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Original Article

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Association of Abortion Event With a History of Endometriosis: A Case-Control Study

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Abstract

Background: Endometriosis is a chronic gynecological disorder characterized by the presence of endometriosis-like tissue outside the uterine cavity, leading to pelvic pain, infertility, and other reproductive complications. Emerging evidence suggests a potential association between endometriosis and an increased risk of abortion events. This study aimed to investigate the association between abortion events and a history of endometriosis using a case-control study design.

Methods: A case-control study was conducted involving 112 women who experienced abortion (cases) and 131 women with successful pregnancies without abortion (controls). Data were collected from Prof. Dr. Margono Soekarjo General Hospital between September 2022 and September 2024. Data on endometriosis history, demographic factors, reproductive history, and potential confounding factors were collected through medical records. Logistic regression analysis was performed to assess the association between endometriosis and abortion events, adjusting for confounding variables. Bivariate and multivariate logistic regression analyses used odds ratios (ORs) with 95% confidence intervals (CIs). Variables were considered statistically significant if the P value < 0.05 in multivariate analysis.

Results: The prevalence of endometriosis was significantly higher in the abortion group (73.2%) compared to the control group (31.3%) with P < 0.001. After adjusting for age, body mass index (BMI), smoking status, and number of previous pregnancies, women with a history of endometriosis had a 2.25-fold increased odds of experiencing an abortion (OR: 2.25; 95% CI: 1.71 - 2.94; P < 0.001). Additionally, severity of endometriosis was positively correlated with the frequency of abortion events (P < 0.001).

Conclusion: This study found a significant association between abortion events and a history of endometriosis. Women with endometriosis are at a higher risk of experiencing abortion, emphasizing the need for targeted reproductive counseling and management in this population. Further research is necessary to elucidate the underlying mechanisms and develop strategies to mitigate this risk.

Keywords: Abortion; Endometriosis; Risk factors

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Introduction

Endometriosis is defined as the chronic inflammatory disease which is a prevalent gynecological condition affecting approximately 10-15% of women of reproductive age worldwide [1, 2]. Out of them, 30% of the affected are represented by Asian women. Endometriosis prevalence rate is higher among Asian women with the odds of 1.63 times higher [3, 4]. It is characterized by the presence of endometrial-like tissue outside the uterine cavity, commonly involving the ovaries, pelvic peritoneum, and other pelvic structures [5, 6]. Endometriosis significantly affects women's quality of life due to its painful symptoms, including pelvic pain and infertility. These challenges often lead to emotional distress and social consequences. Additionally, women with endometriosis are at a higher risk of experiencing abortion, which further complicates their reproductive health. Understanding this connection underscores the importance of targeted reproductive counseling and management for this population [1, 7].

Abortion, defined as the termination of a pregnancy before the fetus is viable, occurs in approximately 10-20% of pregnancies (American College of Obstetricians and Gynecologists) [6, 8]. While various factors contribute to abortion events, including genetic, anatomical, hormonal, and immunological factors, the role of endometriosis in increasing the risk of abortion has garnered interest in recent years. Some studies have suggested that women with endometriosis may have a higher incidence of abortion, potentially due to altered uterine receptivity, inflammatory responses, and hormonal imbalances associated with the condition [5-7].

Abortion rates continue to be a significant public health concern, yet the relationship between abortion events and the presence of endometriosis remains underexplored in the existing literature. While some studies have suggested various associations, gaps persist in understanding the underlying mechanisms and risk factors. This study aimed to address these

gaps by investigating the potential link between a history of abortion and endometriosis. Specifically, we evaluated the association between abortion events and endometriosis through a case-control study, adjusting for potential confounders.

