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# Prenatal diagnosis of abnormally invasive placenta reduces maternal peripartum hemorrhage and morbidity

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## Abstract

*Objective.* Abnormally invasive placenta (AIP) poses diagnostic and therapeutic challenges. We analyzed clinical cases with confirmed placenta increta or percreta. *Design.* Retrospective case series. *Setting.* Multicenter study. *Population.* Pregnant women with AIP. *Methods.* Chart review. *Main outcome measures.* Prenatal detection rates, treatment choices, morbidity, mortality and short-term outcome. *Results.* Sixty-six cases were analyzed. All women and all but three fetuses survived; 57/64 women (89%) had previous uterine surgery. In 26 women (39%) the diagnosis was not known before delivery (Group 1), in the remaining 40 (61%) diagnosis had been made between 14 and 37 weeks of gestation (Group 2). Placenta previa was present in 36 women (54%). In Groups 1 and 2, 50% (13/26) and 62% (25/40) of the women required hysterectomy, respectively. In Group 1 (unknown at the time of delivery) 69% (9/13) required (emergency) hysterectomy for severe hemorrhage in the immediate peripartum period compared with only 12% (3/25) in Group 2 ($p = 0.0004$). Mass transfusions were more frequently required in Group 1 (46%, 12/26 vs. 20%, 8/40; $p = 0.025$). In 18/40 women (45%) from Group 2 the placenta was intentionally left in situ; secondary hysterectomies and infections were equally frequent (18%) among these differently treated women. Overall, postpartum infections occurred in 11% and 20% of women in Groups 1 and 2, respectively. *Conclusions.* AIP was known before delivery in more than half of the cases. Unknown AIP led to significantly more emergency hysterectomies and mass transfusions during or immediately after delivery. Prenatal diagnosis of AIP reduces morbidity. Future studies should also address the selection criteria for cases appropriate for leaving the placenta in situ.

**Abbreviations:** AIP, abnormally invasive placenta.

## Introduction

Abnormally invasive placenta (AIP) renders normal placental delivery impossible and carries a high risk for severe hemorrhage. AIP is associated with a significantly increased maternal morbidity and a reported maternal mortality up to 7% (1).

## Key Message

Unknown abnormally invasive placenta led to significantly more emergency hysterectomies and mass transfusions during or immediately after delivery. Prenatal diagnosis of abnormally invasive placenta reduces morbidity.

Histopathologically, there are three degrees of abnormally deep placental invasion: placenta accreta, increta and percreta (Table 1).

All cases with AIP can be referred to as "placenta accreta" (2), but clinically two main groups should be differentiated based on the extent of invasion: "simple placenta accreta" with abnormally adherent placenta that requires manual removal or curettage, but no further surgical procedures to achieve hemostasis and to restore normal uterine tone (such cases were not included in our study); and the more relevant group of AIP comprising cases with invasion of the uterus only (placenta increta; or placenta percreta with extension limited to the uterine serosa) and AIP with extrauterine invasion (bladder, bowel, other internal organs). In cases with the clinical diagnosis of "simple placenta accreta" pathological confirmation is usually not available.

The reported incidence of abnormally deep placental infiltration varies between 1/1000 and 1/2500 deliveries (1,3,4), but has increased 10-fold over the last 50 years (5), probably as a consequence of rising rates of cesarean deliveries (6). Further risk factors include placenta previa, other previous uterine surgery, multiparity, advanced maternal age, Asherman syndrome and submucous myoma (7). In the presence of placenta previa the risk of "placenta accreta" increases from 24% in a patient with a history of one previous cesarean delivery to 67% in a patient with a history of three or more cesarean deliveries (8).

Combined results from two series using the three-stage definition, comprising a total of 138 histologically confirmed AIPs from hysterectomy specimens, the distribution of stages was 79% placenta accreta, 14% placenta increta and 7% placenta percreta (3,9). Clinical problems occur mostly during the third trimester and delivery, but uterine rupture due to placenta increta/percreta can also occur early in gestation from 14 weeks onwards (10–12).

