# Effects of Placenta Location in Pregnancy Outcomes of Placenta Accreta Spectrum (PAS): A Retrospective Cohort Study

**Shokoh Abotorabi; M.D.[1], Solmaz Chamanara; M.D.[1], Sonia Oveisi; Ph.D.[2], Maryam Rafiei; M.D.[1], Leila Amini; M.D.[1]**

1 Department of Obstetrics and Gynecology, Clinical Research Development Unit, Kosar Hospital, Qazvin University of Medical Sciences, Qazvin, Iran
2 Department of Pediatrics, Metabolic Diseases Research Center, Qazvin University of Medical Sciences, Qazvin, Iran

## Abstract
**Objective:** Placenta Accreta Spectrum (PAS) affects approximately one in a thousand deliveries. Very few studies evaluated PAS risk factors based on their location. In this study, we have investigated the effects of placenta location on placental adhesion-related complications, its risk factors, and outcomes.
**Materials and methods:** We performed a retrospective cohort study of pathology-confirmed cases of PAS from patients with peripartum hysterectomy, at a large educational hospital in Qazvin, Iran, from 2009 to 2019. Placenta location was found by ultrasound reports and intraoperative evaluation. We measured demographic features, basic characteristics, maternal and neonatal outcomes based on placental location including anterior, posterior, and lateral in Placenta Accreta Spectrum. Chi-square, t-test, and one-way ANOVA were used to examine the relation of complications, risk factors, and outcomes in PAS.
**Results:** A review of 70 cases showed the distribution of placenta location as follows: 57% anterior, 27% posterior, and 16% lateral. The mean gestational age at delivery was 35 (33-39) weeks. In 78.6% (n=55) of the patients, an association with placenta previa and in 94/2% (n=66) of cases a history of cesarean section was found, however, it was not significantly correlated with placenta location (p=0.082). We found that surgery duration was significantly longer in patients with lateral PAS (155±38, vs 129.35±33.8 and 133.15±31.5 for anterior and posterior placenta respectively, p=0.09). Patients with lateral PAS also bled more than the remaining two groups (2836 ml for lateral PAS vs 2002 and 1847 for anterior and posterior placenta respectively, p=0.022). Moreover, women with a history of uterine surgery were more likely to have posterior PAS compared to those with anterior and lateral PAS (p=0.035).
**Conclusion:** Differences in complications, risk factors, and outcomes of PAS based on placenta location may lead to improved diagnosis and decreased morbidity in women.

**Keywords:** Hysterectomy; Maternal Mortality; Placenta Accreta; Postpartum Hemorrhage; Placenta Previa

## Introduction
Placenta accreta spectrum (PAS) is a high-risk pregnancy condition that occurs when the placenta deeply attaches to the uterine wall and includes three major types: accreta, Increta, and percreta (1). The most well-known risk factor is placenta previa when there is a history of previous cesarean delivery (2) or other uterine surgeries, such as endometrial curettage

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(3). PAS is usually diagnosed using sonography with a sensitivity of 77-87%, specificity of 96-98%, a positive predictive value of 65%-95%, and a negative predictive value of 98% (4).

PAS is an uncommon complication that affects approximately one per thousand deliveries. However, it has become more common in recent years due to rise in a cesarean deliveries (5). PAS can range from 0.04% to more than 0.9% in one per thousand deliveries (6) and can cause high-risk complications that lead to massive life-threatening Intrapartum and postpartum hemorrhage in most cases (6). Placenta location may allow us to improve diagnosis and decrease the rate of life-threatening risks. For example, research showed that when the placenta previa adheres to the anterior wall of the uterus, it is more likely to have serious complications such as abnormal bleeding and hysterectomy, compared to when it adheres to the posterior wall (7-9). Moreover, PAS with posterior location is normally diagnosed late which results in more complications associated with the anterior location (10).

Although placenta location has been explored in the context of placenta previa, very few studies have examined whether the risk factors vary based on placenta location (10). Understanding the association of placenta location and placental adhesion-related complications is essential in accurate risk management. Given the lack of studies in this context and the crucial nature of the subject in avoiding life-threatening risks in women, we assessed risk factors, side effects, and outcomes of PAS based on the placental location (anterior, posterior, and lateral).

