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Placenta Accreta spectrum (pas) disorders: A 10-year study at tertiary care center, Ahmedabad, western India

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Abstract

Background: The last 30 years have witnessed the dramatic increase in the incidence of placenta accreta spectrum (PAS) disorders from 0.12% to 0.31%. The spectrum of abnormal placental invasion ranges from the subclinical findings of adherent placental basal plate with the myometrial fibres to the substantial presentation of placenta percreta.

Methods: In this retrospective study of 10 years, there were 81,650 deliveries at our tertiary care center and 28 patients were diagnosed with PAS disorders. The placental localization and diagnosis of placental spectrum disorders were confirmed with ultrasound and color doppler.

Results: Total deliveries during the 10 years study were 81,650, out of which 27 cases met the diagnostic criteria of PAS with ultrasound and 1 case diagnosed intraoperatively resulting incidence of PAS to 0.035%. There is increase in incidence of PAS from 0.0125% in 2010 to 0.1% in 2019. All these patients were planned for elective cesarean section at 35 weeks gestation, but 2 of them presented in emergency with bouts of bleeding and required immediate intervention. Massive hemorrhage was reported in 12 (42.8%) cases and 26 (92.9%) cases required blood transfusion. Bladder injury was reported in 6 (21.4%) case. Maternal mortality has been noted in 1(3.5%) case which was complicated with disseminated intravascular coagulation and acute renal failure.

Conclusions: Favorable outcome in PAS disorders can only be achieved with preoperative multidisciplinary input and perioperative measures require adequate time in order to be instituted.

Keywords: Placenta accreta, morbidly adherent placenta, placenta previa

Introduction

The last 30 years have witnessed the dramatic increase in the incidence of placenta accreta spectrum (PAS) disorders from 0.12% to 0.31%. Irving in 1937 first described placenta accreta as the failure of separation of the placenta from uterine wall following delivery of the fetus leading to the often used term morbid placental adherence [1]. Various terminologies has been applied to this condition, however, recent guidelines suggested the adoption of term placenta accreta spectrum (PAS), including accreta, increta and percreta [2]. Invasive placentation is associated with catastrophic hemorrhage and having approximately 7.0% mortality rate [3].

PAS refers to a spectrum of abnormal placental invasion which ranges from the subclinical (mostly microscopic) findings of adherent placental basal plate with the myometrial fibres to the substantial presentation of placenta percreta, where the placental tissues invades through the uterine wall and its serosa into the peritoneal cavity including the bladder most often. PAS is traditionally considered to occur as the consequence of localized uterine injury (previous caesarean section) which leads to locally defective decidualization or scarring and abnormal placental adherence in a subsequent pregnancy. The rising trends of PAS disorder is attributed to advancing maternal age (≥ 35 years) and increasing number of cesarean sections globally [4]. Women having prior myomectomy, vigorous curettage resulting in Asherman syndrome, submucous leiomyomas, thermal ablation and uterine artery embolization is at risk for PAS disorders [4].

Optimal and timely management of women with PAS will help reducing the maternal and perinatal morbidity and mortality [5]. It involves early antenatal diagnosis and recognition of high-risk pregnancy based on clinical risk factors, accurate preoperative diagnosis with dedicated ultrasound and MRI if necessary, proper maternal counselling and multidisciplinary

approach at the time of delivery.

The objective of this study was to evaluate the high-risk factors, early antenatal diagnosis using ultrasonography and color doppler and various management strategies to improve the fetomaternal outcome in PAS disorders at our tertiary care center.

Materials and Methods

In this retrospective study of 10 years from January 2010 to December 2019, there were 81,650 deliveries at our tertiary care center and 27 women were diagnosed with PAS disorders with ultrasound and color doppler, one case diagnosed intraoperatively. Demographic profile including age, parity, gestational age, past obstetric and medical history, general and abdominal examinations, laboratory and radiological investigations were recorded for all these patients. The placental localization and diagnosis of placental spectrum disorders were confirmed with ultrasound and color doppler.

In all the antenatal women at our center, routine ultrasonography is performed at 20 weeks gestation to localize the placenta. In this scan, all the women with suspected diagnosis of placenta previa on transabdominal scan was confirmed by transvaginal scan. Repeat ultrasound with color doppler at 32 weeks gestation was done in women having low-lying placenta at previous scan at 20 weeks. The risk of PAS increases in women with previous cesarean section with placenta previa or anterior placenta underlying old cesarean section scar [6].