We retrospectively analyzed a series of cases of placenta increta and percreta from tertiary centers over the course of 14 years to calculate prenatal detection rates, analyze clinical treatment choices and define risk factors for maternal and fetal outcome and complications.

**Table 1.** Degrees of severity in abnormally deep placentation.

| Type | Clinical presentation, histological finding |
|---|---|
| Placenta accreta | Anchoring villi are attached to the myometrium (as opposed to only the decidua); requires manual removal of curettage to fully retrieve the placenta, but placenta can be removed completely without the need for further procedures |
| Placenta increta | Abnormal invasion of the placenta into the myometrium, not extending to or beyond the serosa/outer layer of the uterus; retrieval by curettage or manually is not possible |
| Placenta percreta | As increta, but extending beyond serosa/outer layer of the uterus, either intraoperatively or histologically |

Modified after Resnik et al. (7)

## Material and methods

Abnormally invasive placenta was staged clinically and histologically as shown in Table 1. All women with confirmed placenta increta or percreta treated between 1998 and 2011 were collected; women with simple placenta accreta as defined above were not included. There was no common treatment protocol. Clinical management for each case was at the discretion of the individual center. Time of diagnosis of AIP was classified as "prenatal" if the condition was recognized before the onset of labor or cesarean delivery. In these cases the gestational ages at the diagnostic scan and the indication for this scan were analyzed. In all other cases the diagnoses were made "intrapartum". The management was categorized into four groups, by time of diagnosis and attempted or deferred manual or operative placental separation (Table 2). Treatment, both at the time of delivery as well as thereafter, was recorded and analyzed including adjunct measures like uterine artery embolization or methotrexate injections. For between-group comparisons, the non-parametric test (Mann–Whitney *U*-test) was used; $p < 0.05$ defined statistical significance.

## Results

Data from 66 women who met the inclusion criteria were analyzed. Anamnestic, clinical and delivery data and maternal and fetal outcomes are shown in Table 3.

**Table 2.** Management categorization into four groups, by time of diagnosis and attempted or deferred manual or operative placental separation.

| | |
|---|---|
| Intra-partum diagnosis (Group 1) | Group 1a: retrieval of the placenta was attempted<br>Group 1b: retrieval was not attempted, but conservative management was promptly instituted once the diagnosis was evident |
| Prenatal diagnosis (Group 2) | Group 2a with attempted retrieval of the placenta by manual separation and/or curettage despite the suspicion<br>Group 2b without attempted placental separation |

**Table 3.** Demographic and obstetrical characteristics of women with abnormally invasive placenta.

| Variable | Group 1 (intrapartum Dx) ($n$ = 26) | Group 2 (prenatal Dx) ($n$ = 40) | $p$-value |
|---|---|---|---|
| Maternal age, (years) | 29 (23–35) | 31 (26–42) | 0.75 |
| Gravidity | 3 (2–7) | 3 (2–12) | 0.58 |
| Parity | 2 (1–3) | 2 (1–8) | 0.55 |
| Gestational age at diagnosis, (weeks) | 36 (25–40) | 31 (14–37) | <0.0001 |
| Gestational ages at delivery (weeks) | 36 (25–40) | 36 (19–38) | 0.28 |
| Number of women with previous cesarean section, (number of CS) | 10 (1–2) | 32 (1–3) | <0.0001 |
| Number of women with previous uterine curettages, (number of D/C) | 11 (1–3) | 18 (1–4) | <0.0001 |

*Note* Data are presented in medians (range). Differences between Group 1 and 2 are analyzed with the Mann–Whitney *U*-test, significant differences are accepted for $p < 0.05$.
Abbreviations: CS, cesarean section; D/C, dilatation and curettage; Dx, diagnosis.

There were no maternal deaths and apart from one fetus in Group 1 (intra-abdominal maternal bleeding at 25 weeks) and two early terminations after early diagnosis all the newborns survived. Of 64 pregnant women with AIP, 57 had previous uterine surgery (89%): either one ($n$ = 26), two ($n$ = 12) or three ($n$ = 3) previous cesarean deliveries; one ($n$ = 14), two ($n$ = 8) or three or more ($n$ = 7) curettages; or other uterine surgery (fibroid resection $n$ = 1; hysteroscopic polyp or septum resection $n$ = 2). In two women there was no information about previous uterine surgery.