## Materials and methods

We performed a retrospective cohort analysis on patients with a history of peripartum hysterectomy associated with PAS, between January 2009 and December 2019 in Kosar Hospital, a tertiary referral educational center in Qazvin, Iran. Kosar Hospital provides care for high-risk pregnancies with patient referrals from across the province. To identify all the cases with PAS, data were extracted from the Hospital information registration system, using specialized code assigned to peripartum hysterectomy. To perform the analysis, we developed a checklist with two main sections. The first section included all of the demographic features and basic characteristics. The second section of the checklist included maternal and neonatal outcomes. A group of expert professors carefully reviewed the checklist and approved its validity. In addition, checklists were later completed by obstetricians and gynecology residents. To confirm the reliability of the checklist, the reviewers randomly selected 15 medical records, reviewed them, and checked them for similarity.

We included all patients undergoing cesarean hysterectomy for PAS that had a complete medical record and ultrasound report and pathology-confirmed PAS, in addition to a clearly defined placenta location in the ultrasound report. We excluded medical records with missing ultrasound placenta location or other missing information. Our protocol for PAS was patients with a planned cesarean hysterectomy at 34 to 35 weeks of pregnancy, with placenta left in situ.

Patients were grouped as anterior, posterior, and lateral based on placental location in the ultrasound report. The following factors were investigated concerning their association with the placental location. Baseline characteristics: PAS suspected prenatally, delivery type (scheduled, emergent), gestational age at delivery, the severity of invasion based on pathology report (accreta/inccreta, percreta), maternal age, prior cesarean-sections, prior uterine surgeries. Outcomes: operating times (minutes), estimated blood loss (estimated blood loss was determined by evaluating the blood in the suction canister and laparotomy sponges), transfusion of blood products, and intensive care unit (ICU) admission. Surgical complications: vascular injury, neurologic injury, bladder injury, and intestinal injury. Postoperative complications: postoperative hemorrhage, ileus, inability to extubate postoperatively, fever, infection, thromboembolic, acute kidney injury (AKI), re-exploration, multi-organ failure, and mortality. Neonatal outcomes: APGAR scores and neonatal intensive care unit (NICU) admission.

The study is approved by the ethical committee of Qazvin University of Medical Sciences, and all the medical records are evaluated and confirmed by a pathology group.

***Statistical analysis:*** We used SPSS statistical software for data analysis. The data is presented by descriptive statistics including mean, median, standard deviation, frequency, and percent. Using the Chi-square test, we compared the proportions, and then we performed an independent t- student test and one-way ANOVA to compare the means. For variables without normal distribution based on Kolmogorov-Smirnov test results, we used equal nonparametric tests. Then, logistic regression was conducted to identify and control the effect of

confounder variables. We considered the P-value of less than 0.05 as significant.

## Results

From January 2009 to December 2019, 33193 cesarean sections with consent to use medical records have been performed at the Obstetrics Department of Kosar Hospital. Among those, 105 (0.31%) cases had a history of peripartum hysterectomy, among which 81 patients (81 out of 105) had PAS. We excluded 11 patients from the study because of missing information. This process resulted in 70 complete cases with confirmed PAS that had a history of hysterectomy.

Placenta accrete/increta was diagnosed in 53 (75.7%) patients and placenta percreta in 17 (24.3%) deliveries. Table 1 shows baseline characteristics. In 54/3% (n=38) of the cases, PAS was unknown preoperative and was only diagnosed during surgery and then was confirmed histopathologically. The mean gestational age at delivery was 35 (33-39) weeks. In 78.6% (n=55) of the patients, an association with placenta previa and in 94/2% (n=66) cases a history of CS was found, however, it was not significantly correlated with placenta location (p=0.082). Three patients had a history of prior uterine surgery such as myomectomy.

PAS was prenatally diagnosed in 17 (53.1%), 8 (25%), and 7 (21.9%) of the patients with anterior, posterior, and lateral placenta, respectively (p=0.43). Our analysis showed that the majority of the patients in the three groups needed emergency delivery before the scheduled delivery, with a similar proportion in the three groups (p=0.16).

Table 2 shows outcomes. The surgery time was longer in the lateral placenta location but the difference was not statistically significant.