Following sonographic and color doppler findings suggested the diagnosis of PAS:

- Multiple linear, irregular vascular spaces within the placenta (swiss cheese appearance)
- Marked thinning or obliteration of the retroplacental hypoechoic zone.
- Interruption of the hyperechoic border between the uterine serosa and bladder.
- Remarkably thin or even non visualized lower uterine segment.

- On color doppler, marked peri-placental vascularity and vascular lakes with turbulent flow (PSV > 15cm/s)

All the diagnosed cases of PAS were planned for elective cesarean section at 35 weeks gestation with the consent for cesarean hysterectomy, while 2 cases were managed conservatively. Preoperatively cross-matched blood products were prepared in all these cases. Histopathological examination was requested for all cases which underwent cesarean hysterectomy. These patients were admitted to ICU.

Inclusion Criteria: All patients diagnosed prenatally as PAS disorders by means of Ultrasound and colour doppler studies and confirmed postoperatively by histopathological examination.

Exclusion Criteria: Any other uterine pathology or cause needing cesarean hysterectomy.

Outcome measures included management plan including intraoperative interventions (cesarean hysterectomy, internal iliac artery ligation, conservative surgery, relaparotomy). Data regarding maternal mortality and morbidity (admission to ICU, massive hemorrhage, blood transfusion, disseminated intravascular coagulation, bladder injury, infection and prolonged hospital stay) and perinatal outcome were collected and analyzed.

Results

Total number of deliveries during the 10 years study period was 81,650, out of which 710 cases (0.87%) were placenta previa. Out of these 710 cases, 27 cases met the diagnostic criteria of PAS disorder and 1 case diagnosed intraoperatively making its incidence 0.035%. There is increase in incidence of PAS from 0.0125% in 2010 to 0.1% in 2019 as depicted in figure 1. Out of 28 cases, accreta was reported in 8 (28%) cases, increta in 13 (47%) and percreta in 7 (26%) cases.

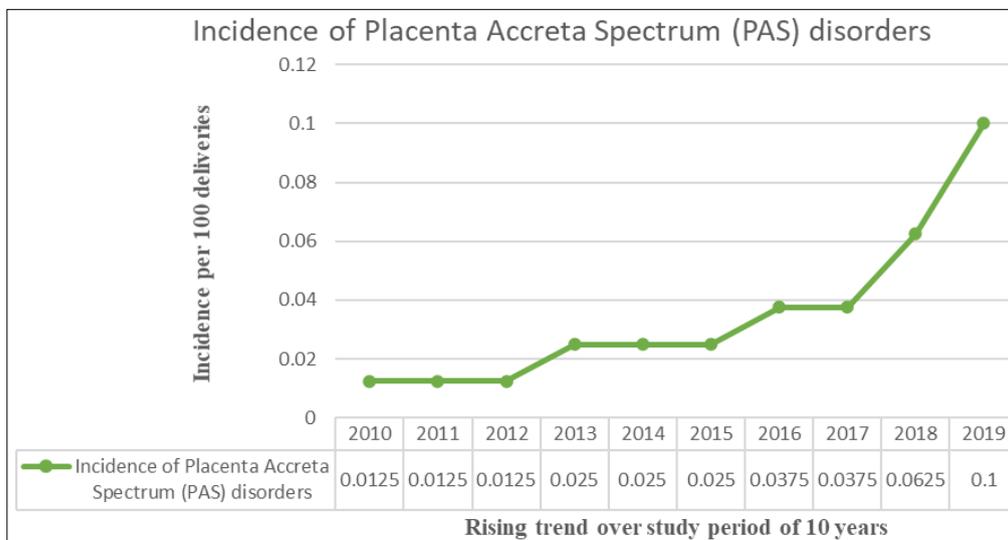


Fig 1: Rising trends in the incidence of Placenta Accreta Spectrum (PAS) disorders (2011-2020)

The mean age of the women was 28.6 ± 4.1 years with 3 women (11.5%) having age above 35 years. The mean gravidity observed was 3.1 ± 0.6 . In these women with PAS, 8 cases had anterior placenta previa type II, 11 cases had anterior placenta previa type III and 9 cases had type IV central placenta previa. In this study of 10 years, an increasing incidence of cesarean section is observed from 39.6% in 2010 to 44.9% in 2019 as

demonstrated in figure 2. There were 10 cases with previous 1 cesarean section, 10 cases with previous 2 cesarean section, 6 cases with previous 3 cesarean sections and 2 cases with previous 4 cesarean sections. This study revealed that the risk for PAS were advanced maternal age (> 32 years), previous cesarean sections (higher the number of cesarean sections, higher is the risk for PAS), multiparity (≥ 3) and placenta previa.

