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# Placenta Accreta Spectrum; Risk Factors, Complications, Advantages and Disadvantages to Decrease Maternal Morbidity and Mortality

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**ABSTRACT**

**Background & Objective:** Placenta Accreta Spectrum (PAS) is a condition in pregnant women where trophoblastic tissue attaches abnormally to the uterus myometrium, causing maternal deaths. Major risk factors include placenta previa and cesarean delivery, which is increasing without medical indication. This study was conducted with aim to explore the risk factors of PAS, clinical outcomes of affected patients, and strategies to minimize maternal morbidity and mortality.

**Materials & Methods:** A total of 142 women who had undergone at least one cesarean delivery in the past were included. Among them, 85 women had placenta accreta spectrum (PAS) in their current pregnancy (group 1), while 57 did not have PAS (group 2). The information regarding their demographics and previous gynecological history, including placenta previa were collected. $P<0.05$ was considered statistically significant.

**Results:** The risk of placenta accreta spectrum (PAS) is significantly higher in cases where there has been a previous cesarean delivery and placenta previa ($p<0.05$). There were no significant differences between past elective or emergent cesarean delivery ($p>0.05$). PAS was associated with more emergent cesarean deliveries ($p<0.001$) and hysterectomies ($p<0.001$). Moreover, 97% of patients with history of placenta previa developed PAS ($p<0.001$). Most of the patients who underwent hysterectomy had PAS and placenta previa ($p<0.001$). There was no significant correlation between previous hysteroscopies and curettages and a higher risk of PAS ($p>0.05$).

**Conclusion:** Women with previous cesarean delivery are significantly at risk of placenta accreta in their future pregnancies. Pregnant women should avoid insisting on elective cesarean delivery without medical indication. Planned cesarean delivery could reduce the maternal complications.

**Keywords:** Cesarean Delivery, Placenta Accreta Spectrum, Repeated Cesarean Section, Pregnancy Outcome

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## Introduction

The maternal mortality rate has been dropped during last decade, but unfortunately it is still high. Most of maternal deaths are belonged to middle to low-income countries (1). According to latest data, world health organization (WHO) declared that 800 mothers died each day in 2020 due to preventable pregnancy complications such as severe bleeding after childbirth (1). Post-partum hemorrhage (PPH) is common during the peripartum period. It is the leading cause of maternal morbidity and mortality around the world (2). Placental abnormalities are one of the risk factors for PPH (2). Placenta Accreta Spectrum (PAS) refers to the unusual adherence of trophoblastic tissue to the myometrium of the uterus during pregnancy (3). This abnormal placentation leads to lethal hemorrhage when myometrium-placenta detachment occurs after delivery. Based on the degree of the trophoblastic invasion to the uterine myometrium, there are three types of PAS, namely placenta accreta, placenta increta, and placenta percreta (3). Placenta previa, history of cesarean delivery (CD), and recurrent abortions are some risk factors of placenta accreta. Maternal complications are more likely to occur in association with PAS complications, such as fever, wound infection, PPH, uterine rupture, third-trimester vaginal bleeding, maternal blood transfusion, post-partum hysterectomy, intensive care unit (ICU) admission, and longer length of hospital stay (4). As

CDs are significantly increasing each year, the incidence of PAS and its complications are raising substantially **(5)**. Therefore, the present study was conducted with aim to investigate the risk factors of PAS in women with at least one CD. Moreover, the pregnancy outcomes and complications of patients with PAS were evaluated.

## Methods

This cross-sectional study was approved by the research ethics committees of Qom University of Medical Science. One hundred and forty-two patients who had at least one cesarean delivery (CD) referred to the teaching hospitals of Qom city between 21 march 2019 and 21 march 2021 were enrolled into the study. Women aged 18-50 years who had a history of cesarean section and no prior uterine manipulation and surgery were eligible to participate in this study. Individuals who had normal vaginal delivery and incomplete data were removed from the research. Patients were divided into two groups: patients with PAS (First group or PAS group) and patients without PAS (Second group).

Before starting the research process, personal consent was obtained from each patient. A researcher-made checklist was utilized in this study. The checklist evaluated the numbers of past CDs, past obstetrics history, past surgical history and curettages, history of ectopic pregnancy, infertility, infectious diseases, financial status, and demographic information such as maternal age, etc. The checklist was completed by the researchers during patients' admission to the general ward following the surgery (cesarean section or hysterectomy).

Data were analyzed using SPSS software (version 20). Frequency tables were used to analyze qualitative variables and means and standard deviations to analyze quantitative variables. The chi-square test was used to compare the classified variables and the independent t-test for quantitative variables. P<0.05 was considered statistically significant.

