis. The inclusion criteria were observational studies (case-control, cohort, and cross-sectional) that explained the association between previous cesarean section and the risk of preeclampsia. Review studies, letters to the Editor, and case reports were excluded from our research.

Two independent authors (EJ and SA) reviewed the retrieved studies, and the following information was extracted: (1) name of the first author, (2) publication year and location of study conduction, (3) total sample size, (4) age of maternal, (5) estimated odds ratio/risk ratio and (95% CIs), and (6) adjustment status (crude/adjusted). Any disagreements were resolved by discussion among researchers. The subgroup analysis was conducted based on the adjusted form of studies.

To assess the quality of the included studies, the present meta-analysis conducted the Newcastle-Ottawa scale (NOS). It has 8 items and uses a star system to assess the quality of studies. According to this scale, studies range between 0 and 9 stars, and scores of the papers were divided into low quality (<7 points) and high quality (≥7 points) [22]. Two investigators performed the quality assessment independently. Any disagreement was resolved by discussion between the authors.

We used Stata software, version 14 for the management and analysis of data. In this study, we evaluated the association between previous cesarean section and the risk of preeclampsia based on the odds ratio (OR) and its 95% confidence interval. A random-effects model was used to analyze of data. We assessed heterogeneity across studies by using the I^2 statistic. The values were 75%, 50%, and 25% based on cut-off points for high, moderate, and low heterogeneity. Publication bias was evaluated by Begg and Egger tests.

Results

We included 1384 studies via electronic databases based on search strategy and 241 studies via checking reference lists. We did not find new studies via searching conference databases. There were 523 duplicate studies. We excluded 1088 studies after reading the title and abstract, and 14 studies were considered for reading full papers. In the end, 7 studies were included in the present meta-analysis (Figure 1). These studies were four cohort studies [15, 20, 23, 24], two case-control [21, 25], and one cross-sectional [26] involving 423940 participants. In this systematic review, 4 studies out of 7 were adjusted based on confounding variables. Three studies were performed in Asia, 2 in America, and 2 in Africa (Table 1). The effect of previous cesarean section exposure on preeclampsia was determined by OR (Figure 2). The findings of studies showed an increased risk of preeclampsia in women with previous cesarean section compared to women without cesarean section: (OR=1.28, 95% CI, 1.15%-1.41%, P=0.001). The heterogeneity was low (I^2=37.2%). The quality of studies was assessed, according to the NOS. The quality of all studies except one study was high.

The subgroup analysis was conducted based on the adjusted form of studies. ORs in crude and adjusted studies were reported at 1.29 (95% CI, 0.13%-2.46%, P=0.2) and 1.29 (95% CI, 1.22%-1.36%, P=0.001), respectively. A significant association was found in crude studies, and the heterogeneity among adjusted studies was low (I^2=2.4%) (Figure 3).

The heterogeneity between studies was evaluated by the I^2 statistics. There was moderate heterogeneity among the results of the studies. There was no publication bias among studies confirmed by Begg and Egger tests (P=0.099 and P=0.280, respectively).

Table 1. Characteristics of included studies in the present meta-analysis

1st author, y	Country	Design	Sample size	OR (Lower-Upper 95% CI)	Estimate	Adjustment	Maternal age (y)	Quality of studies
Saadat, 2007 [25]	Iran	Case-control	250	0.77 (0.43, 1.38)	Odds ratio	Crude	Control group: 39.2±2 Case group: 37.2±2	Low
Ventura Laveriano, 2013 [15]	Peru	Cohort	30935	1.40 (1.20, 1.60)	Odds ratio	Adjusted	Not reported	High
Tandu-Umba, 2014 [26]	Congo	Cross-sectional	2086	1.70 (1.10, 2.50)	Odds ratio	Adjusted	28.1	High
Cho, 2015 [20]	Korea	Cohort	222137	1.23 (1.08, 1.40)	Odds ratio	Adjusted	30.9	High
Dammavalam, 2017 [21]	India	Case-control	950	2.08 (1.14, 3.77)	Odds ratio	Crude	Not reported	High
Mbah, 2007 [24]	USA	Cohort	166712	1.28 (1.20, 1.37)	Odds ratio	Adjusted	Not reported	High
Iyoke, 2014 [23]	Nigeria	Cohort	870	6.67 (1.50, 9.73)	Odds ratio	Crude	32.3	High

Discussion

The findings of this meta-analysis presented a significant association between previous cesarean section and the risk of preeclampsia. We reported a 28% increased risk for preeclampsia in women with previous cesarean section. The heterogeneity among studies was low. According to the NOS, the quality of studies was high, except for one study. The subgroup analysis was based on the adjusted form of studies. OR in crude and adjusted studies were reported at 1.29 and 1.29, respectively.