Materials and Methods

This study employed a case-control method with secondary data (medical records) from all patients who came to polyclinic Fertility and Endocrinology (FER) at Prof. Dr. Margono General Hospital between September 2022 and September 2024. Randomized sampling was used, with a total of 628 subjects. We performed a power analysis using SPSS to determine the sample size needed to achieve a statistical power of 0.80 with a significance level of 0.05. This power analysis was conducted based on the expected effect size and the type of statistical Chi-square test used. Sampling selection of 112 women who experienced abortion (cases) and 131 women with successful pregnancies without abortion (controls) was conducted based on the following inclusion criteria: patients diagnosed with endometriosis based on histopathological evaluation post-surgery, aged 18 - 55 years, and with no history of other gynecological disorders. Exclusion criteria were: patients with incomplete medical records, those diagnosed with endometrial hyperplasia or cancer, or those who have undergone any surgical procedures for endometriosis before the study period, chronic medical conditions (ex diabetes, hypertension, cancer, etc.), history of recurrent pregnancy loss (> 2 consecutive miscarriages), use of assisted reproductive technologies (ARTs) in the past year, or refusal to participate.

The control group was composed of individuals who were also diagnosed with endometriosis, with diagnosis confirmed through histopathological evaluation. This ensures that comparisons between the study groups are made using reliable, accurately diagnosed cases.

Data were collected through medical records then information was gathered including: demographic information (age, body mass index (BMI), educational level, and marital status), reproductive history (number of pregnancies, parity, abortions, and infertility treatment), medical history (diagnosis of endometriosis confirmed by pathology examination, severity of endometriosis with revised American Society for Reproductive Medicine (rASRM) classification assessed from operative report, history of pelvic inflammatory disease and other gynecological conditions) and life style factor (smoking status and use of contraceptive methods). Bivariate and multivariate logistic regression analyses were conducted, using an odds ratio (OR) and a 95% confidence interval (CI). Variables were considered statistically significant if $P < 0.05$ in the multivariates analysis.

Definition operation

Endometriosis diagnosis was confirmed through histopathological evaluation following surgical intervention. Only patients with histopathologically confirmed endometriosis were included in the study, ensuring a reliable diagnostic baseline. Asymptomatic cases or those diagnosed clinically without histopathological confirmation were excluded.

Abortion was defined as termination before 20 weeks of pregnancy including spontaneous abortion, induced abortion, and incomplete abortions.

Data were analyzed using the International Business Machines Statistical Package for the Social Sciences (IBM SPSS) Statistics Version 26 (for Windows). Descriptive statistics summarized demographic and clinical characteristics. Chi-square testing was conducted to assess the association between endometriosis and abortion events. Confounding variables were identified through statistical testing (Chi-square, *t*-tests) and prior literature on endometriosis and reproductive outcomes. Variables that were significantly associated with both the exposure (endometriosis) and the outcome (abortion) in the preliminary analysis were considered as potential confounders. We controlled for age, BMI, parity, and smoking status as confounders based on their established associations with both endometriosis and abortion, as well as their significant impact on the relationship between these two variables in multivariable regression analysis. By controlling for these variables, we aimed to isolate the true relationship between endometriosis and abortion while minimizing the influence of confounders. For all variables with a 95% CI, the results were considered statistically significant with a $P < 0.05$ for all analyzed variables.

This study was submitted to and approved by the Ethics and Research Committee of the Development and Research Department at Prof. Dr. Margono Soekarjo Hospital, Purwokerto, Indonesia, in accordance with Protocol 12/2003 No. 432/03457/Research Permit on September 2, 2024. This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration. All medical record data were used exclusively for the purposes of this research and will not be shared with any parties outside the researchers and research supervisors. The data are intended solely for academic purposes.

Results

According to Table 1, we found that the reproductive age (15 - 45 years old) of the two groups had a significant correlation (75.9% vs. 51.9%; $P < 0.001$). Reproductive age was included as a covariate in the analysis to control for its potential confounding effect on the relationship between endometriosis and abortion. A previous study by Giudice showed that advanced maternal age was associated with both an increased risk of miscarriage and more severe endometriosis, particularly among older women [1]. BMI showed no difference and significance between the two groups ($P = 0.106$). For parity, the primiparous was found to be higher in the endometriosis group than non-endometriosis (35.7% vs. 19.8%; $P = 0.010$). For marital status, both groups had a significant correlation (93.8% vs. 84.7%; $P = 0.026$). Education background for both groups had no difference and significance between levels ($P = 0.051$). The association between endometriosis and a his-

