

SYSTEMATIC REVIEW AND META-ANALYSIS

The association between previous abortion and risk of placenta accreta spectrum: a meta-analysis

Previous abortion and placenta accreta spectrum

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ABSTRACT

Background. Several studies have yielded conflicting results regarding the potential link between previous abortion and placenta accreta spectrum (PAS), contributing to ongoing controversy on the matter. To address this discrepancy, we conducted a meta-analysis to elucidate the association between previous abortion and the risk of PAS.

Methods. To examine the association between prior abortion and PAS, we systematically searched major databases, including PubMed (Medline), Web of Science, and Scopus. A random-effects model was used for the meta-analysis, and study quality was evaluated using the Newcastle-Ottawa Scale (NOS).

Results. The final analysis included five cohort studies and six case-control studies with a total population of 115,422 participants. We examined the association between previous abortion and the risk of PAS based on crude and adjusted studies. The association between previous abortion and the risk of PAS in crude studies was 1.62 (95%CI 1.46- 1.77; I² = 17.8%). In adjusted studies, the association was 2.37 (95%CI 1.62-3.12; I²=79.5%). Substantial heterogeneity was observed in studies using adjusted analyses, while minimal heterogeneity was found in studies reporting crude estimates.

Conclusions. This meta-analysis reported that prior abortion is a risk factor for PAS. Given these significant implications, healthcare providers should incorporate PAS risk assessment into pre-abortion evaluations and carefully consider the choice of termination method.

Key words

Placenta accreta spectrum; abortion; meta-analysis; pregnancy.

INTRODUCTION

Placenta accreta spectrum (PAS) is characterized by pathological placental implantation, classified into three progressive stages: Placenta accreta (Abnormal adherence of villi to the myometrium without invasion), Placenta increta (Penetration of trophoblastic tissue into the uterine muscle), Placenta percreta (Transmural invasion extending beyond the uterus to adjacent organs) [1]. The underlying pathophysiology of PAS is primarily related to defective decidualization of the basal decidua, which allows excessive and uncontrolled trophoblastic invasion into the myometrium. Prior endometrial injury or uterine scarring can disrupt the normal placental–uterine interface, predisposing affected women to abnormal placental adherence. A meta-analysis reported the prevalence of PAS between 0.01% to 0.1% of deliveries [2]. This disorder is rapidly increasing worldwide due to the rising trend of cesarean deliveries [3]. Epidemiologic data indicate a strong association between prior cesarean delivery and PAS risk. In a systematic review, the incidence of PAS increased from approximately 0.3% in women with one previous cesarean to 6.74% in women with five or more cesareans [4]. Other cohort data suggest PAS rates rising from around 0.03% to 2.8% with increasing cesarean number, highlighting the dose–response relationship between surgical scarring and abnormal placentation [5].

PAS disorder represents a critical obstetric complication with potentially life-threatening maternal consequences, including severe hemorrhage and organ damage. [6]. Its significance lies in the increase in maternal and fetal mortality [7]. PAS is a leading cause of severe postpartum hemorrhage, frequently resulting in life-threatening maternal hemorrhage that often requires massive blood transfusion and emergency peripartum hysterectomy. This condition significantly contributes to both severe maternal morbidity and mortality [8].

Some risk factors that increase the risk of PAS include: multiple pregnancies, obesity, in vitro fertilization (IVF), maternal age, smoking and previous cesarean sections [9, 10]. Previous abortion has also been suggested as a potential risk factor for PAS, as it may cause varying degrees of endometrial damage depending on the type and frequency of abortion. Induced abortion, particularly when associated with surgical curettage, may directly injure the endometrium and impair subsequent decidual regeneration. In contrast, spontaneous abortion may exert different effects depending on gestational age and the need for uterine intervention, while recurrent abortions may result in cumulative endometrial injury and uterine scarring [9].

Several epidemiological studies have reported that women with a history of prior pregnancy loss or abortion especially when associated with endometrial injury from uterine procedures such as dilatation and curettage are at increased risk of abnormal placentation including placenta accreta spectrum in subsequent pregnancies. For example, a recent systematic review and meta-analysis found a significant association between prior abortion and PAS (OR 1.65; 95% CI: 1.43–1.92) [11], and a large case–control study in Iran demonstrated a positive link between previous abortion and PAS outcomes [12]. Identifying responsible factors is crucial as it allows for early interventions to improve perinatal outcomes and reduce associated morbidity and mortality [13]. Several observational studies have reported a significant association between previous abortion and the risk of PAS [14,15], whereas other studies have failed to demonstrate such a relationship. These inconsistent findings across the literature have contributed to ongoing controversy regarding the role of prior abortion in the development of PAS. Epidemiologic studies have also suggested that women with a history of fetal loss may be at increased risk of abnormal placentation, including

placenta previa and PAS, in subsequent pregnancies, further supporting the biological plausibility of this association [16,17].