Table 1: Characteristics of patients diagnosed with PAS

	Present study	Eller <i>et al.</i> [30]
Mean age (year)	28.6 ± 4.1	32.4%
Age ≥ 35 years	11.5	-
Gravidity (Mean)	3.1 ± 0.6	5%
Previous CS	36%	33%
Previous 2 CS	36%	24%
Previous 3 CS	21%	34% (Previous ≥3)
Previous 4 CS	7%	
Placenta Previa	100%	77%

All the patients with diagnosed PAS were planned for elective cesarean section at 35 weeks gestation, but 2 of these cases presented in emergency with bouts of bleeding and required

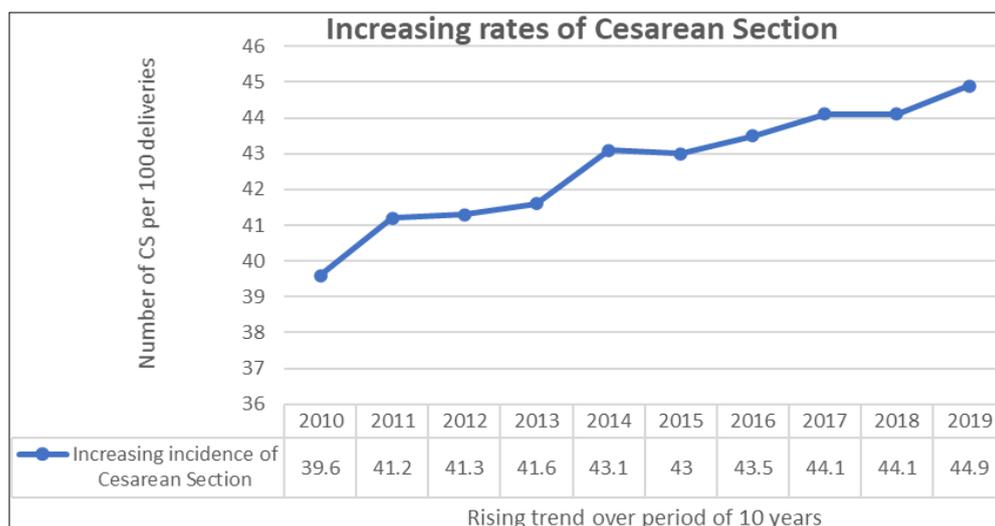
immediate intervention. One case was with previous 3 cesarean section at 29 weeks gestation and emergency cesarean section (posterior fundal incision was kept) was performed and placenta was left in-situ and monitoring by sequential USG and serial β -hCG, placenta resorbed after 16 weeks. Another case was with previous 1 cesarean and aborted in II trimester (20 weeks gestational age) followed by retained placenta due to PAS. As there was no active bleeding, she was managed conservatively by serial USG, β -hCG monitoring and placenta expelled spontaneously after 14 weeks. Obstetric hysterectomy was performed in these 26 cases and 2 cases were managed conservatively. Subtotal hysterectomy (undilated and uneffaced cervix left in-situ) was performed in 20 cases while total hysterectomy was required in 6 cases.

Table 2: Feto-Maternal complications associated with PAS

Complications	Present study No. of cases (N=%)	Eller <i>et al.</i> [30] (%)	Norris <i>et al.</i> [31] (%)
Bladder injury	6 (21.4)	-	36.1
Ureter injury	-	-	4
Bowel injury	-	-	-
Hemoperitoneum requiring relaparotomy	1 (3.5)	3	2
Intra-abdominal pelvic packing	2(7.0)	-	-
Acute respiratory distress syndrome (ARDS)	1 (3.5)	-	-
Disseminated intravascular coagulation (DIC)	1 (3.5)	29	-
Massive hemorrhage	12 (42.8)	-	-
Blood transfusion	26(92.9)	43	-
Prolonged hospital stays	27 (96.4)	49	-
ICU admission	26 (92.9)	43	-
Maternal mortality	01(3.6)	00	00
Neonatal complication	Neonatal mortality	1 (3.5)	-
	Physiological jaundice	5 (17.9)	-

