

Interval Placental Delivery: A New Approach to Deal with Placenta Accreta Spectrum (PAS) Disorders: A Cohort Study

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ABSTRACT

Background: Placenta accreta spectrum (PAS) disorders are one of the most terrible conditions in obstetrics. The major complication associated with PAS disorders is massive hemorrhage, which ultimately may lead to maternal death.

Objectives: This study aimed to detect the optimum time and mode of interventions to remove the morbidly adherent placenta after leaving it in situ for conservative management.

Patients and Methods: This was a cohort study carried out at the Obstetrics and Gynecology Department, Minia Maternity and Children University Hospital through the period from March 2018 to December 2020. The total number of patients with a placenta that was left in place was 20 patients out of 29 patients who were eligible for the study.

Results: This approach of leaving the placenta in place then interval placental delivery was successful in 16 cases (80%). Four cases needed hysterectomy. Placental removal was through spontaneous placental resorption in one case (5%), a spontaneous expulsion of the placenta in one case (5%), in addition to a successful interval placental delivery through D & C in 2 cases (10%) as well as removal by mini-laparotomy in 12 cases (60%). The mean time between the cesarean section and the 2nd set of interventions to remove the placenta was 48.2 ± 6.7 days.

Conclusion: Conservative treatment by leaving the placenta in place followed by interval placental delivery seemed to be an appropriate management choice in selected patients desiring preservation of the uterus, but complications such as sepsis and secondary postpartum hemorrhage should be carefully diagnosed and appropriately managed.

Keywords: Interval placental delivery, PAS disorders, Minia University.

Registration: The findings are part of a study that was registered on ClinicalTrials.gov under the number NCT02590484 (October 29, 2015).

INTRODUCTION

Placenta accreta spectrum (PAS) disorders result from the improper attachment of the placenta either completely or partially to the underlying myometrium. It is a potentially fatal pregnancy condition. Placenta previa accreta is a leading cause of maternal mortality and morbidity. Early diagnosis and advance planning are the key to minimizing complications. These disorders are divided into three types based on the degree of chorionic villi penetration and the area of placental involvement, namely placenta accreta, increta, and percreta, with variable degrees of anchoring placental chorionic villi attachment into the uterine myometrium [1, 2].

PAS abnormalities are linked to significant maternal morbidity, such as a large number of blood transfusions, hysterectomy, cystotomy, ICU admission, infection, and protracted hospitalization [3]. Additionally, maternal mortality may occur because of the risk of serious bleeding during delivery. Fetal outcome may be affected as well in PAS disorders as antepartum hemorrhage may occur, which mandates premature delivery with its consequences [4].

Over the last 50 years, the frequency of PAS disorders has increased tenfold due to rising rates of cesarean sections paired with advanced maternal age. Even in developed countries, reported rates range from 1 in 2,500 to 1 in 530 deliveries [5, 6].

The aim of this study was to detect the optimum time and mode of interventions to remove the morbidly

adherent placenta after leaving it in place at time of cesarean section aiming at conservative management.

PATIENTS AND METHODS

Study design and setting:

This was a single-center cohort research that took place between March 2018 and December 2020 at Minia Maternity and Children University Hospital's Obstetrics and Gynecology Department.

Inclusion criteria: All cases with PAS disorders, which were hemodynamically stable, of low parity, desiring conservation of the uterus, and were diagnosed by ultrasound and MRI as having a complete invasion of the uterine wall, underwent elective cesarean section with leaving the placenta in place then close follow up to determine the optimum time and method of removing the placenta with the goal of managing PAS disorders in a conservative manner.

Exclusion criteria: Patients who refused conservative treatment, had clotting disorders, had impaired liver or renal functions, had spontaneous placenta separation intra-operatively, or had any other uterine disease requiring hysterectomy were excluded.