Preeclampsia leads to inefficient uteroplacental blood loss, negatively affecting perinatal outcomes [27]. A study has reported several fetal complications from placental ischemia: intrauterine growth restriction (IUGR), oligohydramnios, fetal instability, and placental abruption. As a result, these complications increase the risk of premature delivery, whether spontaneous or indicated [28].

The association mechanism between previous cesarean section and the risk of preeclampsia is unclear. The initial pathology in preeclampsia is associated with maternal-fetal complications. It is determined by the invasion of poor trophoblastic of the uterine and changes in uteroplacental blood flow [16]. In addition, it has been reported that a previous cesarean was associated with unexplained stillbirth in a subsequent pregnancy. It has

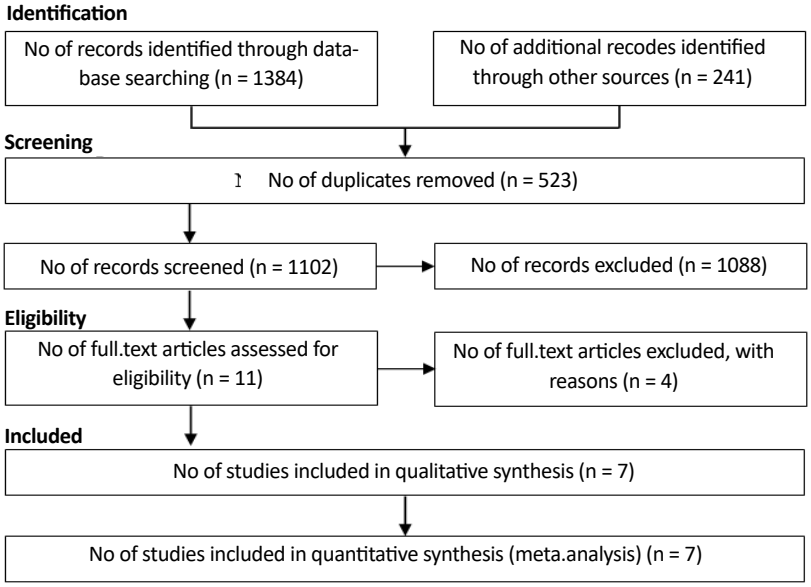

Figure 1. Flow of Information through the different phases of the systematic review

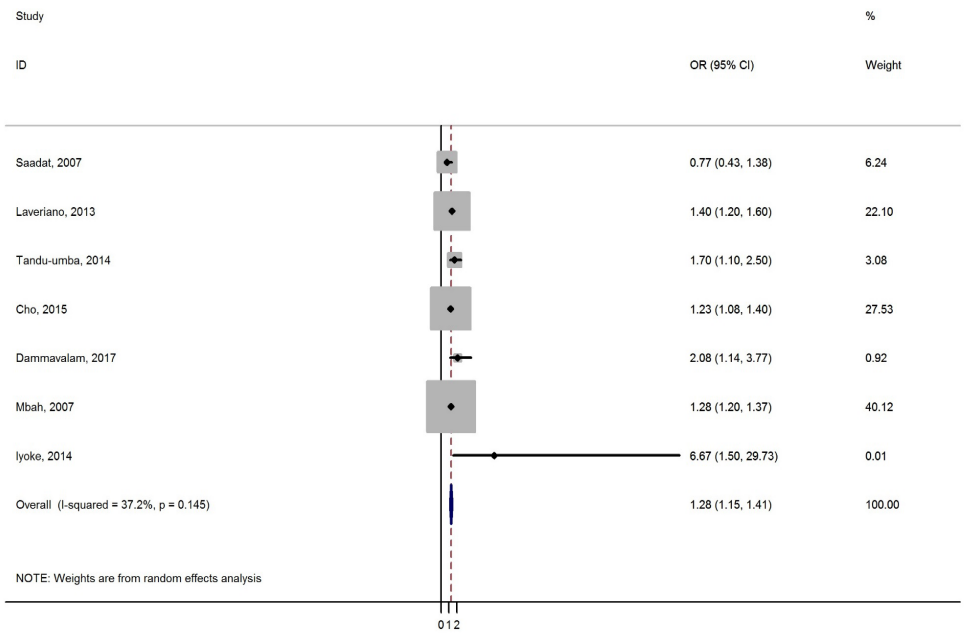

Figure 2. Forest plot of the association between previous cesarean section and preeclampsia

been suggested that this association may be a manifestation of abnormal uterine blood flow caused by intentional or inadvertent occlusion of major uterine vessels during a previous cesarean and abnormal placentation from uterine scar [29].

