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# The impact of antenatal diagnosis of placenta accreta on reducing blood loss: a 57-case monocentre retrospective study

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**ABSTRACT**

**Objective.** The aim of our study was to investigate the impact of antenatal diagnosis of PA on blood loss, blood transfusions, and maternal and neonatal morbidity and mortality.
**Materials and Methods.** This is a monocentre retrospective study including all patients who had failed manual removal of the placenta or evidence of placental invasion at the surgery. The patients included were divided into 2 groups:

- Group 1: patients with an antenatal diagnosis according to the ultrasounds or magnetic resonance imaging data.
- Group 2: patients with unexpected placenta accreta.

Then, we compared blood loss estimated by Gross formula, transfusions, and maternal and neonatal morbidity in both groups.
**Results.** In our series, 57 cases of PA were included: 35 patients with antenatal diagnosis (group 1) and 22 with unexpected PA (group 2). The bleeding estimation was 1,610 ± 908 ml in group 1 *versus* 2,480 ± 1,317 ml in group 2, with p = 0.007. The need for transfusion was reduced from 95.4% to 17% when PA was diagnosed antenatally with p = 0.001. Unexpected PA was correlated with an increased risk of severe bleeding with OR 2.35, 95%CI 1.08-5.62 and transfusion requirements with OR 1.85, 95%CI 1.18-6.1. However, expected PA was correlated with a higher risk of prematurity with OR 2.04, 95%CI 1.05-4.8.
**Conclusions.** The antenatal diagnosis of placenta accreta allowed better maternal outcomes by reducing the blood loss and transfusions requirements. However, it increased the incidence of planned preterm birth.

## INTRODUCTION

Placenta accreta is one of the most serious pregnancy complications in which the placenta is abnormally adherent and invades the uterine wall [1]. Its incidence is increasing all over the world following the trend of rising caesarean delivery and intrauterine interventions [2]. Placenta accreta can lead to a life-threatening severe and catastrophic haemorrhage, resulting in haemostatic hysterecto-

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my, blood transfusion, and significant adverse maternal and neonatal outcomes [1].
Ultrasound is the primary tool in antenatal diagnosing placenta accreta, and magnetic resonance imaging is generally performed to help in the diagnosis [3, 4]. Furthermore, the antenatal diagnosis may allow better organization and some precautions that may improve maternal outcomes. The aim of this study was to investigate the role of antenatal diagnosis of placenta accreta and its impact on blood loss, transfusions, and maternal and neonatal morbidity and mortality.

## MATERIALS AND METHODS

### *Study design*

After obtaining patients' oral consent and the approval from the local ethics committee, we conducted a monocentre retrospective study by analysing the database of patients with confirmed placenta accreta to assess the impact of the antenatal diagnosis on maternal outcomes and particularly the blood loss and the need for transfusions and neonatal outcomes.

### *Study setting*

The study was conducted in the maternity of the Hedi Chaker University Hospital in the region of Sfax in Tunisia. We studied a database of patients who were hospitalized for placenta accreta in the period lasting from January 2016 to March 2021.

### *Study population with selection criteria*

We included patients aged from 18 to 45 years old with placenta accreta (where the chorionic villi attach directly to the surface of the myometrium), increta (where the chorionic villi penetrate deeply into the myometrium), and percreta (where chorionic villi penetrate through the uterine serosa). We considered placenta accreta all patients who experienced failed attempts to remove the placenta during the third stage of labour, evidence of placental invasion at surgery and failed manual removal of the placenta partly or totally.
We did not include patients aged less than 18 years, as well as individuals declining to consent or not being able to consent. We did not include patients with suspected placenta accreta, but not confirmed during the delivery (complete placenta removal after delivery). Patients with confirmed placenta accreta who were operated on in other maternity hospitals and then referred to our tertiary centre were excluded from the study.