Interventions:

Pre-operative stage: Medical history was thoroughly obtained by the treating physician, which included patient's demographic data, history of the major complaint, menstrual history, past medical history, and obstetric history (previous pregnancies, deliveries,

abortions, puerperium and fetuses). Additionally, general examination and abdominal examinations were carried out. Routine laboratory investigations and radiological investigations were performed. Loss of the typical retro-placental clear space, anomalies of the bladder-myometrium interface, large placental lacunae, and enhanced vascularity at the uterus-bladder interface

were all used to diagnose PAS diseases using sonography and MRI [4] (figure 1, 2).

Before participating in the study, all patients were counseled about it and provided an informed written permission. The counseling process involved the aim of the study, procedures, expected outcome and possible complications that may develop.

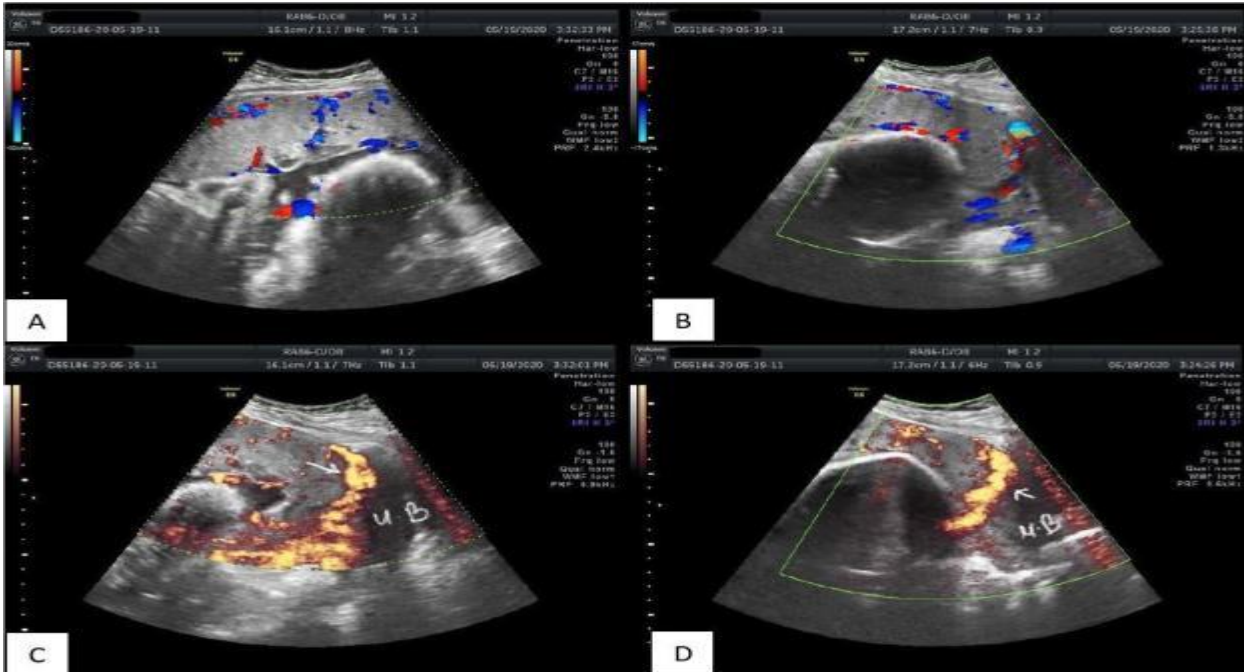


Figure (1): Doppler/ultrasound picture of a case of placenta percreta. A, B, C & D: sagittal duplex ultrasound examination of the lower uterine segment showing placenta previa major anterior, with loss of the sub-placental lucent zone, large blood lakes (white arrow) not clearly separable of the bladder wall



Figure (2): MRI picture of a case of placenta percreta. Two sagittal MRI T2 images showed: Anteriorly low lie located placenta reaching the margin of the internal OS; there is loss of the normal tri-layered myometrium as well as no separation between myometrium and bladder wall with signal void dots seen within (black arrows), urinary bladder (black star).

