

ORIGINAL RESEARCH

Placenta Accreta Spectrum in delivered women is associated with history of curettage: A case-control study at Dr. Moewardi General Hospital, Surakarta, Indonesia

Helena Adelia Prabowo¹, Nutria Widya Purna Anggraini²*, Asih Anggraeni³,
Sigit Setyawan⁴

¹Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia.

²Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Sebelas Maret, Dr. Moewardi General Hospital, Surakarta, Indonesia.

³Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Sebelas Maret, Universitas Sebelas Maret Hospital, Surakarta, Indonesia.

⁴Department of Parasitology, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia.

Article Info	ABSTRACT
<p>Received Aug 25, 2024 Revised Dec 27, 2024 Accepted Jan 10, 2025 Published Apr 1, 2025</p> <p>*Corresponding author: Nutria Widya Purna Anggraini nutria_dr@staff.uns.ac.id</p> <p>Keywords: Placenta accreta spectrum History of curettage Delivered women Maternal health</p>	<p>Objective: Placenta Accreta Spectrum (PAS) is a condition in which the placental villi directly adhere to the myometrium, a leading cause of serious obstetric bleeding. The situation has increased morbidity and mortality in pregnant women due to 3.000 – 5.000 mL blood loss. The incidence of PAS has risen globally from 0.12% to 0.31%, linked to frequent uterine damage from procedures like cesarean sections or curettage. This study aims to determine the association between history of curettage and PAS.</p> <p>Materials and Methods: The type of research used is analytic observational with a case-control approach. The sampling technique used in this study is purposive sampling, and 134 samples match the inclusion criteria. The samples used are delivered women referred to Dr. Moewardi General Hospital, Surakarta, Indonesia, from May 2022 until May 2024. Data analysis utilizing IBM SPSS 25. Chi-square test determines the association between two variables at a significance level of $p < 0.05$, while logistic regression is used to determine the most influential variables.</p> <p>Results: The sample consisted of 67 patients with PAS and 67 without PAS. There was a significant association between the history of curettage and PAS, as determined by a Chi-square test, with a p-value of 0.000. Further analysis using logistic regression on the history of curettage obtained a value of $p = 0.001$ and $OR = 5.769$ (CI95% 2.090 – 15.928).</p> <p>Conclusion: The history of curettage is significantly associated with PAS. Patients who have had curettage in the past are 5.769 times more likely to experience PAS than patients without a history of curettage.</p>

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Highlights:

1. Placenta Accreta Spectrum cases rise in proportion to the high frequency of uterine wall damage.
2. A significant association was found between curettage history and Placenta Accreta Spectrum.



INTRODUCTION

Indonesia continues to face a significant health problem concerning the Maternal Mortality Rate (MMR), which is still a long way off from achieving the Sustainable Development Goals (SDGs) target of reducing the global MMR to less than 70 per 100.000 live births by 2030.¹ According to the Long Form Population Survey conducted by Badan Pusat Statistik (BPS), the MMR in Central Java is slightly lower than the national MMR, which is reported to be 183 per 100.000 live births by 2020.² Pregnancy-related hypertension, hemorrhage, and infection are the three primary causes of maternal mortality in Indonesia. The hemorrhage that resulted in the mother's death can be classified as either antepartum or postpartum hemorrhage.^{3,4} Postpartum hemorrhage can be caused by several factors, including uterine atony, laceration of the genital tract, blood clotting disorders, and the most recent of these is retained placenta.^{5,6}

The term "Placenta Accreta Spectrum" (PAS) refers to the condition where the villi of the placenta are directly attached to the myometrium, with absence of decidua basalis and Nitabuch layer. It is the most common cause of significant obstetric bleeding. The global incidence of PAS has increased from 0.12% to 0.31%.⁷ The rise in cases is linked to high rates of uterine damage, such as caesarean and curettage procedures, both of which can damage endometrial tissue and result in abnormal placenta implantation.⁸ Various risk factors contribute to the development of PAS, including a prior cesarean section, placenta previa, curettage, advanced maternal age, multiparity, and smoking.⁹ A prospective cohort study conducted at the University of Kobe, Japan, revealed that women who underwent curettage had a 2.8-fold increased risk of developing PAS.¹⁰ According to a case-control study in Egypt, women who had a history of curettage were 3.996 times more likely to have a PAS than women who did not have a history of curettage.¹¹ Scars resulting from curettage, cesarean section, or infection can cause the Nitabuch layer to become thin or vanish.¹²