(155±38, vs 129.35±33.8 and 133.15±31.5 for anterior and posterior placenta respectively, p=0.09). In addition, 98% of the patients needed a blood transfusion. Vascular and bladder injuries were the most common surgical-related complications; and fever (n=11), post-operative hemorrhage (n=8), ileus (n=5), and re-exploration were the most common post-surgery complications (Table 2).

Furthermore, our results revealed that the lateral placenta location group had greater blood loss relative to the other two groups (2836 ml vs 2002 and 1847 for anterior and posterior placenta respectively p=0.022) (Table 2). We considered blood loss equal to 1500 ml or greater as significant because a pregnant woman can tolerate blood loss equal to 1500 ml or less without hemodynamic changes. In fact, in normal pregnancy in an average size woman, the amount of pregnancy-induced hypervolemia is about 1500-2000 ml. Moreover, our analysis showed that even after adjustment for other variables such as the number of prior cesareans, the severity of placental adhesion, delivery type, positive prenatal diagnosis, gestational age at delivery, prior uterine surgery, and having placenta previa, these differences remain statistically significant (Table 3). We have not had any mortality related to PAS in the past ten years.

## Discussion

Placenta Accreta Spectrum (PAS) is becoming increasingly common with significant life-threatening risks. Knowledge of risk factors, pre-preparation, and postpartum care can allow decreasing the morbidity and mortality rate of PAS. In our study, we examined a large cohort of patients over 10 years to examine how risk factors, diagnosis, and outcomes vary based on placenta location.

**Table 1:** Baseline characteristics of participants

|  | Anterior (n=40) | Posterior (n=19) | Lateral (n=11) | P-value |
|---|---|---|---|---|
| PAS suspected prenatally, n(%) | 17(53/1%) | 8(25%) | 7(21/9%) | 0.43 |
| Delivery Type, n (%) |  |  |  |  |
| Scheduled | 15(75%) | 3(15%) | 2(10%) | 0.16 |
| Spontaneous/ Emergent | 25(50%) | 16(32%) | 9(18%) |  |
| Gestational age at Delivery (mean ±SD) | 36.3±2.4 | 34.3± 5.1 | 34.7±4.8 |  |
| Severity of Invasion, n (%) |  |  |  |  |
| Accreta/ Increta | 30(56.6%) | 14(26.4%) | 9(16.9%) | 0/71 |
| Percreta | 10(58.8%) | 5(29.4%) | 2(11.7%) |  |
| Maternal age | 17-42 | 24-43 | 24-40 |  |
| Prior cesarean-section or prior uterine surgeries, n (%) | 39(59%) | 16(24.2%) | 11(16.6%) |  |
| Prior C-section | 0(0%) | 3(100%) | 0(0%) | 0.082 |
| Prior uterine surgeries |  |  |  | 0.035 |
| Placenta Previa in this pregnancy | 31(56.3%) | 16(29%) | 8(14.5%) | 0.73 |

PAS: Placenta Accreta Spectrum

**Table 2:** Surgical and neonatal outcomes and post-operative complications

| Outcomes | Anterior (n=40) | Posterior (n=19) | Lateral (n=11) | P-value |
|---|---|---|---|---|
| Operating time, minutes (mean ±SD) | 129.35±33.8 | 133.15±31.5 | 155±38.2 | 0.095 |
| Bleeding (EBL) ml, (mean ± SD) | 2002(300-6000) | 1847(200-4500) | 2836(200-5000) | 0.088 |
| Transfusion of Blood products during delivery, n(%) | 40(57.9%) | 18(26%) | 11(15.9%) | 0.26 |
| ICU admission, n(%) | 30(17.5%) | 12(63/2%) | 11(100%) | 0.127 |
| Surgical Complications, n (%) | | | | |
| Vascular Injury | 1(16/7%) | 3(50%) | 2(33/3%) | 0.10 |
| Neurologic Injury | 0 | 0 | 0 | |
| Bladder Injury | 10(66.6%) | 3(20%) | 2(13/3%) | 0.69 |
| Ureteral Injury | 0 | 1(100%) | 0 | 0.25 |
| Intestinal Injury | 0 | 0 | 0 | |
| Postoperative Complications, n (%) | | | | |
| Post-operative hemorrhage | 6(75%) | 1(12/5%) | 1(12/5%) | 0.52 |
| Ileus | 3(60%) | 2(40%) | 0(0%) | 0.554 |
| Inability to extubate post-operatively | 1(50%) | 1(50%) | 0(0%) | 0.69 |
| Fever | 7(63/6%) | 1(9/1%) | 3(28/3%) | 0.25 |
| Infection | 1(50%) | 0 (0%) | 1(50%) | 0.34 |
| Thromboembolic | 0(0%) | 1(100%) | 0(0%) | 0.25 |
| Acute kidney injury | 1(50%) | 1(50%) | 0(0%) | 0.34 |
| Re-exploration | 3(7/5%) | 1(5/3%) | 1(9/1%) | 0.91 |
| Multi-organ Failure | 0(0%) | 1(100%) | 0(0%) | 0.25 |
| Mortality | 0(0%) | 0(0%) | 0(0%) | |
| Neonatal Outcome | | | | |
| Apgar score at 5 minutes | 8.2±1.7 | 8.1± 2.0 | 7.0± 2.6 | |
| Apgar score at 10 minutes | 9.4±1.2 | 9.1± 2.l2 | 8.2± 2.9 | |
| NICU admission | 7(17/5%) | 3(15/8%) | 4(36/4%) | 0.57 |