To date, only one meta-analysis has examined the association between prior abortion and the risk of placenta accreta spectrum. This meta-analysis, which included six studies published up to February 2017, found no significant increase in the risk of abnormally invasive placenta associated with previous abortion [18]. However, this study had several important limitations, including the small number of included studies, heterogeneity in the definition and classification of abortion, and insufficient differentiation between induced and spontaneous abortions. Furthermore, in recent years, additional epidemiological studies with larger sample sizes and improved study designs have been published, which were not incorporated into the previous meta-analysis. These developments may substantially influence the pooled risk estimates.

Therefore, given the rising incidence of PAS and the need for up-to-date and robust evidence to inform clinical practice, an updated meta-analysis incorporating newly published studies, addressing heterogeneity, and more carefully evaluating abortion types is warranted. The present study was conducted to fulfill this need.

Materials and Methods

This meta-analysis was conducted in strict accordance with the 2020 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, ensuring comprehensive reporting of all methodological processes and results. We followed PECO framework for performing this study: **P**opulation: pregnant women, **E**xposure: Women with previous abortion, **C**omparison: women without previous abortion and **O**utcome: risk of PAS.

Inclusion and exclusion criteria

We included primary studies that assessed the association between previous spontaneous abortion and the risk of PAS, encompassing observational studies such as cohort, case-control, and cross-sectional studies. Studies with inadequate data for outcome measurement were excluded. Additionally, we excluded letters to the editor, case reports, case series, systematic reviews, as well as in vitro and animal studies.

Information sources and search

PubMed (Medline), Web of Science, and Scopus were systematically searched up to March 30, 2024, using combinations of keywords: (morbidly adherent placenta OR placenta accreta OR placenta increta OR placenta percreta OR abnormally invasive placenta) AND (previous abortion OR previous miscarriage OR history of miscarriage OR history of abortion OR prior miscarriage OR prior abortion)(Table S1). Additionally, reference lists were examined to identify additional sources.

Study selection

We employed the Population, Exposure, Comparison, and Outcome (PECO) model to select eligible studies. The Population consisted of pregnant women, the Exposure was previous abortion, and the Comparison was made with non-previous abortion. The Outcome of interest was PAS. Two investigators (EJ and SA) independently screened all titles and abstracts, and subsequently reviewed the full texts that were deemed definitely or possibly eligible. Any disagreements between the two authors were resolved through discussion.

Data extraction

Data extraction was performed using Stata software (version 13.0), capturing the following variables from each included study: first author, publication year, study design, diagnostic criteria, study population characteristics, maternal age distribution, and adjusted confounding variables.

Methodological quality

Study quality was assessed using the modified Newcastle-Ottawa Scale (NOS) for observational studies[19]. This instrument evaluates three domains: (1) participant selection criteria, (2) comparability between PAS and non-PAS groups, and (3) outcome assessment methodology. Based on the standard NOS scoring system (range 0-9), we classified studies scoring 7-9 as high quality and those scoring ≤ 6 as low quality.

Heterogeneity and reporting biases

To evaluate heterogeneity among studies, we utilized the chi-square test[20] and the I^2 statistic. An I^2 statistic greater than 50% was considered indicative of high heterogeneity[21]. Additionally, regression tests, including Egger's and Begg's[22] were employed to examine publication bias.

Summary measures

Primary outcomes were analyzed as dichotomous variables (PAS vs. non-PAS groups), with effects estimated as odds ratios (ORs) and corresponding 95% confidence intervals. All analyses employed a DerSimonian-Laird random-effects model to account for between-study heterogeneity[23]. Statistical significance was defined as $p < 0.05$ using two-tailed tests, with all computations performed in Stata/Version 13.0 (StataCorp LP, Texas, USA).

Results

Description of studies

Our systematic search identified 439 potentially relevant records through initial screening. After title/abstract review and evaluation of 17 full-text articles until March 30, 2024 (Figure 1), 11 studies met our inclusion criteria. The excluded studies ($n=6$) comprised one systematic review and five articles failing eligibility requirements. The final analysis included five cohort studies[14, 15, 24-26] and six case-control studies[16, 17, 27-30], all published in English, encompassing a total population of 115,422 participants (Table 1). The total number of included cases was 3381 participants.