In three of the 66 women, placenta percreta extended to the bladder (bladder wall invasion) and in one woman to the mesocolon. In the remaining 62 women there was either placenta increta or placenta percreta, extending only up to the uterine serosa.

There were 36/66 (54%) women who had placenta previa; in only three women the main placental insertion was on the posterior uterine wall. In another 13 women the placenta was not previa, but low anterior.

In 40/66 (61%) women the condition had been diagnosed or suspected before delivery. In these women the diagnosis had been made by ultrasound at a median age of 31 weeks of gestation (range 14–37). Indications for these scans were "routine scan" ($n$ = 17), "previa" ($n$ = 10), "bleeding" ($n$ = 6) and "(other) suspected placental anomaly or percreta" ($n$ = 4) or were not specified ($n$ = 3).

The 66 women were divided in four groups according to prenatal diagnosis status and management approach (Table 2). In 96% (25/26) of the women in Group1 retrieval of the placenta was attempted (Group 1a). From Group 2, in 25% (10/40) of women retrieval of the placenta by manual separation and/or curettage was attempted (Group 2a), whereas for the remaining women placental separation was not tried (Group 2b); the latter group contained women with elective primary cesarean hysterectomies. Nine of 66 women (14%), all in Group 1, gave birth vaginally; none had placenta previa. All other women had cesarean deliveries (plus two terminations at 19 and 20 weeks with diagnoses at 14 and 17 weeks, respectively).

The median gestational ages at delivery were 35.9 weeks (range 25.0–40.0) in Group 1 and 36.0 weeks (range 19.0–38.4) in Group 2 ($p$ = 0.28). In the two cases with the earliest diagnoses, i.e. at 14 weeks (routine scan) and 17 weeks ("query placental site", previa), termination of pregnancy was offered and performed (by fundal hysterotomy, leaving the placenta in situ); in these two cases the placenta resolved spontaneously and completely (confirmation by ultrasound and diagnostic hysteroscopy after 12 and 18 months, respectively).

In both groups, many women underwent hysterectomies, either at the time of delivery or later (then, typically, because of complications). In Group 1, 13/26 (50%) of the women required hysterectomy. All nine spontaneous deliveries were in Group 1, and none of them had a hysterectomy. Subtracting these cases with less severely abnormal placentation (non-previa) from the calculation yielded a hysterectomy rate of 76% (13/17) for Group 1, with two-thirds (69%, 9/13) as emergency hysterectomy because of severe bleeding. In Group 2, all women were delivered by elective cesarean delivery and 25 of them (62%) underwent hysterectomy.

In 10/40 cases placental retrieval was attempted (Group 2a) despite the known diagnosis, comprising six women with primary hysterectomy, two with focal resections and two requiring emergency hysterectomy because of severe bleeding. When retrieval was not attempted (Group 2b, 30 cases), one woman required emergency hysterectomy because of bleeding, 10 had primary hysterectomy and six had delayed hysterectomy. When retrieval was not attempted (Group 2b; 30/40), 17/30 (56%) eventually had a hysterectomy.

Of the 18 women in Group 2 in whom the placenta was left in situ, 11 (61%) avoided a hysterectomy.

Delayed hysterectomy for bleeding or infection was required for 7/18. There were significantly more emergency hysterectomies (unscheduled due to unexpected excessive blood loss) for severe bleeding in Group 1 compared with Group 2 (9/13 vs. 3/25; $p = 0.0004$).

Without prepartum diagnosis, slightly more women required blood products, but significantly ($p = 0.025$) more women required mass transfusions (more than eight red blood cell concentrates). In Group 1, 15/26 (58%) required blood products in the course of the treatment, 13/17 (76%) in the cesarean section group, and 12/26 (46%) as a mass transfusion. Only two of the nine women with placenta increta who delivered vaginally required transfusions, none of them had a mass transfusion. In Group 2, 20/40 (50%) required blood products, eight (20%) of them as mass transfusions.