Table 1. Variable Description, Sample and Data Characteristics

Analyzed variable	Endometriosis (n = 112, 100%)	Non-endometriosis (n = 131, 100%)	P-value (sig two-sided)
N	112	131	
Age			0.001*
Reproductive age (18 - 45 years)	85 (75.9)	68 (51.9)	
Non-reproductive age (> 45 years)	27 (24.1)	63 (48.1)	
BMI			0.106
Underweight (< 18.5 kg/m^2)	14 (12.5)	8 (6.1)	
Normoweight (18.5 - 24.9 kg/m^2)	44 (39.3)	58 (44.3)	
Overweight (25 - 29.9 kg/m^2)	29 (25.9)	45 (34.4)	
Obese (> 30 kg/m^2)	25 (22.3)	20 (15.3)	
Obstetric status			0.010*
Nullipara (0)	10 (8.9)	2 (1.5)	
Primipara (1)	40 (35.7)	26 (19.8)	
Multipara			
2	35 (31.3)	52 (39.7)	
3	17 (15.2)	28 (21.4)	
4	7 (6.3)	13 (9.9)	
≥ 5	3 (2.67)	10 (7.63)	
Marital status			0.026*
Married	105 (93.8)	111 (84.7)	
Divorced	7 (6.3)	20 (15.3)	
Education level			0.051
Elementary school	24 (21.4)	47 (35.9)	
Junior high school	22 (19.6)	18 (13.7)	
Senior high school	34 (30.4)	28 (21.4)	
Diploma	6 (5.4)	3 (2.30	
Bachelor degree	8 (7.1)	7 (5.3)	
Magister degree	3 (2.7)	1 (0.8)	
None	15 (13.4)	27 (20.6)	
Abortion			0.001*
Normal	30 (26.8)	90 (68.7)	
Previous abortion	82 (73.2)	41 (31.3)	
rASRM			0.001*
Normal		131 (100)	
Stage 1	2 (1.78)		
Stage 2	33 (29.46)		
Stage 3	67 (59.82)		
Stage 4	10 (8.9)		
Anemia			0.578
Normal (Hb > 11 g/dL)	51 (45.5)	55 (42)	
Anemia (Hb < 11 g/dL)	61 (54.5)	76 (58)	
Acceptor contraceptive			0.57
Yes	76 (67.85)	93 (70.9)	
No	36 (32.1)	38 (29)	
Smoking status			0.42
Yes	5 (4.46)	4 (3.05)	
No	107 (95.5)	127 (96.9)	

If the Chi-square condition is not satisfied, the P-value for categorical data is determined using Fisher's exact tests. *P value < 0.05 for statistically significant. BMI: body mass index; rASRM: revised American Society for Reproductive Medicine.

Table 2. Comparison of Endometriosis and Previous Abortion Between the Two Groups

Variable	Group		OR (95% CI)	P value
	Endometriosis (%)	Non-endometriosis (%)		
N	112	131		
Abortion			2.25 (1.717 - 2.949)	< 0.001
Normal	30 (26.8)	90 (68.7)		
Previous abortion	82 (73.2)	41 (31.3)		

If the Chi-square condition is not satisfied, the P-value for categorical data is determined using the Fisher's exact tests. P value < 0.05 for statistically significant. CI: confidence interval; OR: odds ratio.

tory of abortion had been proved by the data in which the endometriosis group was higher than non-endometriosis (72.2% vs. 31.3%; P < 0.001). In addition, higher stage rASRM had a significant correlation with the severity of the symptoms actually for stage III-IV (68.72%; P < 0.001). For anemia, acceptor contraceptive and smoking status showed no difference and significance between both groups.

Data adjustments for age, BMI, smoking status, and number of previous pregnancies were made (Table 2) and analyzed using Chi-square statistics concerning the association between both groups. It was proven that endometriosis had a significant correlation with previous abortion approximately 2.25 times higher than non-endometriosis (OR: 2.25; 95% CI: 1.717 - 2.949; P < 0.001). Additionally, severe endometriosis was independently associated with a higher risk of abortion (OR: 1.67; 95% CI: 0.95 - 0.291; P < 0.001).