Effects of exposure

Figure 2 presents the meta-analysis results evaluating the association between prior abortion and PAS risk, stratified by crude and adjusted analyses. Crude analyses demonstrated a statistically significant increased risk of PAS (OR = 1.62; 95% CI: 1.46–1.77), with low heterogeneity ($I^2 = 17.8\%$). Adjusted analyses revealed a stronger association (OR = 2.37; 95% CI: 1.62–3.12), though with substantial heterogeneity ($I^2 = 79.5\%$). Heterogeneity was markedly higher in adjusted studies compared to crude analyses (Figure 2). Notably, Ogawa et al. (2024) provided stratified results, reporting both crude and adjusted estimates for women with 1–2 prior abortions and ≥ 3 prior abortions [26].

Subgroup analysis

We stratified crude analyses by study design to evaluate the association between prior abortion and PAS risk. The association between previous abortion and the risk of PAS in cohort studies was significant [2.15(95% CI: 1.74, 2.57; $I^2=82.2\%$)]. In case-control studies, the association was significant [1.64 (95% CI: 1.35, 1.92; $I^2=0.0\%$)]. The heterogeneity was substantially higher in cohort studies compared to case-control designs

Publication bias

Publication bias was evaluated using Begg's rank correlation test ($p=0.323$) and Egger's linear regression test ($p=0.143$). Both tests indicated no statistically significant evidence of publication bias among the included studies (Figure 3).

Quality of the studies

Quality assessment using the NOS demonstrated that all included studies except one met our pre-defined threshold for high methodological quality (scores ≥ 7), with detailed scoring presented in Table 2.

Discussion

The meta-analysis demonstrates a consistent association between prior abortion and increased PAS risk. While substantial heterogeneity was detected in adjusted analyses, crude estimates demonstrated remarkable consistency across studies, suggesting that variability in covariate adjustment approaches may contribute to between-study differences.

Only a meta-analysis has been conducted regarding the association between prior abortion and the risk of PAS and they included six studies in PubMed and Scopus published through February 2017. The findings indicate that previous abortion did not significantly increase the risk of abnormally invasive placenta (OR: 1.36; 95% CI: 0.84, 2.20) [18]. While comprehensive searches were performed in PubMed and Scopus, the exclusion of Web of Science may have introduced selection bias. These methodological constraints should be considered when interpreting the findings. In the present meta-analysis, PubMed (Medline), Web of Science, and Scopus were systematically searched with 11 studies.

Studies have shown that women with a history of fetal loss are at a higher risk of abnormal placentation. An et al., based on a multivariable logistic regression model, reported an association between increased occurrence of placenta percreta and a higher number of previous miscarriages [31]. While our meta-analysis identified a significant association, these findings contrast with a Japanese cohort study [32]. PAS disorders may develop following any iatrogenic or spontaneous endometrial injury that disrupts the decidua basalis [33]. Uterine curettage, as a fundamental technique for induced abortion, can lead to endometrial damage [34]. It should be noted, however, that combining medical and surgical abortions may dilute the observed effect if the mechanism is primarily one of mechanical trauma.

Multiple theories have been proposed to explain the mechanism of PAS. It's possible that mechanical factors such as primary defects in the decidua due to trauma from surgery or biological factors such as abnormal uterine decidual response to trophoblast infiltration, or a combination of both, may be involved [35]. In PAS, invading trophoblast cells penetrate deep into the uterine wall, becoming hypertrophic and increasing in number, while large trophoblast cells with multiple nuclei decrease [34]. Previously, it was thought that a fundamental defect in trophoblast biological function led to excessive invasion beyond the physiological attachment zone of the endometrium to

the myometrium. The current hypothesis suggests that a defect at the junction of the endometrium-myometrium, possibly due to previous surgeries, prevents proper decidualization of the endometrium, allowing for abnormal trophoblast invasion [8].

The heterogeneity between the results could be due to the fact that the studies included in this meta-analysis did not specify the type of abortion (medical versus surgical).

This meta-analysis had several limitations: 1) Heterogeneity Concerns: Considerable heterogeneity was observed among adjusted studies ($I^2 = 79.5\%$). However, interpretation requires caution, as the Q-test has limited power with few studies. 2) Unadjusted Confounding: Some included studies did not fully account for potential confounders (e.g., prior cesarean delivery, maternal age), which may introduce residual information bias. However, there is a risk that the association found is driven by the correlation between abortion history and multiparity/prior cesareans rather than abortion itself.