## Results

A total of 142 with prior CD were enrolled in the current study. Participants were divided into two groups. Eighty-five patients were in the PAS group who had PAS and 57 individuals were in the second group who had no PAS in their current pregnancy. The mean age of patients was 34.12 ± 5.55 years, ranging from 20 to 48 years old. The mean age for first and second groups were 33.8±5.1 years and 34.5±6.09 years, respectively (p=0.67) (Table 1).

**Table 1. Maternal characteristics of the study participants**

| | | *PAS group (n=8٥)* | *Second group (n=5٧)* | *P-value* |
|---|---|---|---|---|
| ***Age*** | | 33.86 ± 5.17 | 34.50 ± 6.09 | 0.67 |
| ***Iranian nationality*** | | 78% | 74% | 0.58 |
| ***Economical state*** | ***Low*** | 31 (37.4%) | 17 (29.3%) | 0.41 |
| | ***Middle*** | 42 (50.6%) | 30 (51.7%) | |
| | ***High*** | 10 (12%) | 11 (19%) | |
| **Primary cesarean** | ***Elective*** | 59 (71.1%) | 35 (28.9%) | 0.18 |
| | ***Emergent*** | 24 (60.3%) | 23 (39.7%) | |
| **Presence of underlying diseases** | | 43 (51.2%) | 34(58.6%) | 0.38 |
| **History of curettage or hysteroscopy** | | 8 (9.6%) | 1 (1.7%) | 0.11 |
| **Placenta previa** | | 34 (40.5%) | 1 (1.7%) | < 0.0001 |
| **Current Cesarean Delivery** | **Elective** | 19 (22.6%) | 41 (70.7%) | < 0.0001 |
| | **Emergent** | 65 (77.4%) | 17 (29.3%) | |
| **History of AUB** | | 2 (2.5%) | 0 | - |
| **Hysterectomy** | | 13 (92.8%) | 1 (7.2%) | 0.004 |
| **History of infertility** | | 3 (3.8%) | 3 (5.2%) | - |
| **Opioid Addiction** | | 1 (1.2%) | 4 (6.9%) | - |
| **History of EP** | | 1 (1.2%) | 0 | - |

**AUB: Abnormal Uterine Bleeding; EP: Ectopic Pregnancy**

The presence of past CD was associated with more prevalence of placenta accreta (p=0.003). Most of the cesarean deliveries in the first and second group were elective and without medical indication (71.1% and 60.3% respectively). According to the finding, most of our cesarean deliveries are without medical indication. Both elective and emergent CDs increased the risk of PAS and there was no significant difference between these deliveries (p=0.1). Moreover, 77% of the patients with PAS needed emergent cesarean delivery in their current pregnancy, whereas, 29% of the patients without PAS underwent emergent CD (p<0.0001). In this study, 14 patients had undergone hysterectomy. All of these hysterectomies were performed in patients with PAS. Almost all of these 92.8% (13/14) hysterectomies were performed in emergent cesarean deliveries (P=0.004). This finding shows the importance of antenatal diagnosis and planned cesarean section in patients with PAS.

Placenta previa was significantly associated with placenta accreta. Nearly all of the patients (97.1%) who had history of placenta previa in their last or current pregnancies developed PAS in their subsequent pregnancies (OR= 38.7, p<0.0001). In addition, 28.5% of the patients with placenta previa underwent hysterectomy. On the other hand, just 3.7% of the patients without placenta previa needed hysterectomy (P<0.0001). Hysteroscopy and curettage did not increase the risk of placenta accreta in subsequent pregnancies (9% vs. 1.7%, p<0.05). Moreover, 65 patients (78.3%) of the first group and 74% in the second group were Iranian (p<0.05). In this study, 42 patients in the PAS group had a moderate economic state versus 32 patients in the second group. No significant differences were seen between the economic state and increased risk of PAS. The presence of underlying diseases does not differ between the two groups (p=0.38). In addition, 30% of the PAS group and 29% in the second group had at least one underlying disease (p=0.3).

## Discussion

According to the latest WHO agencies, a mother dies during pregnancy or childbirth every two minutes. Severe blood loss after childbirth is the main cause of maternal deaths (1). The incidence of placenta accreta spectrum (PAS) varies from 1.7 to 14.1 per 10000 deliveries depending on regions **(6)**. Raised cesarean deliveries (CDs) rate led to an increased prevalence of PAS during recent years. The majority of studies revealed that women with a history of CD are at increased risk of placenta accreta **(6, 7)**. Some studies, on the other hand, suggested that increased PAS may not be due to past CDs **(4, 6)**. Recognizing modifiable risk factors such as cesarean delivery, a significant risk factor for placenta accreta, helps clinicians to decrease the incidence of this disorder **(4)**. The rate of advanced maternal age raised in developed countries during the last decades **(8)**.