There were no women with coagulation disorders as a consequence of the condition or the treatment. In Group 1, of the women who delivered vaginally ($n = 9$), two had endometritis, one of them requiring intensive care unit treatment. In the women with immediate hysterectomy ($n = 9$) there were four complicated cases: one women required intraoperative resuscitation, two had bladder and/or ureter repair and one required unilateral adnexectomy. There was one women with previous diagnosis but no attempted placenta retrieval at delivery who required antibiotics for endometritis. Three women (3/26, 11%) had infectious complications in Group 1.

In Group 2, the placenta was intentionally left in situ in 18 of 40 women (45%); six of these women eventually required or requested secondary hysterectomy. Another three women experienced additional complications: one woman had a chest infection, wound dehiscence and relaparotomy for adhesions; one woman had septic shock 10 weeks after cesarean section and one woman had clostridial enteritis. In total, eight patients (8/40, 20%) from Group 2 developed infectious complications, more than in Group 1, but not significantly different ($p = 0.55$).

Uterine artery embolization, methotrexate treatment and uterine artery ligature were performed in three, five and no cases in Group 1 (11%, 19% and 0%) and in seven, eleven and four cases in Group 2 (17%, 27%, 10%), respectively.

## Discussion

We studied deliveries with clinically relevant AIP and analysed the outcomes by time of diagnosis (before delivery or during delivery) and overall treatment approaches. Having made the diagnosis before delivery and avoiding attempted separation of the placenta decreases maternal complications.

Due to the increase of uterine surgery, mainly cesarean deliveries (by a factor of 10 in the last 50 years), the number of pregnancies complicated by abnormally invasive placentation has increased (5). In our series, 89% of women with AIP had a history of previous uterine surgery, typically, but not only, cesarean sections, confirming previous reports (13).

We did not include cases with "simple placenta accreta" because the clinical diagnosis of this entity is in part subjective and the outcome is generally favorable. Among the 66 women included, 62 had placenta increta or percreta not extending beyond placenta serosa; we consider them one clinical entity. Four women had more severe disease, with either bladder or bowel invasion. These proportions are in accordance with published series (7,14). We also confirmed the association between AIP and placenta previa (8). Placenta previa was present in 54% of women in our study.

Prenatally, ultrasound is the diagnostic method of choice for AIP (2,6). However, the prenatal diagnosis remains challenging. In our study, prenatal diagnosis was achieved in almost two-thirds of women (40/66, 61%). We cannot report positive or negative predictive values of ultrasound for the detection of severe AIP; however, in another study of 453 women presenting with a low-lying placenta and with a history of previous cesarean section or myomectomy, comprising 8.5% with AIP, ultrasound had a sensitivity of 77% and specificity of 96% for a positive predictive value of 65% and a negative predictive value of 98% for AIP (15).

The combination of placenta previa in women with previous uterine surgery, typically cesarean sections, but also curettage, hysteroscopic septum or fibroid resection and other similar conditions, should raise the suspicion of a possible AIP and prompt targeted evaluation (2). We suggest combining transabdominal and transvaginal ultrasound to possibly increase the detection rate of the proposed sonographic markers of AIP: placental lakes, absent hypoechogenic (vascular) layer between placenta and myometrium, reduced myometrial thickness (<1 mm) at the site of the placental bed, in particular between uterus and bladder (6). Another sonographic sign is the presence of characteristic bridging vessels between placenta and adjacent organs, such as the bladder (16). The most predictive ultrasound marker seems to be the presence of increased placental lakes (17).

In our material no maternal death occurred; there were three fetal losses: two very early diagnoses followed by abortion and one uterine rupture at 25 weeks. Uterine rupture and massive hemorrhaging have been reported for AIP as early as the second trimester (18,19).