### *Data collection*

We collected data about demographic parameters like age, weight, size, gestity, parity, and past history of caesarean delivery and intrauterine curettage. We also collected the clinical and biological features when admitted to the hospital like bleeding during the third trimester, transfusion during the current pregnancy (before delivery), the haemoglobin concentration, the prothrombin ratio, and platelet count.
The per-operative management including the mode of delivery, the anaesthesia technique, and the surgical technique was also assessed.
The surgical technique includes the radical treatment based on total surgical removal of the placenta (hysterectomy), or conservative treatment when the placenta was left *in situ* and the surgeon opted for haemostatic suture techniques, arterial ligation, and medical treatment using methotrexate.
The blood loss was calculated according to the Gross formula [5]:
*Blood loss = total blood volume of a pregnant woman (80 ml/kg) × weight (kg) × [(Hb.i − Hb.d2)/((Hb.i + Hb.d2)/2] + 500 ml for every RBC unit transfused.*
Hb.i: haemoglobin concentration before delivery.
Hb.d2: haemoglobin concentration of the second day after delivery.
To assess the impact of antenatal diagnosis of placenta accreta, we compared the blood loss, the transfusions required, the need for catecholamines, and the anaesthesia and surgery-related complications. A massive transfusion was defined by the transfusion of more than 4 RBC units within the first hour or 10 RBC units within the first 24 hours after delivery. The duration of hospital stay was also compared. The neonatal outcomes including the term at delivery, the incidence of prematurity, the need for neonatal intensive care unit referral, and stillbirth were also assessed.

### *Study size*

The sample size determination was based on data from the preliminary results of the 20 last patients enrolled in this study (10 with antenatal diagno-

sis and 10 without). The incidence of blood loss exceeding 2 L was 10% in the antenatal diagnosis group and 80% in the second group. So, we determined that a study sample of 14 patients in each group is required for a 95% confidence level and a 5% margin of error.

### *Bias*

All patients had the same therapeutic protocol. All patients had an ultrasound examination in the third trimester of pregnancy. In the case of uncertain diagnosis of PA with ultrasounds, a MRI was done.

Patients with antenatal diagnosis of placenta accreta had elective caesarean section scheduled at the 35$^{th}$ or 36$^{th}$ gestational weeks. Special precautions were used. A multidisciplinary team, including 2 experimented obstetricians, an anaesthesiologist, an interventional radiologist, a neonatologist, and in some cases, an urologist, was involved in delivery. Two red blood cell (RBC) units were ready to use in the operation room. Patients with antenatal diagnosis were operated on under general anaesthesia. If placental removal failed, a caesarean hysterectomy or conservative treatment may be performed. In cases with extensive bladder involvement, when a caesarean hysterectomy was considered unsafe, a hysterectomy with bladder reconstruction and ureterostomy can be performed.

The transfusion protocol was the same for both groups (the protocol was approved by the department and the institution). The thresholds of transfusion were 7 g/dL of haemoglobin, 50% of prothrombin ratio, and $20 \times 10^6$/L of platelet count.

As the blood loss clinical estimation (blood collection) was operator dependent, we used an objective method based on the variation of haemoglobin concentration in the first two days after delivery (Gross formula) to calculate the blood loss.

### *Groups definition*

To assess the impact of the antenatal diagnosis on maternal outcomes (blood loss, transfusions, and maternal morbidity and mortality), the patients included were divided into two groups:

- Group 1: patients with antenatal diagnosis of placenta accreta according to the ultrasounds or the MRI data.
- Group 2: patients with an intrapartum diagnosis of placenta accreta (unexpected PA).

### *Statistical analysis*

Statistical analyses were performed using the SPSS 23.0 (SPSS, Chicago, IL, USA) statistical package. Continuous variables were presented as means value ± standard deviation. We distinguished two groups according to the antenatal diagnosis of placenta accreta. The comparison between groups was achieved by the Student's t-test and Chi$^2$ test for continuous variables and categorical variables, respectively. The Fisher exact test was used when the Chi$^2$ test was not applicable. The Mann-Whitney U test was used for non-parametric continuous variables. A binary logistic regression analysis was done to investigate the impact of antenatal diagnosis on maternal outcomes. Odds ratios (OR) and a confidence interval of 95% (95%CI) were reported. The significance threshold was set at $p < 0.05$.