Discussion

This case-control study identifies a significant association between abortion events and a history of endometriosis. Women with endometriosis were found to have a 2.25-fold increased odds of experiencing an abortion compared to those without the condition, even after adjusting for potential confounders. Furthermore, the severity of endometriosis was positively correlated with the frequency of abortion events. Our findings are consistent with previous research indicating that endometriosis is associated with adverse reproductive outcomes including increased risk of miscarriage. However, our study provides new insights by focusing on reproductive age group, particular type or severity of endometriosis, and behavioral factors that have been underrepresented in the literature [5, 6, 9]. Unlike earlier studies, which often relied on retrospective data and self-reported miscarriage rates, our study used a case-control design and clinical confirmation of endometriosis diagnosis by histopathology examination which improves the accuracy and reliability of the findings. The elevated risk observed in this study aligns with studies by McCallion et al (2022), who reported that chronic inflammation and altered immune responses in endometriosis may impair implantation and embryo development, leading to higher abortion rates [10].

Early diagnosis of endometriosis is essential, as it can impact fertility and quality of life [9, 11]. Endometriosis is a chronic disease that commonly affects women during their reproductive age (25 - 35 years old) [5, 6]. However, the condition can also occur in adolescent and older women with diagnosis often delayed due to non-specific symptoms or misdiagnosis [7, 12]. The prevalence of endometriosis is particularly high among women in their later 20 years old and early 30 years old, though symptoms can start in adolescence, highlighting the need for early awareness and intervention [9, 11]. This study found that reproductive age had a significant correlation with endometriosis which aligns with the studies by Vercellini and Kvaskoff et al showing that diagnosing endometriosis in younger women and adolescents was often delayed with an average of 7 - 12 years and endometriosis was less commonly diagnosed in post-menopausal women, though the condition may persist or become symptomatic in a subset of older women [5, 7, 12].

Several studies have explored the correlation between parity and the risk of developing endometriosis. Parity has been identified as a protective factor against endometriosis. A meta-analysis conducted by Jenabi proved that women with higher parity had a significantly reduced risk of endometriosis compared to nulliparous women [13]. Farland et al investigated epidemiological and clinical risk factors for endometriosis and found that parity was inversely correlated with the risk of developing endometriosis. Multiple pregnancies can reduce the occurrence and severity of endometriosis, likely due to hormonal changes during pregnancy that inhibit the growth of ectopic endometrial tissue. This finding underlined the inverse correlation between parity and endometriosis suggesting that hormonal factors are related to pregnancy, particularly increased progesterone levels may help suppress or mitigate the disease [2, 12].

Our study found that marital status holds significance towards endometriosis. However, this contradicted a previous research by Emarefa The North African Journal of Scientific that stated that there was no significant relationship between marital status and endometriosis, indicating that whether a woman was single, married, divorced, or widowed did not substantially affect her risk of having the condition. National Health and Nutrition Examination Survey (NHANES) 2001 - 2006 analyzed various factors including marital status in relation to endometriosis: prevalence varied slightly among different marital groups; marital status was not a statistically significant predictor of the condition once other factors such as age, socioeconomic status, and health history were accounted for [14].

The association between endometriosis and abortion can be explained by several mechanisms such as inflammatory environment, hormonal imbalances, immunological factors, and

anatomical abnormalities. Vercellini et al stated that endometriosis is characterized by pro-inflammation which can negatively affect implantation and placental development [5, 6]. Altered estrogen and progesterone levels in endometriosis can disrupt the hormonal milieu necessary for maintaining pregnancy [7, 9]. Endometriosis may involve immune dysfunction leading to an increased risk of immune-mediated rejection of the embryo [14, 15]. Richani et al argued that severe endometriosis can cause pelvic adhesions and anatomical distortions, potentially impacting uterine receptivity and increasing the likelihood of abortion [13, 16, 17]. The cohort study examined the impact of endometriosis on *in vitro* fertilization (IVF) outcomes and found that women with endometriosis had a significantly higher rate of spontaneous abortion compared to women without the condition [18]. The hypothesis is that poor oocyte quality might be a contributing factor to the increased miscarriage rate in women with endometriosis. The cohort study involving 29,000 women with endometriosis and over 295,000 controls found that endometriosis was associated with an increased risk of recurrent pregnancy loss (RPL) [17]. Specifically, the study reported that women with endometriosis were more likely to experience two or more miscarriages, especially in the first trimester [2, 4, 12]. According to European Journal of Obstetrics and Gynecology, researches followed 174 women with laparoscopically confirmed endometriosis and compared their pregnancy outcomes with a control group, finding that the miscarriage rate among women with endometriosis was 29%, significantly higher than the 18% rate observed in the control group [5, 6].