Several factors (such as maternal obesity, diabetes mellitus, etc.) that are risk factors for preeclampsia are also risk factors for cesarean section. Therefore, these risk factors that were the cause of cesarean in the first pregnancy, but not the cesarean itself, are attributed to preeclampsia in the next pregnancy. Furthermore, a higher recurrence risk of preeclampsia is known to be associated with earlier gestational age at delivery in a previous pregnancy complicated by preeclampsia [30].

These abnormalities may be ascribed to placenta ischemia that releases factors into the mother's circulation.

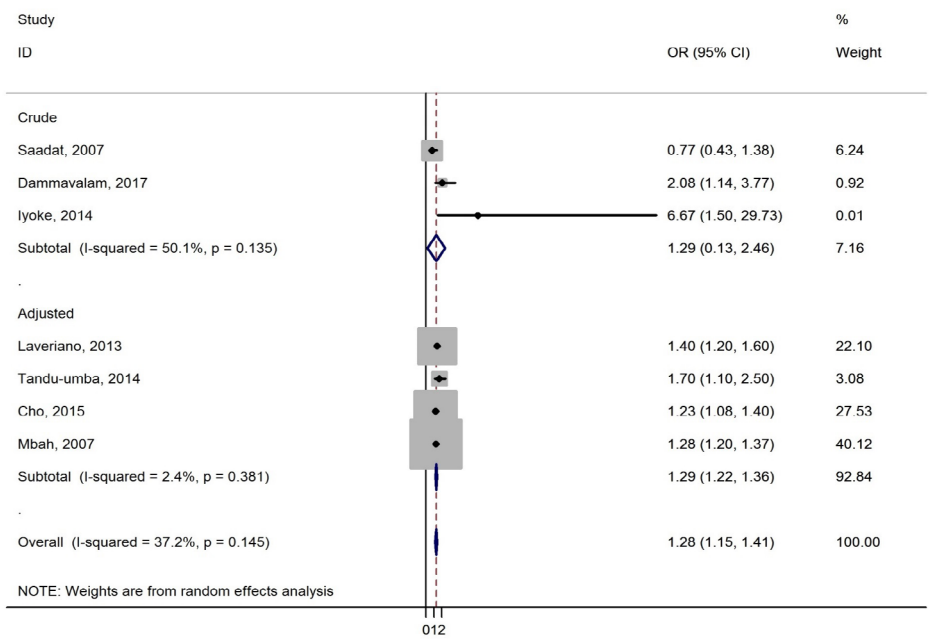

Figure 3. Forest plot of the association between previous cesarean section and preeclampsia based on the adjusted form of studies

These factors can show the clinical manifestations of the disease [31]. Thus, the changes in the uterus are due to surgery or manipulation of the uterus during cesarean section. This change may interfere with normal trophoblastic invasion and changes in placental uterine blood flow in subsequent pregnancies, leading to preeclampsia. On the other hand, the scar tissue of the cesarean section shows significant pathological changes such as lower uterine distortion, upper endometrial scarring, lymphocytic infiltration, the suture material of residual with cell reactions, capillary dilatation, fragmentation and breakdown of the endometrium. Also, biochemical behaviors show decreased levels of transforming factor beta3 and connective tissue growth factor but a slight increase in tumor necrosis factor [32].

The no publication bias and low heterogeneity are the strengths of this study. However, there were a few limitations in our study. We could not evaluate the effect of confounding variables in all studies. Three studies were reported in crude form. Therefore, this issue may raise the possibility of bias. Also, data extracted by the studies included in the meta-analysis were insufficient to conduct some subgroup analyses based on the number of previous cesarean sections. Therefore, we cannot subgroup analysis based on the number of previous cesarean sections and preeclampsia. However, the findings with 423940 participants and low heterogeneity showed that previous cesarean section is a risk factor for preeclampsia. This issue should be considered, especially for pregnant women who undergo cesarean delivery based on their request without any maternal or fetal indication.

In summary, these findings showed that previous cesarean section is a risk factor for preeclampsia. Therefore, programs and educational interventions should be considered to reduce elective cesarean section on maternal request.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by Hamadan University of Medical Sciences (Project Code: 9811088568 and Ethical Code: IR.UMSHA.REC.1398.891).

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Authors' contributions

Study design: Ensiyeh Jenabi and Soodabeh Aghababaei; Data conduction and data analysis: Salman Khazaei; Preaparing the manuscript: Ensiyeh Jenabi and Soodabeh Aghababaei; Final approval: All authors.

Conflict of interest

The authors declared no conflict of interest.

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