Out of 28 cases, 26(92.9%) required blood transfusion. Massive hemorrhage (> 1.5L) was noted in 20(71.4%) cases and multiple blood products were transfused ranging from 4 units to 21 units. There was inadvertent bladder injury in 6 (21.4%) cases, out of them 5 cases had placenta percreta and one case had placenta increta. Bladder injury was repaired in 2 layers with vicryl no 3-0. In 6 cases (23%) with excessive bleeding bilateral internal iliac artery was ligated that helps to control hemorrhage by reducing the pulse pressure. Two (7.0%) cases required intra-abdominal pelvic packing for 48 hours as there was persistent oozing from vault and bladder serosa even after bilateral internal iliac artery ligation. After the cesarean hysterectomy (performed at outside hospital for PAS) in 1 case,

hemoperitoneum was reported that required emergency exploratory re-laparotomy and all the pedicles were secured again and intraperitoneal drain inserted. Postoperative ventilatory support was needed for 48 hours in 2 cases which developed ARDS. There was prolonged hospital stay of 10 days in 27 cases. The case of retained placenta was discharged after one week with advice of regular follow-up. Maternal mortality has been noted in 1(3.5%) case which was complicated with disseminated intravascular coagulation (DIC) and acute renal failure (ARF). There has been one neonatal mortality which was delivered at 29 weeks of gestation and physiological jaundice was observed in 5 neonates and required phototherapy.

**Fig 2:** Increasing number of cesarean sections over 10 years

Discussion

Abnormal adherence of the placenta to the myometrium is established very early in pregnancy and it's been classified into 3 types, placenta accreta where chorionic villi gets implanted directly on the myometrium, placenta increta where chorionic villi invades inside the myometrium and placenta percreta where chorionic villi invades through the entirety of myometrium and involves the surrounding organs^[8]. Most common type is placenta accreta accounting for 75% of cases^[8] but the present study reports accreta in only 28% of cases. The widely accepted hypotheses regarding the etiology for PAS is the underlying defect at the endometrial-myometrial interface at the scar of previous cesarean section or any other uterine surgery which injures the endometrium, which leads to abnormal decidualization in the scar area and causes deep anchoring of chorionic villi and trophoblast infiltration^[9]. But this could not justify the rare occurrence of PAS in nulliparous women without any previous uterine surgery. A probable explanation for this can be obtained from the recent article by Helena *et al.* which describes the similarities between the molecular biology of PAS and 8 hallmarks of carcinogenesis^[10, 11].

The increasing incidence in the placenta accreta spectrum is quite evident from the observational studies across the past decades. It's been observed that the prevalence of PAS described in studies from 1970 to 1980 were between 1 in 2,510 and 1 in 4,017 compared to which the rate reported was 1 in 533 from 1982 to 2002^[7]. In the United States overall incidence of PAS in 2016 study using National Inpatient Sample was 1 in 272, which is strikingly high when compared to any other published study^[7]. Our study reports the incidence of 0.035% (1 in 2857 deliveries) over the span of 10 years which reports increasing trends from 0.0125% (1 in 8000 deliveries) in 2010 to 0.1% (1 in 1000 deliveries) in 2019. The increasing trend is also observed in the incidence of cesarean section from 39.6% in 2010 to 44.9% in 2019.

Several risk factors have been implicated for the PAS. The most common is previous cesarean delivery and the incidence rises with the higher order of prior cesarean deliveries^[12]. Another significant risk factor is placenta previa but there is dramatic increase in the PAS incidence in the cases of previa with prior cesarean section as reported by Silver *et al.*^[13] In present study, out of 28, 10 cases (36%) were previous 1 CS and previous 2 CS each, 6 cases (21%) were previous 3 CS and 2 cases (7%) were previous 4 CS having placenta previa in all cases. In comparison to previa in all the 28 cases in present study, Eller *et al.* reported it in 77% of cases^[30].