### *Ethical approval*

The approval of the Hedi Chaker University Hospital Local Ethics Committee was obtained before beginning the study.

## RESULTS

In this study, we included 57 patients with placenta accreta over 44578 deliveries during the study period. Two patients who were initially taken in charge in other hospitals and secondly referred to our centre were excluded from the study. Placenta accreta was confirmed by anatomopathological examination in 53 cases (all cases treated by a hysterectomy). The incidence of placenta accreta was 0.13% (1/782 deliveries). All patients had obstetric ultrasounds examination but placenta accreta was suspected in only 35 patients (61.4%). Of these 35 suspected patients, only 15 patients had a MRI examination. The MRI confirmed the diagnosis of placenta accreta in all cases.

Then patients were divided into the antenatal diagnosis group (group 1, n = 35) and the unexpected PA group (group 2, n = 22).

The demographic parameters (age, weight, high) and historical characteristics (gravidity, parity, history of caesarean delivery or uterine surgery) of the women were comparable in both groups (**Table 1**). The current pregnancy characteristics and preoperative management were also comparable in both groups (**Table 2**).

**Table 1.** *Demographic parameters.*

| | Group 1 (n = 35) | Group (n = 22) | P-value |
|---|---|---|---|
| Age (Years) | 36.47 ± 3.54 | 34.7 ± 3.39 | 0.112 |
| Weight (Kg) | 75.73 ± 6.69 | 76.37 ± 9.37 | 0.817 |
| Patients high (cm) | 162 ± 11 | 164 ± 12 | 0.800 |
| Gestity (mean) | 4.73 ± 2.37 | 4.47 ± 1.67 | 0.61 |
| Patients with 1 gravidity | 0 (0%) | 0 (0%) | |
| Patients with 2 or more gravidities | 35 (100%) | 22 (100%) | |
| Parity (mean) | 3.73 ± 1.79 | 3.63 ± 0.99 | 0.873 |
| Patients with 1 parity | 0 (0%) | 0 (0%) | |
| Patients with 2 or more parities | 35 (100%) | 22 (100%) | |
| History of caesarean deliveries | | | 0.789 |
| Patients with 0 caesarean delivery | 0 (0%) | 1 (4.5%) | |
| Patients with 1 caesarean delivery | 6 (17%) | 5 (22.7%) | |
| Patients with 2 or more caesarean deliveries | 29 (82.5%) | 19 (86.3%) | |
| Patients with History of curettage | | | 0.745 |
| 0 | 30 (85.7%) | 17 (77.2%) | |
| 1 | 4 (11.4%) | 4 (18.1%) | |
| 2 or > 2 | 1 (2.8%) | 1 (4.5%) | |

Significant P-value ≤ 0.05.

**Table 2.** *Current pregnancy characteristics and per operative management.*

| | Group 1 (n = 35) | Group 2 (n = 22) | P-value |
|---|---|---|---|
| Placenta previa in current pregnancy | 35 (100%) | 22 (100%) | 1 |
| Placenta accreta | 29 | 21 | |
| Placenta increta | 5 | 1 | 0.259 |
| Placenta percreta | 1 | 0 | |
| Preoperative haemoglobin concentration (g/dL) | 11.1 ± 1.67 | 11.18 ± 1.28 | 0.848 |
| Prothrombin ration (%) | 94.3 ± 2.8 | 95.1 ± 3.1 | 0.745 |
| Platelet level $10^6$/mL | 174 ± 31 | 186 ± 22 | 0.215 |
| Bleeding during 3rd trimester of pregnancy | 17 (48.5%) | 11 (50%) | 0.892 |
| Transfusion during pregnancy | 0 | 0 | - |
| Mode of delivery | | | 0.911 |
| Caesarean section | 35 (100%) | 21 (95.4%) | |
| Vaginal delivery | 0 (0%) | 1 (4.5%) | |
| Anaesthesia | | | 0.908 |
| General anaesthesia | 34 (97.1%) | 21 (95.4 %) | |
| Loco regional anaesthesia | 1 (2.8%) | 1 (4.5%) | |
| Hysterectomy | 35 (100%) | 18 (81.8%) | 0.558 |
| Conservative treatment | 0 (0%) | 4 (18.1%) | |
| Uterine artery embolization | 0 (0%) | 0 (0%) | |