Intra-operative phase:

General anesthesia was used as per our hospital protocol. Elective cesarean section was done in the following steps: Positioning (dorsal lithotomy position or supine position), sterilization & draping, followed by an abdominal incision through a midline or para-median incision, opening anterior abdominal wall in layers. The following step was a vertical upper segment cesarean section. After the fetus is delivered, the placenta was observed for 15 minutes for spontaneous separation added with gentle cord traction. If no signs of spontaneous separation after 15 minutes, the placenta was left in place and the cord was clipped short. Vicryl zero was used to close the uterus in two layers, followed by abdominal repair and a vaginal examination for blood clots. A broad-spectrum antibiotic was given.

Post-operative follow up:

The patient was admitted to high dependency unit (HDU) for close follow-up of vital data and serial investigations to early detect any complications. After ensuring medical and hemodynamic stability, the patient was discharged with scheduled follow-up visits every three weeks with strict recommendations regarding rapid transfer to the hospital in case of any bleeding attack. In every follow-up visit, we asked for any vaginal bleeding or discharge, fever and abdominal pain and check for her CBC. Additionally, follow up ultrasound, Doppler and MRI were performed to detect signs of placenta involution, size, vascularity regression and line of cleavage to date the optimum time for the 2nd set of interventions.

In some cases of placenta percreta and/or significant placental vascularity, postoperative uterine artery embolization (UAE) was performed. Based on clinical and radiological criteria such as ultrasound, Doppler, and MRI, a dedicated team trained in treating cases with PAS disorders determines the best timing and mode of intervention to remove the placenta. In the 2nd set of intervention, if the bleeding is excessive after removing the placenta during abdominal approach, to reduce bleeding from the placental bed, the cervix was employed as a natural tamponade, and/or uterine artery ligation was performed [7, 8].

Ethical considerations:

The Research Ethics Committee of the Department of Obstetrics and Gynecology, Faculty of Medicine, Minia University, granted institutional research ethics board permission. Before participating in the trial, all patients were counseled about it and provided an informed written permissions. The study's goal, procedures, expected outcome, and potential complications were all discussed during the counseling process. All methods were performed in accordance with the relevant guidelines and regulations (Declaration of Helsinki).

Statistical analyses

For categorical variables, data were represented using frequencies and valid percentages. P values of less than 0.05 were deemed statistically significant. To compare the means of the different groups, Chi-square analysis was utilized. All statistical computations were carried out using IBM SPSS version 21 (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA).

RESULTS

The total number of patients with a placenta that was left in place was 20 patients out of 29 patients who were eligible for the study. There was one case refused conservative management, and two cases had done primary Caesarean hysterectomy due to developing severe attack of antepartum hemorrhage, and six cases developed accidental intraoperative placental separation.

The study enrolled the twenty women who met the inclusion criteria. Participants' demographics are described in table (1). The hemoglobin level of patients was evaluated before and after the CS. The mean preoperative Hb was 11.3 ± 0.4 g/dl, while the postoperative Hb was 10.7 ± 0.5 g/dl. This difference was not statistically significant. Regarding estimated blood loss (EBL) during the 1st set of intervention (Cesarean section), the mean EBL was 1.1 ± 0.2 (L) and the mean units of transfused blood was 2.1 ± 0.3 (units). Hospital stay ranged from 6 to 14 days with a mean duration of 9.8 ± 0.5 days.

Table (1): Description of demographic data of all studied cases

Demographic data	Descriptive statistics (n=20)
Maternal age (years) Range Mean ± SD	(23-34) 26.25±3.22
Parity P1 P2	7 (35%) 13 (65%)
Number of living children No living One living Two living	2 (10%) 12 (60%) 6 (40%)
Body mass index Range Mean ± SD	(19.5-25) 21.94±1.61
Gestational age at delivery (weeks) Range Mean ± SD	(34-38) 35.7±1.34
Mode of previous deliveries Previous one Cesarean section Previous two cesarean section	7 (35%) 13 (65%)
Previous dilatation and curettage and myomectomy No Previous dilatation and curettage Previous myomectomy	14 (70%) 5 (25%) 1 (5%)

Table (2) showed complications that occurred in the studied group. One case (5%) developed sepsis, which was managed by broad-spectrum antibiotics, antipyretics and ICU admission till improvement. There were two cases (10%) developed wound infection, and they were managed by using broad-spectrum antibiotic therapy and repeated dressings.