Recent studies in literature demonstrate that the abnormal levels of placental biomarkers increase the risk of PAS. Elevated levels of pregnancy associated plasma protein A (PAPP-A), low hCG and β -hCG in first trimester (11-12 weeks) have been observed in women with PAS disorders^[10]. During second trimester (14–22 weeks) women having placenta previa are at greater risk of PAS disorders if serum β -hCG and α -fetoprotein (AFP) are >2.5 MoM^[10, 14]. No difference was noted in the level of cell free fetal DNA (cff-DNA) in the serum of women having PAS disorders compared with normal controls^[15]. By contrast, The level of cell-free placental mRNA was significantly greater in patients having PAS disorders than in those without it^[10]. The level of cell-free placental mRNA is found to be associated with the degree of placental invasion and having high negative predictive value that increases the accuracy of USG and color Doppler in prediction of PAS^[10]. In present study none of the women advised biomarkers. If done, it would have picked up a case that was missed on USG and would have helped in

preoperative counseling for the need of obstetric hysterectomy. It is essential to diagnose PAS as early as possible in the pregnancy and to strategize its management in order to reduce its high maternal morbidity and mortality. Features of PAS visible in ultrasonography may be present as early in the I trimester as low implantation of gestational sac in cases of prior cesarean section. The pregnant women at high risk for PAS such placenta previa and scarred uterus, should be evaluated with experienced sonologist having expertise in this field to establish early diagnosis. In the II or III trimester, the most important USG finding to suspect the PAS is the presence of placenta previa which is reported to be in association with more than 80% of accreta in major studies^[16, 17, 18]. A systematic review, including 23 studies and 3,707 pregnancies, noted an average sensitivity of 90.72% and specificity of 96.94%^[19]. In present study, 27 (96.4%) cases were diagnosed in antenatal period with grey scale ultrasonography and color Doppler and in one case it was diagnosed during surgery. In cases of unexpected and unplanned intraoperative diagnosis of PAS disorder, avoid placental removal and proceed to hysterectomy as judiciously as possible^[33]. The clinical risk factors should be considered equally important as a predictor of PAS disorder even in the absence of USG findings^[33]. Other major modality to diagnose PAS is magnetic resonance imaging (MRI). The reported sensitivities of MRI in various studies are 75-100% and specificities 65-100%^[19]. In difficult cases such as posterior placenta previa, MRI comes in very handy to assess the depth of placental invasion in PAS suspect. None of the woman was advised MRI in present study. According to ACOG, MRI is not recommended as an initial evaluation of PAS disorders^[33].

As the estimates of perioperative blood loss in cases of PAS is higher, prior notification to blood bank is essential for the readiness of cross-matched blood for the frequent need for multiple blood products transfusion in every elective cesarean delivery^[20]. Pre-operative maximization of hemoglobin is advisable. The dynamic traction of invaded myometrial tissue may activate coagulation cascade system- active fibrinolysis and considerable hypofibrinogenemia (between 100 and 200 mg/dl) resulting capillary and continuous hemorrhage after removing the placenta or performing the hysterectomy. If pre-operative level of plasma fibrinogen <250 mg/dl, cryoprecipitate (1U/10kg body weight) must be infused before surgery begins.³² The present study reported pre-operative transfusion of PCV in 8 cases to correct anemia and cryoprecipitate in 3 cases that showed level of plasma fibrinogen <250 mg/dl. Total 26 cases required transfusion of blood and blood components.

There are conflicts in opinion regarding the ideal gestational age for elective cesarean section. An analytical study suggests that 34 weeks of gestation is minimum given that most large centers are competent to tackle the neonatal complications at this maturity and tops the gestation age at 36 weeks in view of increased risk of bleeding after 36 weeks^[21, 33]. In our study, no increase in the incidence of neonatal mortality and morbidity has been observed despite being delivered at 35 weeks which makes this gestational age favorable for both maternal and neonatal outcome. Twenty-six cases (93%) required preterm elective cesarean hysterectomy at 35 weeks of the gestational age in present study considering the degree of invasion and amount of bleeding encountered during the cesarean section. Bilateral internal iliac artery was ligated in 6 cases (23%), and 2(7.0%) cases required intra-abdominal pelvic packing for 48 hours as there was persistent oozing from vault and bladder serosa even after bilateral internal iliac artery ligation. During the cesarean hysterectomy in PAS cases, the most accepted approach is