We found that posterior PAS is more likely to develop in women with a history of uterine surgery. Moreover, PAS with lateral placenta location is associated with surgical complications such as greater blood loss and longer surgery duration relative to the posterior and anterior PAS. These differences based on placenta location could help improve diagnosis and reduce morbidity of cesarean hysterectomy in women.

In our study cases, no maternal mortality occurred, despite massive hemorrhage in some women, which we associate to highly qualified experts. We also used a team-based approach and infusion of adequate blood products to prevent mortality. Because a patient's outcome depends not only on the surgical skills of the attending obstetrician at performing a complex hysterectomy procedure but also on immediate access to blood products for massive transfusion and postoperative intensive care (11).

**Table 3:** Results of logistic regression considering predictors of abnormal bleeding volume post cesarean hysterectomy

| Dependent Variables | B | S.E. | Wald | Sig. | Exp(B) | 95% C.I.for EXP(B) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower | Upper |
| Number of prior cesarean | .081 | .437 | .034 | .853 | 1.08 | .461 | 2.551 |
| Severity of placental abnormal adhesion | | | | | | | |
| Accrete | | | | Reference Group | | | |
| Increta | .468 | .627 | .557 | .455 | 1.60 | .467 | 5.457 |
| Percreta | 2.028 | .886 | 5.238 | .022 | 7.60 | 1.338 | 43.118 |
| Placenta site | | | | | | | |
| Anterior | | | | Reference Group | | | |
| Posterior | -.035 | .632 | .003 | .955 | .97 | .280 | 3.332 |
| Lateral | 2.543 | 1.199 | 4.502 | .034 | 12.72 | 1.214 | 133.271 |
| Delivery type (Emergent vs. Scheduled) | -.967 | .699 | 1.914 | .167 | .38 | .097 | 1.496 |
| Positive prenatal diagnosis | .379 | .678 | .313 | .576 | 1.46 | .387 | 5.517 |
| Gestational age (> 34 weeks) | -.224 | .655 | .117 | .732 | .80 | .221 | 2.887 |
| Positive history of prior uterine surgery | -.119 | .518 | .053 | .819 | .89 | .322 | 2.451 |
| Having placenta previa | .380 | .366 | 1.077 | .299 | 1.46 | .714 | 2.996 |

Maternal mortality of PAS was previously reported to be as high as 7% of cases (11), because of different conditions such as lack of access to prenatal diagnosis, specialist surgeons, blood transfusion, and intensive care facilities (11). A recent study by Bekhosian et al reported no maternal mortality in a study of 442 women with PAS (12), so a team-based approach along with access to adequate blood products is necessary to avoid maternal mortality.

In our study, the mean blood loss was 300-6000 ml in anterior PAS, 200-4500 ml in posterior PAS, and 200-5000 ml in lateral PAS. Schwickert et al reported placenta accreta or increta (lower grades) can be associated with blood loss of more than 3500 to 5500 ml (13). Research shows that, in placenta percreta (higher grades), a blood loss of more than 3500 ml usually occurs in cases where the placental invades into other organs, whereas, without invasion of placental into other organs, the blood loss usually is lower (13). In this study, for patients with PAS, the mean estimated blood loss ranged from 2000 to 7800 ml. Many patients required multiple blood transfusions and each patient received a median of five units of pRBC (13). Research has demonstrated that massive hemorrhage is a major concern in patients with PAS that experience a median blood loss of 2500 to 3000 ml at the time of surgery (14, 15). However, there are a few reliable predictors of life-threatening blood loss in PAS, which is the same in all placenta location groups (16).