Significant P-value ≤ 0.05.

The antenatal diagnosis of placenta accreta reduced significantly the blood loss from 2,480 ± 1,317 ml in group 2 to 1,610 ± 908 ml in group 1 with p = 0.007.

Severe bleeding (blood loss superior to 2 L) was more frequent in patients without antenatal diagnosis of placenta accreta (81.8% *versus* 5.7% when diagnosed prenatally with p = 0.001 and OR 2.35,

95%CI 1.08-5.62). The antenatal diagnosis of PA reduced the need for transfusion. In group 1, only 10 patients needed transfusion (28.5%) *versus* 21 patients (95.4%) in group 2; p = 0.001. The risk of transfusion was higher when the placenta accreta was not diagnosed prenatally with OR 1.85, 95%CI 1.18-6.1. The transfusion details are summarized in **Table 3**.

Massive transfusion was higher in the unexpected PA group, but this difference was not statistically significant (**Table 3**). In our study, we noted 3 cases of haemorrhagic shock that needed the administration of catecholamines per-operatively. All of them were unexpected PA. Surgical and anaesthesia complications were comparable between both groups. Per- and post-operative maternal complications were also comparable between both groups (**Table 4**). For neonatal outcomes, preterm birth was more frequent when the PA was diagnosed antenatally (**Table 4**). Expected PA was correlated with a higher risk of prematurity with OR 2.04, 95%CI 1.05-4.8. However, the birth weight and the incidence of referral to the NICU were comparable in both groups. Any case of stillbirth was noted in our study.

**Table 3.** *Blood loss and the need of transfusion.*

| | Group 1 (n = 35) | Group 2 (n = 22) | P-value and OR [95%CI] |
|---|---|---|---|
| Blood loss (ml) | 1,610 ± 908 | 2,480 ± 1317 | **0.007** |
| Blood loss > 2 L | 2 (5.7%) | 18 (81.8%) | **0.001** and 2.35 [1.08-5.62] |
| Red cell unit transfused per patient | 0.93 ± 1.33 | 1.87 ± 1.57 | 0.045 |
| Patients needed RBC | 10 (28.5%) | 21 (95.4%) | **0.001** and 1.85 [1.18-6.1] |
| Patients needed massive transfusion (> 4 RBC/1hour) | 1 (2.8%) | 5 (22.7%) | **0.055** |
| FFP transfused per patient | 0.80 ± 2.24 | 1.40 ± 3.15 | 0.515 |
| Patients needed FFP | 1 (2.8%) | 7 (31.8%) | 0.066 |
| Platelets transfused per patient | 0 | 1.13 ± 3.09 | 0.165 |
| Patients needed Platelets transfusion | 0 (0%) | 3 (13.6%) | 0.084 |

OR: odds ratio; CI: confidence interval; RBC: red blood cells; FFP: fresh frozen plasma; significant P-value ≤ 0.05 in bold.