Advanced maternal age is associated with higher maternal and fetal complications such as abnormal placentation **(9)**. Some studies reported that patients with PAS had younger maternal age compared to those without PAS **(7)** While other authors found that PAS patients had older age compared to other patients **(10, 11)**. The rate of CD and elective CDs without medical indication raised worldwide during the last few years **(12)**. The age of the patients was not found to be associated with an increased risk of PAS in the present study. In other words, age does not have an impact on the risk of PAS. Another study suggested no relationship between the type of CD and increased risk of PAS **(13)**. Some authors, in contrast, suggested that primary elective CD increased the risk of placenta accreta in future pregnancies **(7, 14)**. In the current research also, women with primary elective or emergent CDs were at increased risk of PAS in their subsequent pregnancies and there was no significant difference between these two types of CD.

Planned delivery for patients with PAS is associated with decreased pregnancy complications such as hemorrhage and blood transfusion **(15, 16)**. An international multicenter study which evaluated 338 women with PAS demonstrated that planned hysterectomy is associated with less peripartum blood loss **(17)**. Ornaghi, et al. **(18)** showed that antenatal suspicion of PAS reduces peripartum blood transfusions **(18)**. To reduce unscheduled deliveries in patients with PAS, Saccone, et al. **(19)** suggested planning a cesarean hysterectomy at $34^{0/7}$- $34^{6/7}$ gestational weeks. This strategy increases neonatal intensive care unit (NICU) stay **(19)**. In contrast, Morlando, et al. **(20)** revealed emergent deliveries are not associated with increased maternal complications, such as blood loss, compared with planned deliveries. They reported that antenatal hemorrhage is the only risk factor for an emergent delivery **(20)**. Morlando, et al. **(20)** study concluded that in the presence of adequate expertise and resources, delivery could be postponed until gestational age >$36^{0/7}$ weeks, if patient has no preterm labor risk and antenatal hemorrhage **(20)**. It is important to note that Morlando et al. performed a study in highly experienced referral centers. Thus, this strategy may not suitable for less experienced centers.

According to the findings of the present study, pregnancies complicated by PAS were associated with more emergent cesarean deliveries subsequently and emergent CDs were associated with more maternal complications such as hysterectomy. Tinari, et al. **(21)** provided evidence that undergoing curettage is a contributing factor to the development of PAS. They suggested that patients with posterior placenta previa and other PAS risk factors such as curettage, need magnetic resonance imaging (MRI) to rule out PAS if classic ultrasound (US) signs are not present in detailed US **(21)**. However, Amirabi, et al. **(22)** reported US has a positive predictive value of 100% in diagnosis of PAS **(22)**. In the current research, although more patients in

PAS group underwent hysteroscopies and curettages compared to another group, no significant difference was found between the two groups. Han, et al. **(23)** demonstrated that placenta previa increases maternal complications and treatment costs. Thus, they suggested that measures must be taken to lower the maternal morbidity and mortality rate in mothers with PAS and placenta previa **(23)**. Some authors concluded that the main risk factor for PAS in women without placenta previa was pregnancy by assisted reproductive technology (ART) not previous CD. They reported that prior cesarean delivery is the major risk factor for PAS in women with placenta previa **(24)**. A review article demonstrated that in vitro fertilization (IVF), dilation and curettage, and myomectomy are the leading predictors of PAS in pregnancies without placenta previa **(25)**. PAS in pregnancies without placenta previa had less maternal mortality and morbidity compared to pregnancies complicated with PAS and placenta previa **(25)**. In the current study, six patients had history of infertility. No significant difference was observed between the PAS group and the second group (those without PAS) in terms of IVF and ART. It may be due to that the majority of infertile patients who conceived through ART did not undergo CD in our center. They undergo CD in private centers.

There are some limitations in the present study. First, some covariates may not be evaluated accurately, due to the small sample size of the study. Second, maternal and fetal outcomes were not evaluated completely and properly in the two groups. Third, most of the patients were from one center, and it is better to evaluate the patients in a multicenter study. Evaluation of some factors such as economic state, history of curettage and hysteroscopy, and underlying disease is the strength of our study.

## Conclusion

As evidenced by the findings of the present study, women who have previously undergone a cesarean delivery and have a history of placenta previa are at a significantly higher risk of developing placenta accreta spectrum (PAS) in subsequent pregnancies. It does not matter whether the prior CD was performed electively or emergently. Of note, most of the pregnancies complicated with PAS needed emergent CD, with serious complications such as hysterectomy. The women of reproductive age are advised that don't postpone their pregnancies and avoid elective CD without medical indication. It is also recommended that clinicians inform their patients that cesarean is not a totally safe surgery and its complications may reveal in the future. It seems antenatal diagnosis of PAS and planned CD may reduce maternal complications.

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Not applicated.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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