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

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ABSTRACT

Objective: Placenta Accreta Spectrum (PAS) involves abnormal placental adherence to the myometrium, causing severe obstetric hemorrhage and increased maternal morbidity and mortality (3,000–5,000 mL blood loss). Its global incidence has risen from 0.12% to 0.31%, linked to uterine trauma from cesarean sections or curettage. This study evaluates the association between curettage history and PAS.

Materials and Methods: This study employed an analytical observational design with a case-control approach. Purposive sampling was utilized, resulting in the inclusion of 134 participants who met the predefined criteria. The study population consisted of women who delivered and were referred to Dr. Moewardi General Hospital, Surakarta, Indonesia, between May 2022 and May 2024. Data were analyzed using IBM SPSS version 25. The Chi-square test was applied to assess the association between variables at a significance level of $p < 0.05$, while logistic regression analysis was conducted to identify the most influential variables.

Results: The study cohort comprised 67 patients diagnosed with PAS and 67 without PAS. A statistically significant association was observed between a history of curettage and PAS, as determined by the Chi-square test, with a p-value of 0.000. Logistic regression analysis further confirmed this association, yielding a p-value of 0.001 and an odds ratio (OR) of 5.769 (95% CI: 2.090–15.928) for a history of curettage.

Conclusion: A history of curettage is significantly associated with the development of PAS. Patients with a prior curettage procedure are 5.769 times more likely to develop PAS compared to those without such a history.

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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 encounter a major public health challenge regarding the Maternal Mortality Rate (MMR), which remains considerably distant from achieving the Sustainable Development Goals (SDGs) target of reducing the global MMR to fewer than 70 per 100,000 live births by 2030.[1] Data from the Long Form Population Survey conducted by Badan Pusat Statistik (BPS) indicate that the MMR in Central Java is slightly below the national figure, which reached 183 per 100,000 live births as of 2020.[2] The three leading causes of maternal mortality in Indonesia include hypertensive disorders of pregnancy, hemorrhage, and infection. Hemorrhagic events contributing to maternal death are classified as either antepartum or postpartum hemorrhage.[3,4] Postpartum hemorrhage can arise from various etiologies, such as uterine atony, genital tract lacerations, coagulopathies, and more recently recognized, retained placenta.[5,6]

The term “Placenta Accreta Spectrum” (PAS) denotes a condition in which placental villi abnormally adhere directly to the myometrium, due to the absence of the decidua basalis and Nitabuch’s layer. PAS is the most frequent cause of major obstetric hemorrhage. The global incidence of PAS has increased from 0.12% to 0.31%.[7] This rising trend is attributed to the prevalence of uterine injury from procedures such as cesarean section and curettage, both of which compromise the integrity of the endometrial lining and lead to abnormal placental implantation.[8] Multiple risk factors are associated with the development of PAS, including previous cesarean section, placenta previa, uterine curettage, advanced maternal age, multiparity, and tobacco use.[9] A prospective cohort study at the University of Kobe, Japan, demonstrated that women with a history of curettage had a 2.8-fold increased risk of developing PAS.[10] Similarly, a case-control study conducted in Egypt found that women with a history of curettage were 3.996 times more likely to develop PAS compared to those without such a history.[11] Scarring from curettage, cesarean sections, or infections may lead to thinning or loss of the Nitabuch layer.[12]

Impaired wound healing can result in permanent dysregulation of myofibrous tissue, leading to inflammation, reduced connective tissue elasticity, interstitial edema, and localized hypoxia.[13] Relative hypoxia activates the Hypoxia Inducible Factor-1 (HIF-1) pathway, which signals blastocyst implantation at specific sites. Elevated HIF-1 levels promote collagen synthesis in the myometrium. However, collagen-rich healing tissue tends to be structurally weaker, less elastic, and poorly vascularized.[14] In view of this background, the present study aims to investigate the association between a history of uterine curettage and the occurrence of PAS, particularly as there has been no prior investigation into PAS risk factors at Dr. Moewardi General Hospital, Surakarta, Indonesia.

MATERIALS AND METHODS

This study adopted an analytical observational design with a case-control approach, comparing two groups: women who delivered with Placenta Accreta Spectrum (PAS) complications and those without PAS complications. In this context, "complications" denotes PAS, encompassing placenta accreta, increta, and percreta, based on the extent of villous invasion. The control group, defined as "without PAS complications," included cases without PAS.