transverse fundal incision or classical incision on uterus to deliver the fetus, not to attempt removing the placenta as manual removal of placenta involves vulnerable risks of torrential hemorrhage and it is strongly discouraged [23]. One case required posterior fundal incision as it was preterm cesarean section at 29 weeks and placenta was extending from fundus to internal os of cervix. In present study, in all cases of cesarean hysterectomy, the attempt to separate placenta was not preferred to minimize blood loss. Subtotal hysterectomy (undilated and uneffaced cervix left in-situ) was performed in 20 (71.4%) cases while total hysterectomy was required in 6(21.4%) cases. However, in cases of PAS disorders with deep invasion up to serosa and presence of cervical involvement, subtotal hysterectomy may not be an effective option. In cases of PAS disorders, subtotal hysterectomy has not been found protective against urologic injury in comparison to total hysterectomy [26]. The survey conducted by SMFM specialists reported that 55% surgeons performed total hysterectomy and 45% surgeons performed supracervical hysterectomy for PAS disorders [27].

In 2007, POBC (prophylactic occlusion balloon catheter) program was introduced which advocated the insertion of balloon catheter into both internal iliac arteries before elective cesarean section in PAS, which aimed to reduce blood flow to uterus after cesarean, preventing hysterectomy and massive hemorrhage by allowing timely progression to arterial embolization if necessary [24]. A modified surgical technique-Triple-P procedure was introduced in 2010 which involves 3 steps:

- Preoperative localization of the placenta and delivering fetus by incision above the upper border of placenta.
- Pelvic devascularization by inflating balloon catheter in both internal iliac arteries.
- Placental non-separation with myometrial excision and uterine wall reconstruction [25].

The present study did not opt modified surgical technique-Triple-P procedure in any cases as non-availability of interventional radiology facility at our center.

The systematic review by Tam *et al.* regarding surgical techniques opted for Placenta accrete spectrum disorders, reported 29% (83/285) unintentional urologic injury during cesarean hysterectomy. Out of them 78% had urinary bladder and 17% ureter injury which is remarkably higher than hysterectomies for gynecological pathology [28]. The present study reported bladder injury in 6 (21.4%) cases and no ureteric injury which is lesser in incidence to the study by Norris *et al.* which reported bladder injury in 36.1% and ureteric injury in 4% [31]. Pre-operative ureteric stenting was not done in any cases. Pre-operative placement of ureteric decreased the risk of urologic injury from 33% to 6% [28]. Adequate sharp bladder dissection before keeping uterine incision reduces bladder injury, as it provides enough time to identify vesico-uterine plane in clear field and facilitates the identification of the different tissues [28]. Massive hemorrhage hampers visibility and necessitates urgency for urinary bladder dissection and in pool of blood it is difficult to get vesico-uterine plane. In some cases of PAS, abundant neovascularization makes bladder dissection difficult. Smulian *et al.* found greater incidence of urinary tract injuries when massive hemorrhage during surgery [29]. According to our experience in cases of bladder injury, holding post bladder wall of rent with Babcock forceps and proceeding for sharp dissection towards lower segment has helped in getting vesico-uterine plane. Scheduled delayed hysterectomy is another option to avoid massive hemorrhage during primary surgery and it also

reduces the chances of urological injuries. During cesarean section the cord is tied and the placenta is kept in situ and hysterectomy is planned after 4-6 weeks [33].

The present study reported 1 (3.5%) maternal mortality which was complicated with disseminated intravascular coagulation (DIC) and acute respiratory distress syndrome (ARDS) while the studies by Eller *et al.* [30] and Norris *et al.* [31] reported no maternal deaths. The reported incidence of DIC is 29% in the study by Eller *et al.* which is very high compared to 3.5% in our study.

Conclusion

Placenta accreta and its variants, placenta increta and placenta percreta, are rare complications of human placentation. It may threaten maternal life due principally to their potential for torrential hemorrhage. Its incidence is rising due to the increasing caesarean rates worldwide and hence aim should be to cut down the rates of primary cesarean section. Early preoperative diagnosis in the suspected women is the key to save the woman's life and adherent placenta should be suspected even in first trimester in women with known high-risk factors. Favorable outcome can only be achieved with preoperative multidisciplinary input and perioperative measures require adequate time in order to be instituted.

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