An ineffective wound healing process will permanently impair the regulation of myofibrous tissue, resulting in inflammation, loss of connective tissue elasticity, tissue edema, and relative hypoxia.¹³ Blastocysts are prompted to implant in a specific area by the Hypoxia Inducible Factor-1 (HIF-1) signal, which is activated by relative hypoxia. Elevated levels of HIF-1 trigger the myometrium to produce collagen. Healing tissue with high levels of collagen is weaker, less elastic, and has decreased vascularization.¹⁴ Based on the explanation, this study is intended to analyze the association between history of curettage with PAS because no further study

has been found on PAS risk factors at Dr. Moewardi General Hospital, Surakarta, Indonesia.

MATERIALS AND METHODS

This type of research was analytical observational with a case-control approach. A comparison of two groups: the group of women who gave birth with PAS complications and without PAS complications. In the context of this study, "complications" refers to the presence of PAS, including placenta accreta, increta, and percreta, depending on the level of villous invasion. The control group or "without PAS complications" refers to cases where PAS does not occur. Placenta previa was chosen as a control because it has several common risk factors like PAS, such as endometrial disruption, scarring from intrauterine or intraoperative procedures, and manual placenta removal.^{3,4} The definitive diagnosis of PAS in this study was established based on histopathological examination and intraoperative observations. Medical records of patients from May 2022 to May 2024 were gathered for this research. Overall, 134 patients were included in the sample for this study, which used purposive sampling.¹⁵ The study's inclusion criteria were as follows: (1) Women who were in delivery with or without PAS complications, (2) A confirmed diagnosis of PAS through histopathological confirmation, and (3) Women with a history of curettage or not.

An independent variable in the study is the history of curettage, which is divided into two groups: those who had curettage in the past and those who have not. The Placenta Accreta Spectrum is a dependent variable in this study that is divided into two groups: the PAS group and non-PAS group. This study analyzes the confounding variables, which include previous CS, mother's age, previous placenta previa, and parity, in order to minimize bias. Bivariate analysis applies the Chi-square or Fisher test for nonparametric comparative hypotheses, as well as multivariate logistic regression to identify the most influential variables. The level of significance used in this study is $\alpha = 0.05$ (95% confidence interval). The hypotheses is accepted if $p < 0.05$, which indicates a significant association between the two variables being tested. Each variable that had a p-value < 0.25 in the bivariate analysis was considered for the logistic regression analysis. Prior to the data collection process, the study received ethical approval from the Health Research Ethics Commission, Dr. Moewardi General Hospital, Surakarta, Indonesia under the Number: 677/III/HREC/2024. Next, the data is processed using SPSS 25, which was developed by IBM company in New York.

RESULTS AND DISCUSSION

The number of samples that were acquired in accordance with the large sample formula's calculation and that satisfied the inclusion criteria of 134 samples at a 1:1 ratio for each case group and control group, resulting in 67 samples being set aside for each group. From 67 patients, more than half of women with PAS (64.2%) do not have a history of curettage, while only 24 samples (35.8%) indicate a history of curettage. A higher incidence of CS, at least twice as much, was observed in women with PAS (52.2%). In contrast, most of women without PAS had never experienced CS or had a frequency of less than twice (83.6%). The presence of placenta previa in previous pregnancies was less common in both PAS and non-PAS samples; only 9 (13.4%) experienced PAS, while 7 (10.4%) did not. Most of the women who gave birth with PAS were multiparous or grand multiparous (98.5%), only one woman was a primiparous. The age group of 42 (62.7%) women with PAS belonged to the age category of <35

years, but the number of women in the <35 and ≥35 years age groups without PAS was nearly equal (Table 1).