3) Lack of Abortion-Type Stratification: Subgroup analysis by abortion method (surgical vs. medical) was not possible due to insufficient reporting in primary studies. 4) We did not use other electronic databases such as Cochrane Library and Embase in this study, which is a limitation of the present study. Despite these limitations, our findings, based on 115,422 participants across 11 studies, consistently demonstrate that previous abortion is associated with an increased risk of PAS.

Conclusions

This meta-analysis reported that prior abortion is a risk factor for PAS. These findings suggest clinicians should incorporate PAS risk assessment into abortion counseling, particularly for patients with additional risk factors (e.g., multiparity, advanced maternal age). Procedure selection may benefit from considering potential differential effects on endometrial integrity. Although endometrial injury may influence PAS risk, the current evidence does not allow definitive recommendations regarding the abortion procedure. Further research is required to clarify whether the method of abortion affects endometrial integrity and subsequent PAS risk.

COMPLIANCE WITH ETHICAL STANDARDS

Authors' contribution

EJ and SA participated in Conceptualization, Data curation, Investigation, Methodology. EJ and SA contributed to the writing of the paper, EJ and SA and FK participated in the performance of the research, S Kh were involved in data analysis, and the final manuscript was edited by all authors.

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Study registration

Not applicable.

Disclosure of interests

The authors declare that they have no conflict of interests.

Ethical approval

This study received ethical approval from the Institutional Review Board of Hamadan University of Medical Sciences (IR.UMSHA.REC.1403.226; July 13, 2024). All procedures were conducted in strict compliance with the ethical principles outlined in the Declaration of Helsinki (2013 revision).

Informed consent

Not applicable.

Data sharing

Access to data is possible with permission from the responsible author.

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

1 st Author, year	Design	Sam ple	Mean of materna l age (Year)	Diagnosis criteria	Aborti on type	Estim ate	Adjustme nt	Qual ity
Eshkoli, 2013[14]	Cohort	3486 9	<i>Not reported</i>	Clinical and histopathol ogical reports	Recurr ent abortio ns	OR	Crude/Adj usted	High
Sun, 2023[15]	Cohort	7577 3	Not reported	Not reported	Previou s abortio n	OR	Crude/Adj usted	High
Tadayon, 2022[28]	Case- control	739	Case:32 .8, Control: 28.7	Surgeon's confirmatio n during delivery and histopathol ogical findings	Previou s abortio n	OR	Crude	High
Moeyini, 2021 [30]	Case- control	513	Case:32 .6, Control: 31.6	By second or third month ultrasonog raphy and confirmed by a perinatolo gist	Previou s abortio n	OR	Crude	High
Ogawa, 2022[26]	Cohort	2253	<i>Not reported</i>	Obstetricia ns, such as difficult piecemeal manual removal of the placenta	History of miscarr iage	RR	Crude/Adj usted	High
Parra-Herran, 2016 [29]	Case- control	61	Case:35 .0, Control: 34.4	Histopatho logic diagnosis	History of miscarr iage	OR	Crude	High

1 st Author, year	Design	Sample	Mean of maternal age (Year)	Diagnosis criteria	Abortion type	Estimate	Adjustment	Quality
Alchalabi, 2014[25]	Cohort	81	Case:34.7, Control: 31.1	Ultrasonography	History of miscarriage	OR	Crude	High
Klar, 2013[27]	Case-control	483	Case:32.47, Control: 31.39	Histopathologic confirmation	Previous abortion	OR	Crude/Adjusted	High
Wu, 2005[17]	Case-control	450	<i>Not reported</i>	Histopathologic confirmation	Previous abortion	OR	Crude	High
Elbery, 2020[24]	Cohort	33	31.33	Ultrasonography and histological diagnosis	Previous abortion	OR	Crude	Low
Kamara, 2013[16]	Case-control	167	<i>Not reported</i>	Clinical and histological diagnosis	Previous miscarriage	OR	Crude	High

In study of Eshkoli: variables controlled were the year of birth, maternal age, recurrent abortions, second-trimester vaginal bleeding, previous CD, and placenta previa. In study of Sun: variables controlled were pre-pregnancy BMI, maternal age, mode of delivery, and parity. In study of Ogawa: variables controlled were the year of birth, maternal age, parity, history of miscarriage, conception method, previous cesarean and smoking. In study of Klar: Variables controlled were previous abortions, Previous curettages, previous cesarean sections, maternal age, parity, gravity and smoking.