Additionally, there were three cases (15%) that had a low-grade fever managed by using broad-spectrum antibiotic therapy and antipyretics. four cases (20%) required a delayed hysterectomy, where two cases had a severe attack of secondary post-partum hemorrhage & and the other two cases due to failure of interval placental delivery at the 2nd set of intervention due to development of severe intraoperative bleeding.

Table (2): Description of complications in all studied cases

Complication	Descriptive statistics (n=20)
Sepsis	1 (5%)
Wound Infection	2 (10%)
Postpartum hemorrhage Primary Secondary	0 (0%) 2 (10%)
Postpartum low-grade fever	3 (15%)
Delayed hysterectomy	4 (20%)
Bladder injury	1(5%)
Coagulopathy	0 (0%)
Intensive care unit admission	4 (20%)
Re-exploration	0 (0%)
Maternal mortality	0 (0%)

Table (3) showed the time and mode of 2nd set of interventions to remove the placenta after conservative management of PAS disorders (interval placental delivery). This approach (leaving the placenta in place followed by interval placental delivery) was successful in 16 cases of the cohort (80%). Four cases (20%) needed hysterectomy; two cases due to severe attack of secondary postpartum hemorrhage during the expectant period and two cases due to failure of interval placental delivery after the period of conservative management.

Table (3): Time and mode of interventions to remove the placenta

Time of intervention (days) Range Mean ± SD	(34-63) 48.2 ±6.7
Mode of intervention Spontaneous placental resorption Spontaneous placental expulsion Removal by dilatation and curettage Removal by mini laparotomy	1 (5%) 1 (5%) 2 (10%) 12 (60%)
Successful placental removal Yes No	16 (80%) 4 (20%)

Finally, placental MRI findings were recorded and compared at ten days and three weeks' time points post-surgical using a chi-square test. There was a statistically significant difference in the appearance of the line of cleavage, calcification, and necrosis between follow-up at the third week and the tenth day postoperatively, as shown in table (4).

Table (4): Description of placental MRI findings during post-operative follow up in studied cases

Placental MRI findings	After ten days (n=20)	After three weeks (n=20)	P-value
Size Decrease Increase	20(100%) 0(0%)	20(100%) 0(0%)	1
Vascular leaks Decrease Increase	20(100%) 0(0%)	20(100%) 0(0%)	1
Necrosis Appear Didn't appear	2(10%) 18(90%)	14(70%) 6(30%)	0.001*
Line of cleavage Appear Didn't appear	0(0%) 20(100%)	14(70%) 6(30%)	<0.001*

* Significant difference at p-value < 0.05

DISCUSSION

One of the most serious complications in obstetrics is placenta accreta spectrum (PAS) diseases. It occurs as a result of the decidua basalis' partial or complete absence, as well as the fibrinoid or Nitabuch's layer's incomplete development [9]. Previous uterine scars, including cesarean sections and uterine curettage, are frequently linked to the illness. Other risk factors for placenta accreta include multiparity, placenta previa, past intrauterine infections, increased maternal blood alpha-fetoprotein, and maternal age greater than 35 years [10].

The present study investigated the optimum time and mode of interventions to remove the morbidly adherent placenta after leaving it at time of cesarean section for conservative management. It was revealed that placental removal was through resorption in one case (5%), spontaneous placental expulsion in another case (5%) in addition to a successful interval placental delivery through D & C in two cases (10%) as well as successful placental removal through abdominal approach in 12 cases (60%). The overall success of this approach of conservative management was 80%. Conservative management of placenta accrete was evaluated in different settings. **Sentilhes et al.** [5] evaluated the success rate of conservative treatment in 167 cases of placenta accrete & percreta. Conservative therapy failed in 22% of the time necessitating a hysterectomy, either primary or delayed, in the majority of cases, due to significant hemorrhage. Conservative therapy was shown to be effective in 131 women (78.4%), which is similar to our findings. In a comparable study conducted at our institution, expectant care of PAS disorders by leaving the placenta

in place resulted in preservation of the uterus in 14 of 16 cases (87.5%) [11].