In our study PAS with lateral placenta location is associated with surgical complications such as greater blood loss and longer surgery duration relative to the posterior and anterior PAS. Previous research also has confirmed that lateral placenta location in Previa and PAS patients affects prenatal outcomes such as blood loss (17). Furthermore, in placenta previa, non-lateral placenta showed a higher volume of blood loss than placenta present in lateral uterine wall (18), which can be due to placenta with central part being fed by both uterine arteries, rather than just one in lateral uterine wall (18). Therefore, it is essential to do the surgery in centers capable of rapid transfusion of a large volume of blood products. However, in the presence of focal PAS, lateral placenta previa with anterior dominancy has shown greater blood loss (19). In fact, the thicker part of myometrium in the patients with anterior dominancy might increase the blood loss from the incision location (20). Although these findings are in contrast to our results about the increase of blood loss in lateral PAS, our medical records did not specify dominancy (anterior or posterior) of lateral PAS in the ultrasound reports. Therefore, the anterior or posterior dominancy might affect the amount of blood loss in patients with lateral PAS.

Our study also showed that posterior PAS is more likely to occur in women with a history of uterine surgery. PAS can occur after any procedure or operation that harms the endometrium, which includes uterine curettage, myomectomy, endometrial ablation, uterine artery embolization, or manual removal of the placenta (21). Identifying risk factors for posterior PAS is a challenging task because of the abnormal invasion of the placenta to the posterior wall of the uterus (22). Previous research has confirmed that placenta previa and previous uterine surgery are the most common risk factors of posterior PAS (22). And, our results align with previous studies that have confirmed there is a higher chance of developing posterior placenta adhesion in women with previous uterine surgery (23) that needs to be analyzed for heightened awareness and decreased rate of mortality in women with PAS.

Furthermore, about 77% of patients with PAS in our study had Previa, of which 93.9% were women with previous cesarean surgery. Previous research has confirmed the significant association of the increase in the number of previous cesarean sections with a higher risk of PAS (24-30). Moreover, pregnancies with PAS have a higher risk of neonatal and pregnancy complications, which appears to be the result of implantation and interference with normal placental function (28-30). In addition, in our study, the median gestational age at delivery in lateral and posterior placenta adhesion was 34 weeks (range 29–39) relative to the 36 weeks (range 33–39) in anterior placenta adhesion, which is similar to another study that reported gestational age of 37 weeks in women with placenta accreta (31). The most relevant factor influencing the neonatal outcome in women with PAS is gestational age at delivery, with higher gestational ages leading to better neonatal outcomes (32). In this study, we had one patient with multiple organ failure related to invasion of posterior placenta to pelvic organ vessels.

To our knowledge, this is the first study on the effects of placenta location on PAS in Iran. Our study calls for more preoperative considerations such as adequate blood products and expert surgical teams with a team-based approach in patients with lateral PAS, to decrease the morbidity and mortality rate of PAS patients. However, the retrospective nature of

our study can be a limitation to the study. Moreover, the quality of the documentation over the 10-year study period affected the number of the patients and the lack of a few variables such as dominancy (anterior or posterior) of lateral PAS on ultrasound reports. While our study is a major step towards identifying the association of placenta location and placental adhesion-related complications to develop accurate risk stratifications, future studies need to consider using data from different hospitals with a larger study cohort.

## Conclusion

PAS is a life-threatening disorder that is most common in women with placenta previa and previous cesarean sections. The differences in complications, risk factors, and outcomes of PAS based on placenta location may allow us for improved diagnosis and decreased morbidity in women. Therefore, the goal of obstetrical management should be to identify women with PAS by obstetric history and imaging techniques; And to ensure delivery by multidisciplinary teams in specialized obstetric referral centres whenever possible. Even in expert hands, blood loss can still be massive and difficult to manage.

## Conflict of Interests

Authors have no conflict of interests.

## Acknowledgments

The authors thanks to all the participants of this study. There is no conflict of interest in this study.

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