Placenta previa was selected as a control due to shared risk factors with PAS, such as endometrial disruption, scarring from intrauterine or intraoperative procedures, and manual placental removal.[3,4] The definitive diagnosis of PAS was confirmed through histopathological examination and intraoperative findings. Medical records from May 2022 to May 2024 were collected for this study. A total of 134 patients were included using purposive sampling.[15] The inclusion criteria were: (1) women delivering with or without PAS complications, (2) a confirmed PAS diagnosis via histopathological verification, and (3) women with or without a history of curettage.

The independent variable was a history of curettage, categorized into two groups: those with prior curettage and those without. The dependent variable, Placenta Accreta Spectrum, was divided into PAS and non-PAS groups. Confounding variables, including prior cesarean section, maternal age, previous placenta previa, and parity, were analyzed to minimize bias. Bivariate analysis employed the Chi-square or Fisher test for nonparametric comparative hypotheses, while multivariate logistic regression identified the most influential variables. A significance level of $\alpha = 0.05$ (95% confidence interval) was applied. The hypothesis was accepted if $p < 0.05$, indicating a significant association between tested variables. Variables with a p-value < 0.25 in bivariate analysis were included in the logistic regression. Ethical approval was obtained from the Health Research Ethics Commission, Dr. Moewardi General Hospital, Surakarta, Indonesia, under Number: 677/III/HREC/2024 prior to data collection. Data were analyzed using SPSS 25, developed by IBM in New York.

RESULTS AND DISCUSSION

The number of samples obtained in accordance with the large sample formula and meeting the inclusion criteria amounted to 134, with a 1:1 allocation ratio between the case and control groups, resulting in 67 samples for each group. Among the 67 patients, more than half of the women diagnosed with PAS (64.2%) had no history of curettage, while only 24 individuals (35.8%) reported a history of the procedure. A notably higher incidence of cesarean section (CS) was observed in the PAS group, with at least two previous CS in 52.2% of cases. In contrast, the majority of women in the non-PAS group had either no CS history or fewer than two cesarean deliveries (83.6%). The occurrence of placenta previa in prior pregnancies was relatively low in both groups; only 9 women (13.4%) in the PAS group and 7 women (10.4%) in the non-PAS group reported such history. Most women who delivered with PAS were either multiparous or grand multiparous (98.5%), with only one woman classified as primiparous. Among women with PAS, 42 (62.7%) were under 35 years of age, while the distribution of age categories <35 and ≥35 years in the non-PAS group was nearly equivalent (Table 1).

The bivariate analysis presented in Table 1 assesses the association between a history of curettage and the occurrence of PAS using the Chi-square test. The resulting p-value was $p = 0.000$, signifying a statistically significant association between a curettage history and PAS ($p < 0.05$). No significant associations were observed between PAS and previous placenta previa ($p = 0.594$; Chi-square test), maternal age ($p = 0.221$; Chi-square test), or parity ($p = 0.062$; Fisher's exact test), based on the bivariate analysis of potential confounders—all demonstrating p-values > 0.05. Table 2 outlines the PAS risk factors, with the strength of association ranked from highest to lowest: previous CS ($p = 0.000$; OR = 7.549), history of curettage ($p = 0.001$; OR = 5.769), and maternal age ($p = 0.041$; OR = 0.418). Individuals with a history of curettage were found to be 5.769 times more likely to develop PAS compared to those without such a history.

Table 1. Basic characteristics of research samples and bivariant 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

This investigation identified a significant association (p = 0.000; Chi-square test, Table 1) between prior curettage and Placenta Accreta Spectrum (PAS) in women delivering at Dr. Moewardi General Hospital, Surakarta. Multivariate logistic regression analysis (Table 2) established that a history of curettage is the second most significant risk factor for PAS, following prior cesarean section (p = 0.001; OR = 5.769; 95% CI 2.090–15.928). Women with a history of curettage exhibited a 5.769-fold increased risk of developing PAS compared to those without such a history. These findings align with a case-control study conducted in China between 2015 and 2021, which reported a significant association in bivariate analysis (p < 0.001) between curettage and PAS, with multivariate analysis indicating an odds ratio of 2.54 for a single curettage procedure.[16] Baldwin et al.[17] observed that women with a history of curettage had a 2.1-fold higher risk of PAS compared to those without. Similarly, a prospective cohort study at Kobe University found a 2.8-fold increased risk of PAS among women with prior curettage.[10] A case-control study in Egypt demonstrated that women with a history of curettage had a 3.996-fold higher risk of PAS compared to those without.[11] Experimental studies in the United States identified disruptions in myometrial integrity and deeper trophoblastic invasion in mice with surgical scars from curettage, mirroring the histological characteristics of PAS.[18]