The bivariate analysis in [Table 1](#) examines the association between history of curettage and PAS applying the Chi-square test. The obtained p-value is $p = 0.000$, indicating a significant association between the history of curettage and PAS ($p < 0.05$). There is no significant association between PAS and previous placenta previa ($p = 0.594$; Chi-square test), mother's age ($p = 0.221$; Chi-square test), and parity ($p = 0.062$; Fisher test) based to the bivariate analysis conducted on the confounding variables, which has a value of $p > 0.05$. Table 2 displays PAS risk factors with the strength of the association ranging from greatest to the smallest are previous CS ($p = 0.000$; OR = 7.549), history of curettage ($p = 0.001$; OR = 5.769), followed by mother's age ($p = 0.041$; OR = 0.418). Samples with the history of curettage were 5.769 times more likely to have PAS than patients without a curettage history.

Table 1. Basic characteristics of research samples and bivariate analysis of PAS risk factors

Variables	Placenta Accreta Spectrum		p-value
	No	Yes	
History of curettage (n, %)			
No	60 (89.6)	43 (64.2)	0.000 ^a
Yes	7 (10.4)	24 (35.8)	
Total	67 (100.0)	67 (100.0)	
Previous CS (n, %)			
Never and <2 times	56 (83.6)	32 (47.8)	0.000 ^a
≥2 times	11 (16.4)	35 (52.2)	
Total	67 (100.0)	67 (100.0)	
Previous PP (n, %)			
No	60 (89.6)	58 (86.6)	0.594 ^a
Yes	7 (10.4)	9 (13.4)	
Total	67 (100.0)	67 (100.0)	
Mother's age (n, %)			
<35	35 (52.2)	42 (62.7)	0.221 ^a
≥35	32 (47.8)	25 (37.3)	
Total	67 (100.0)	67 (100.0)	
Parity (n, %)			
Primiparous	7 (10.4)	1 (1.5)	0.062 ^b
Multiparous and grand multiparous	60 (89.6)	66 (98.5)	
Total	67 (100.0)	67 (100.0)	

CS = cesarean section

PP = placenta previa

^a Chi-square test

^b Fisher test

Table 2. Multivariate logistic regression of history of curettage, previous CS, and mother’s age

Variables	p-value	OR	CI 95%	
			Min	Max
History of curettage	0.001	5.769	2.090	15.928
Previous CS	0.000	7.549	3.060	18.624
Mother’s age	0.041	0.418	0.181	0.965

The study found a significant association ($p = 0.000$; Chi-square test in Table 1) between the history of curettage and PAS in women undergoing deliveries at Dr. Moewardi General Hospital Surakarta. Based on multivariate logistic regression analysis, Table 2 shows that history of curettage is the second most significant risk factor, after previous CS ($p = 0.001$; OR = 5.769; CI95% 2.090 – 15.928). Individuals who had previously undergone curettage had a 5.769-fold increased risk of developing PAS compared to those who had not. The findings align with a case control study conducted in China between 2015 and 2021, which found a significant association in bivariate analysis ($p < 0.001$) among curettage and PAS. In multivariate analyses, the odds of having PAS is 2.54 for a single curettage variable.¹⁶ Baldwin et al.¹⁷ reported that women with a history of curettage had a 2.1 times higher risk of developing PAS than women without a curettage history. A prospective cohort study conducted at Kobe University discovered that women with the history of curettage had a 2.8 times higher chance of developing PAS.¹⁰ Women with a history of curettages had a 3.996 times higher risk of developing PAS than women without a history of curettages, as shown in a case control study conducted in Egypt.¹¹ In experimental studies conducted in the United States, myometrial integrity disturbances and deeper trophoblastic invasions were observed in mouse with surgical scars caused by curettage, which is similar to the PAS histological picture.¹⁸

On the other hand, a retrospective study concerning the Placenta Accreta Index Score found that, with a value of $p = 0.82$, there was no significant association between the history of curettage and PAS.¹⁹ According to a study conducted at Dr. M. Djamil General Hospital Padang, $p = 0.114$, indicated that there was no significant association between prior curettage and PAS.²⁰ In addition, a study conducted in Iran by Kasraeian et al.²¹ found that a bivariate analysis between prior curettage and PAS produced the $p = 0.381$. A retrospective study conducted in Italy between 2014 and 2019 found that the $p < 0.357$ concluded that there was no significant association between previous curettage and PAS.²² A cohort study in Japan with patients from 2011 to 2014 found that previous curettage was not a risk factor for PAS ($p = 0.468$).²³