For women with a prenatal diagnosis of AIP, the timing of delivery is debated (20). A compromise has to be

made between the risk of onset of spontaneous labor and a subsequent emergency intervention and prematurity. Warshak et al. reported fewer hemorrhagic complications when cesarean delivery/hysterectomy was performed at 34–35 weeks compared with later, but the rate of admissions to and time spent in neonatal intensive care unit was higher (21). Others have proposed delivery at 36–37 weeks (14). Typically, the timing of planned delivery when AIP is known is an individual decision depending on the placental location, extent of infiltration and previous episodes of bleeding (2,22), as well as maternal choices. One study in women with simple placenta previa indicated that a cervical length measurement <30 mm predicted the likelihood of spontaneous onset of labor and bleeding (23), but its value in AIP diagnosis is unknown.

Different therapeutic strategies for AIP exist: surgical removal of the uterus and involved tissues or conservative therapy with the placenta left in situ after delivery of the fetus. The strategy depends on the risk of bleeding, the hemodynamic situation and the patient's desire to preserve fertility (2,14,24).

The therapeutic approach to AIP known before delivery as proposed by the American College of Obstetricians and Gynecologists and the Society of Maternal–Fetal Medicine is a planned cesarean delivery with preparation for immediate hysterectomy without attempted removal of the placenta (2,25). However, the possibility of false-positive prenatal diagnoses has to be considered. In a series, nine of 40 (22%) women with antenatally suspected placenta accreta in whom placental removal was not attempted at cesarean hysterectomy, the diagnosis of AIP could not be confirmed by pathology (26).

An alternative approach is to leave the placenta in situ after cesarean delivery of the fetus. In our study, this was attempted in 18 women; 11 women (61%) eventually avoided hysterectomy, possibly preserving their fertility chances. This "conservative" approach was also investigated in a large retrospective study including 167 patients (24). Uterine preservation was possible in 78%, but there were 6% with severe complications. The main risks are infection and severe bleeding; in addition, this approach requires lengthy follow-up under close surveillance, and the recurrence risk for AIP is as high as 30% (27).

When there is extensive pelvic organ involvement, in particular pelvic floor or wall invasion or massive pelvic hyperemia, the conservative approach may be the only possible option; a delay of definitive hysterectomy of only a few days may be helpful to achieve a marked reduction of pelvic bleeding complications and can allow for optimized pro-operative preparation, for example prophylactic placement of common iliac artery balloon catheters and/or ureteric stents (22,28).

Surgical uterine devascularization for AIP may help to achieve hemostasis, but is technically challenging (29,30). Pelvic artery embolization is an effective adjunct to surgery in controlling obstetric hemorrhage and as a fertility-saving and life-saving procedure (31). In our study, 10 women were treated by uterine artery embolization, either as sole treatment or preventively after focal resection.

Half of the patients in both groups in our study required blood transfusions, but mass transfusions (more than eight red blood cell packages) were more than twice as frequent if the diagnosis had not been made prenatally (46% in Group 1 versus 20% in Group 2, $p = 0.025$), confirming that antenatal diagnosis of AIP reduces peripartum blood loss and the need for blood transfusion (14,26).

Infections are more common when the placenta is left in situ in AIP (22,24,32). In our study, three patients from Group 1 (11%) and eight of Group 2 (20%) experienced infectious complications, but this difference was not significant ($p = 0.55$). These infection rates are in accordance with the literature (24).

The main limitation of our study was its retrospective design, its observational nature and the multicenter data contribution with different management approaches. AIP is rare in pregnancies without risk factors, but a considerable problem in cases with the combination of previous uterine surgery and placenta praevia or low lying placenta. Only a prospective multicenter design with a management protocol may address the remaining open questions, in particular when to offer primary surgery compared with leaving the placenta in situ after delivery of the baby.

## Conclusion

Abnormally invasive placenta carries significant maternal morbidity. Previous uterine surgery is a major risk factor. Prenatal diagnosis is possible in about two-thirds of the cases and shows better outcomes, because fewer emergency operations and mass transfusions are required. Leaving the placenta in situ offers the opportunity to preserve fertility, but further studies are needed to identify the best subgroup eligible for this treatment.

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