The researcher used rASRM classification to evaluate the extent of endometriosis during exploratory laparotomy with four mains focusing on the location of endometrial implants, depth of infiltration, presence and severity of adhesions, and size of ovarian endometriomas (endometriotic cysts) [19]. rASRM used a scoring system for numerical value of peritoneal implants, size and presence of ovarian endometriomas and adhesions extent, and location of adhesions [20, 21]. Johnson et al evaluated over 1,000 women with different rASRM stages of endometriosis and found a higher miscarriage rate among women with severe (stage III-IV) endometriosis compared to those with mild (stage I-II) endometriosis [22]. The miscarriage rate was 35% for women with severe endometriosis compared to 21% for women with mild forms. The study concluded that advanced endometriosis, due to its more extensive pelvic inflammation and adhesions, may negatively impact early pregnancy and lead to a higher risk of miscarriage [4, 23]. Another study focusing on rASRM and pregnancy outcomes in women with endometriosis found that those with stage III-IV endometriosis had a significantly higher risk of spontaneous abortion compared to women with stages I-II. This research also pointed out that the risk of miscarriage increases with the severity of adhesions and ovarian involvement [15, 16]. A larger retrospective analysis of women undergoing fertility treatment showed that miscarriage rates were notably higher in women with advanced rASRM stage endometriosis. The study highlighted that women with stage IV endometriosis had nearly doubled miscarriage rate of those with stage I-II, with the risk particularly elevated in natural conception compared to ARTs [6, 24]. Although previous studies have explored the relationship between endometriosis and abortion, many have focused on general associations without considering factors such as age group, disease severity, or treatment history. Our study aimed to fill this gap by examining the impact of age group, behavioral factors, and severity of endometriosis on the association between endometriosis and reproductive outcomes.

Our findings contribute to the growing body of evidence suggesting a potential link between abortion events and endometriosis. However, further studies are needed to investigate the underlying biological mechanisms and to explore the role of various risk factors. Future research should focus on larger cohorts and include diverse populations to confirm these findings. This study has several limitations such as recall bias due to self-reported abortion events and endometriosis history, selection bias because we used medical records from a single institution which may limit the generalizability of the findings, and confounding factor although adjustment was made but unmeasured variable (genetic and detailed lifestyle factors) had not been assessed. A future study considering prospective cohort designs to better establish causality and explore the underlying biological mechanisms linking endometriosis to abortion is much needed. Additionally, research into targeted therapies that address the inflammatory and hormonal aspects of endometriosis may provide strategies to reduce the risk of abortion in affected women.

Conclusion

In this study, a significant association between abortion events and a history of endometriosis was demonstrated. Women with endometriosis are at higher risk of experiencing abortions, particularly those with severe forms of the condition. These findings underscore the importance of early detection, comprehensive management, and targeted reproductive counseling for women with endometriosis to improve their reproductive outcomes and overall quality of life.

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Financial Disclosure

None to declare.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Informed Consent

Not applicable.

Author Contributions

Study concept and design was done by YPD and EP; data collection and statistical analysis by YPD and MEG; data interpretation and presentation by YPD, EP and WP; manuscript drafting by YPD and EP; and research supervision by EP and WP. All authors discussed the results, contributed to the final manuscript and approved the version for publication.

Data Availability

The datasets used and/or analyzed the current study are available from the corresponding author on reasonable request.

Abbreviations

ACOG: American College of Obstetricians and Gynecologist; ART: assisted reproductive technologies; BMI: body mass index; CI: confidence interval; FER: fertility and endocrinology reproductive; IBM SPSS: International Business Machines Statistical Package for the Social Sciences; IVF: *in vitro* fertilization; NHANES: National Health and Nutrition Examination Survey; OR: odds ratio; rASRM: revised American Society for Reproductive Medicine; RPL: recurrent pregnancy loss

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