Curettage damages the endometrial tissue, resulting in abnormal placental attachment. An ineffective wound healing process will permanently disrupt the regulation of myofibers, inflammation, tissue oedema, loss of elasticity in connective tissue, and relative hypoxia.¹³ Blastocysts implant in the scar area in response to relative hypoxia via the HIF-1 signal. Healing tissue with a high collagen content is weaker, less elastic, and has less vascularization, allowing the trophoblast and corialis vili to penetrate deep into the myometrium and satisfy the fetus nutritional requirements. Women who had previously undergone curettage had decreased blood flow and increased vascular resistance in their uterine. Focal myometrial degeneration is influenced by poor vascularization, which prevents re-epithelization and decidualization from taking place in the affected area.¹⁴ Around the curettage area, there is a thinning of the decidua basalis and Nitabuch layer, which divides the corialis vili from the myometrium. A low oxygen condition provided by the basalis deficit induces trophoblastic invasion into the myometrium.²⁴ The architecture and integrity of the endometrial layer will be impaired by repeated curettage, which involves removing tissue from the uterine layer (niche formation occurs). Extravillous Trophoblast (EVT) invade uncontrollably as a result of this condition. Because of the loss of the Nitabuch layer, high HIF-1 activity will promote angiogenesis without being neutralized by the presence of inhibitory factors.²⁵

The study findings indicate that among women giving birth at Dr. Moewardi General Hospital, a significant association was observed between a history of CS and PAS ($p = 0.000$; Chi-square test in Table 1). Table 2 illustrates that the most significant risk factor for the development of PAS in logistic regression is a history of CS ($p = 0.000$; OR = 7.549; CI95% 3.060 – 18.624). Patients who have previously undergone a CS have 7.549 times higher odds of experiencing PAS compared to patients without a history of CS. This result coincides with a study held in France from 2013 to 2015, which concluded that a history of CS has a significant association with PAS, as evidenced by a p-value of less than 0.001.²⁶ In the study, the highest frequency of CS history for both patients with PAS and those without PAS was once, with 216 samples and 50 samples, respectively. Based on the findings of a study conducted in Utah, United States, the highest frequency of CS



history in patients who had PAS was not fewer than two times, which amounted to 99 (50.5%) out of a total of 196 samples. When applying multivariate analysis, a history of two CS is associated with a 4.61 times greater likelihood of experiencing PAS.²⁷

The underlying disease progression of PAS is the presence of scarring on the uterus. A cross-sectional study of maternal hemodynamics and fetoplacental circulation in Norway found that after CS, the average uterine vascular resistance increased ($p = 0.026$) but the average blood flow to the endometrium decreased ($p = 0.038$).²⁸ Blood flow disruption around scar tissue blocks scars from vascularizing, which results in the myometrium to permanently degeneration and interrupts the processes of decidualization and re-epithelialization.¹²

This study still has some limitations, such as the failure to investigate other risk factors that increase the probability of PAS (Body Mass Index of mother, In-Vitro Fertilization, multiple pregnancies, smoking, uterine abnormalities, and more), which may bias the study due to uncontrolled confounding variables.^{16,23,29-34} Additionally, this study was limited to Dr. Moewardi General Hospital Surakarta, making it less representative of the overall population. In order to obtain more representative and accurate results, it is suggested that similar research occur with a wider population and a different approach while keeping considering the confounding variables.

CONCLUSION

There is statistically significant association between the history of curettage and PAS. The probabilities of developing PAS were 5.769 times higher in patients with a history of curettage compared to those without. Based on the study's findings, the researchers suggest conducting further research using larger-scale and other methods to explore the correlation and causation between the history of curettage and PAS.

DISCLOSURES

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Conflict of interest

All of the authors do not have any conflicts of interest.

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Author contribution

HAP: develops a research proposal and study design, collects data, analyzes data, and writes manuscript. NWP & AA: develops a research proposal and writes manuscript. SS: analyzes data and writes manuscript. All authors gave contributions to the article and also provided approval to the submitted version.

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