Table 2. Score of Quality of studies based on the Newcastle Ottawa Scale (NOS)

First author, Year	Selection	Comparability	Exposure	Total quality score
Eshkoli, 2013	4	2	2	8
Sun, 2023	3	2	3	8
Tadayon, 2022	3	1	3	7
Moeini, 2021	4	1	2	7
Ogawa, 2022	4	2	3	9
Parra-Herran, 2016	3	1	3	7
Alchalabi, 2014	3	1	3	7
Klar, 2013	3	2	3	8
Wu, 2005	3	1	3	7
Elbery, 2020	2	1	2	5
Kamara, 2013	3	1	3	7

Low quality (<7 points); High quality (>7 points)

Figure 1: Flowchart of the process selection of the studies

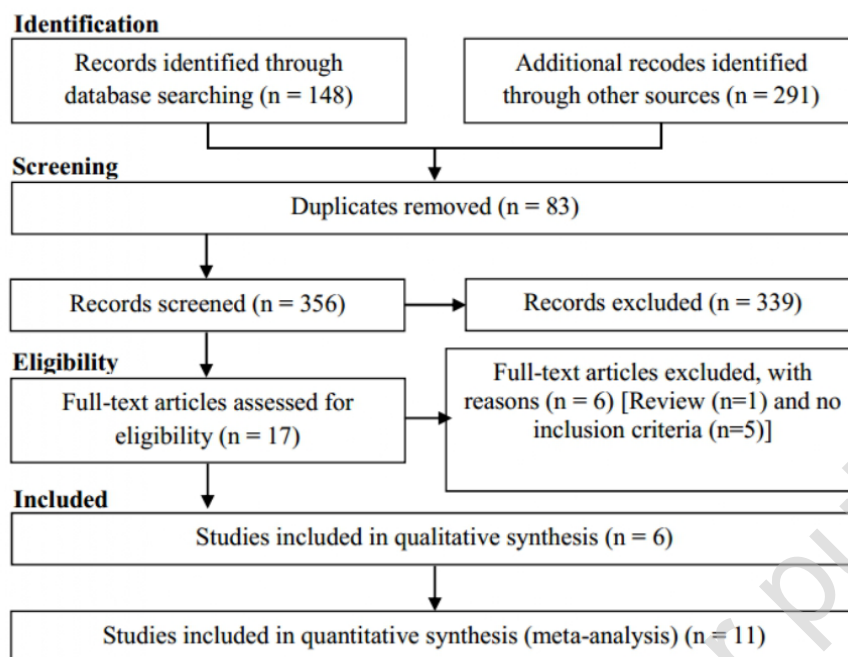


Figure 2: The association between previous abortion and risk of placenta accreta spectrum (PAS)

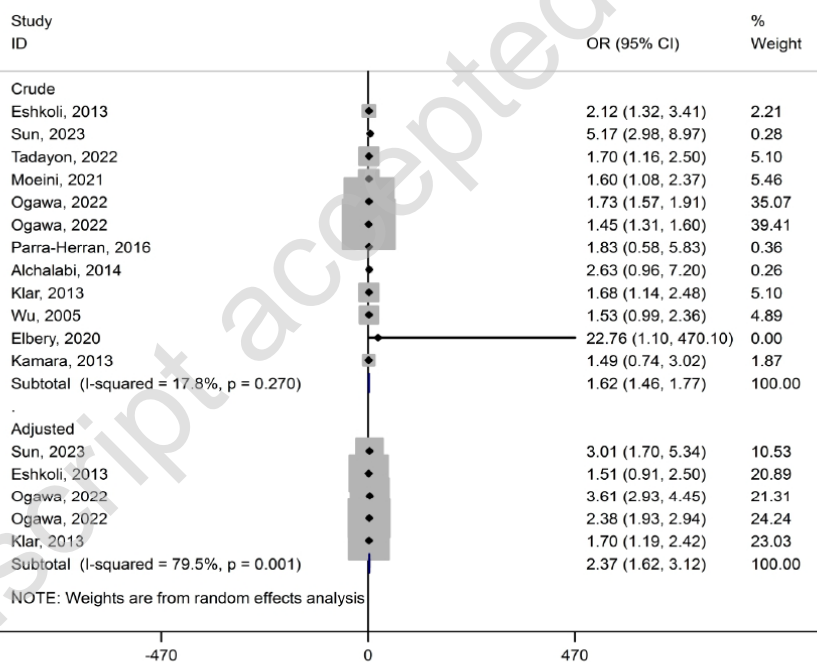


Figure 3: Funnel plot of previous abortion and risk of placenta accreta spectrum (PAS)