In contrast, a retrospective study evaluating the Placenta Accreta Index Score found no significant association between prior curettage and PAS (p = 0.82).[19] Similarly, a study at Dr. M. Djamil General Hospital, Padang, reported no significant association (p = 0.114).[20] In addition, a study conducted in Iran by Kasraeian et al.[21] in Iran found a non-significant association in bivariate analysis between prior curettage and PAS (p = 0.381). A retrospective study in Italy from 2014 to 2019 concluded no significant association (p = 0.357).[22] Additionally, a cohort study in Japan from 2011 to 2014 determined that prior curettage was not a risk factor for PAS (p = 0.468).[23]

Curettage compromises endometrial tissue, leading to abnormal placental attachment. Ineffective wound healing disrupts myofiber regulation, resulting in inflammation, tissue edema, loss of connective tissue elasticity, and relative hypoxia.[13] Hypoxia Inducible Factor-1 (HIF-1), activated by hypoxic conditions, promotes blastocyst implantation in scarred areas. Healing tissues with elevated collagen content are weaker, less elastic, and exhibit reduced vascularization, allowing trophoblasts and chorionic villi to invade deeply into the myometrium to fulfill fetal nutritional demands. Women with prior curettage experience diminished uterine blood flow and increased vascular resistance. Poor vascularization contributes to focal myometrial degeneration, impeding re-epithelialization and decidualization in affected areas.[14] The thinning of the decidua basalis and Nitabuch layer around the curettage site, which normally separates chorionic villi from the myometrium, facilitates trophoblastic invasion into the myometrium under hypoxic conditions.[24] Repeated curettage impairs the endometrial architecture by removing uterine tissue, leading to niche formation and uncontrolled invasion by extravillous trophoblasts (EVT). The absence of the Nitabuch layer, combined with elevated HIF-1 activity, promotes angiogenesis without regulation by inhibitory factors, further exacerbating the risk of PAS.[25]

The study findings demonstrated a statistically significant association between a history of cesarean section (CS) and the occurrence of PAS among women delivering at Dr. Moewardi General Hospital (p = 0.000; Chi-square test in Table 1). As presented in Table 2, logistic regression analysis identified prior CS as the most significant risk factor for PAS (p = 0.000; OR = 7.549; CI95% 3.060–18.624). Patients with a previous history of CS were found to have 7.549 times higher odds of developing PAS compared to those without such a history. These findings align with a study conducted in France from 2013 to 2015, which demonstrated a significant association between previous CS and PAS, as indicated by a p-value of less than 0.001.[26] In that study, the highest frequency of CS for both PAS and non-PAS patients was one prior CS, with 216 and 50 cases, respectively. In contrast, a study conducted in Utah, United States, found that the majority of PAS cases had a history of at least two cesarean deliveries, with 99 (50.5%) out of 196 patients reporting this. Multivariate analysis in that study indicated that having undergone two cesarean sections

increased the likelihood of developing PAS by 4.61 times.[27]

The pathophysiological basis of PAS involves the formation of uterine scar tissue. A cross-sectional study on maternal hemodynamics and fetoplacental circulation in Norway revealed that following CS, average uterine vascular resistance significantly increased ($p = 0.026$), while endometrial blood flow significantly decreased ($p = 0.038$).[28] This disruption in blood flow impairs vascularization of the scar tissue, which in turn contributes to permanent myometrial degeneration and interferes with key physiological processes such as decidualization and re-epithelialization.[12]

Nevertheless, this study has certain limitations. One of the major constraints is the absence of analysis for other known risk factors that may influence PAS, such as maternal Body Mass Index, use of In-Vitro Fertilization, multiple gestations, tobacco use, and uterine anomalies, among others.[16,23,29–34] The omission of these variables could introduce potential bias due to the presence of uncontrolled confounding factors. Furthermore, this study was conducted exclusively at Dr. Moewardi General Hospital, Surakarta, which limits the generalizability of the findings and may not adequately represent the broader population. To obtain more robust and representative results, future studies should be conducted across multiple centers using broader population samples and study designs that better account for confounding variables.

CONCLUSION

A significant association was identified between a history of curettage and the occurrence of PAS. Patients with a history of curettage were more likely to develop PAS compared to those without such a history. Based on these findings, the researchers recommend further studies involving larger populations and alternative methodologies to better investigate the relationship and potential causality between prior 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. NWPA & 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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