These findings are supported by two studies conducted by **Kayem et al.** [10, 12] who investigated the influence of conservative and extirpative methods for PAS abnormalities on maternal mortality and morbidity over two consecutive periods, one of which was to leave the placenta in situ versus manual removal of the placenta. In the two studies, **Kayem et al.** [10, 12] found that there was a decrease in the percentages of hysterectomy when placental retention was allowed as well as reduction in the rates of blood transfusion and the incidence of DIC. There was, however, a higher rate of sepsis in patients whose placenta was left in place. In many cases, further pregnancies occurred following expectant management. These pregnancies passed uneventfully with no abnormalities in the placental site and terminated by the usual cesarean section [10, 12]. There are many studies in the literature reporting that expectant management of PAS disorders is linked with less maternal morbidity and less requirement for hysterectomy and transfusion of blood compared to extirpative management [10-13].

In our case series, UAE was performed in 12 cases (60%). We have found that cases underwent UAE had marked reduction in placental size and vascularity when compared to cases that did not. This agrees with previous studies [11, 14, 15]. Complications observed with UAE in the present study included mild reaction from the embolizing material in two cases and low-grade fever in one case.

Serious complications were encountered in three cases in our study (15%); one patient was complicated by sepsis but responded to conservative management. Two cases had an attack of severe 2ndry postpartum hemorrhage treated by immediate hysterectomy. Other less serious complications included wound infection in two cases (10%), postpartum low-grade fever in three cases, (15%), bladder injury in one case (5%) and ICU admission in four cases (20%). All complications were managed successfully with no residual morbidity. Additionally, no cases of maternal mortality reported in our series. **Sentilhes et al.** [5] found significant maternal morbidity in ten cases (6.0%, 95 % CI 2.9-10.7%) and one case died from methotrexate toxicity in a large multicenter trial. In the current study, ultrasonography and MRI follow-up revealed a progressive shrinking of the placenta with reduced blood flow in all cases.

Furthermore, there was a statistically significant difference in calcification, necrosis, and line of cleavage between follow up at 3rd week and at 10th-day postoperatively (P-value <0.001). As regards postoperative follow up, **Lam et al.** [16] described a case of successful conservative treatment of placenta previa accreta during Cesarean surgery with the placenta remaining in place. The placenta shrank gradually with diminished vascularity during the ultrasound follow-up, and a greyish white tissue was passed out on day 56 with

some fresh vaginal bleeding. She started menstruating again five months after giving birth. At six months, certain echogenic foci suggestive of the calcified placental remnant were discovered.

In the present study, the appearance of placental calcifications & areas of necrosis occurred in 70% of cases three weeks postoperatively. Also, it was noticed that there was a line of cleavage between the placenta and uterine wall appeared partially in 70% of cases three weeks postoperatively. **Timmermans *et al.***^[17] backed up these findings, recommending that women with unusually invasive placentation must be followed up with imaging modalities such as ultrasonography or MRI. The current study adds to the growing body of evidence that conservative management of PAS disorders is possible in some cases, avoiding the complications of Cesarean hysterectomies and the danger of serious damage to the implicated nearby organs. However, the present study had some limitations. These included the small sample size recruited and that the study was a single center, so, the generalizability may be limited.

CONCLUSIONS

At present study, there was no agreement about the ideal management for PAS disorders. Conservative treatment by leaving the placenta in place followed by interval placental delivery seems to be an appropriate management choice in selected patients desiring preservation of the uterus, but complications such as sepsis and secondary postpartum hemorrhage should be carefully diagnosed and appropriately managed.

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