**Table 4.** *Maternal and neonatal morbidity.*

| | Group 1 (n = 35) | Group 2 (n = 22) | P-value and OR [95%CI] |
|---|---|---|---|
| **Maternal outcomes** | | | |
| Haemorrhagic chock (need for catecholamine) | 0 (0%) | 3 (13.6%) | 0.24 |
| Surgical complication | 3 (8.5%) | 3 (13.6%) | 0.652 |
| Urinary tract injury | 2 | 2 | - |
| Digestive tract injury | 0 | 0 | - |
| Postoperative infections | 1 | 1 | - |
| Late bleeding or haematoma | 0 | 0 | - |
| Anaesthesia complication | 0 (0%) | 0 (0%) | - |
| Transfusion complication | 0 (0%) | 1 (4.5%) | - |
| Duration of hospitalization (days) | 5.13 ± 1.5 | 6 ± 3.59 | 0.379 |
| **Neonatal outcomes** | | | |
| Term at delivery | 35.4 ± 5.1 | 37.3 ± 3.8 | 0.089 |
| Preterm delivery ≤ 37 WG | 31 (88.5%) | 4 (18.1%) | **0.001** and 2.04 [1.05-4.8] |
| Birth weight (g) | 2,851 ± 345 | 3,010 ± 285 | 0.095 |
| Referral to the NICU | 32 (91.4 %) | 21 (95.4%) | 0.845 |
| Stillbirth | 0 | 0 | - |

OR: odds ratio; CI: confidence interval; WG: weeks of gestation; NICU: neonatal intensive care unit; significant P-value ≤ 0.05 in bold.

## DISCUSSION

In this study, we showed that the antenatal diagnosis of placenta accreta using ultrasounds technique and MRI allowed a significantly reduced blood loss and lower rates of transfusions requirements as a consequence. We showed also that the absence of this antenatal diagnosis was correlated with an increased risk of severe bleeding (blood loss superior to 2 L) and RBC transfusion.

So, this study emphasizes the role of the antenatal diagnosis that allows planned and organized management by a multidisciplinary team and thus can reduce haemorrhagic morbidity, compared with unexpected placenta accreta [6]. Our study has a clinical implication as it emphasizes the role of prenatal ultrasound and MRI as promising diagnostic tools for PA in the third trimester, in reducing the maternal blood loss and maternal morbidity as a consequence. As a low-income country, access to healthcare structures can be difficult at times, and high-level maternity hospitals with multidisciplinary teams are not available in all regions of our country [7]. So, we still have an important group of patients who did not have a correct antenatal screening of the placenta accreta. Furthermore, patients can sometimes neglect the utility of prepartum consultations, particularly multiparous ones. This study shows that gynaecologists as well as patients should be aware of the higher risk of postpartum complications due to the absence of an antenatal diagnosis of the placenta accreta [8].

The placenta accreta spectrum in our study was comparable with the literature data. The incidence was 1/782 which is near 1/1,000 of recent publications [9, 10]. The main risk factors including placenta previa, previous caesarean section, uterine surgeries, *in vitro* fertilization, and advanced maternal age were identified in our cases [6, 11]. Understanding placenta accreta spectrum risk factors may facilitate patient identification and may help in prenatal diagnosis. We suggest particular caution for patients at risk of abnormal placentation and we think that using advanced techniques like MRI for prenatal diagnosis seems to be reasonable [12]. MicroRNAs (miRNAs) are small non-coding RNA molecules (~22 nucleotides long) that suppress gene expression by binding to the 3′ end of the untranslated region (3′-UTR) of target mRNAs [13]. It has been reported that miR-34a, miR-29a/b/c, and miR-125a are significantly down-regulated in placenta accreta but the mechanisms by which miRNAs might contribute to PAS pathogenesis have yet to be determined [14]. Nevertheless, these biomarkers demonstrated modest screening efficiency [15].

The ultrasounds remain the primary tool in diagnosing placenta accreta [9]. Although the increasing role of MRI in placenta accrete diagnosis is evident, it requires experienced readers [16]. The literature reveals several disparate but conceptually overlapping MRI signs. Identifying and differentiating between placenta increta and percreta on imaging may be quite challenging even with MRI and sometimes even on final pathology [12, 16].

In our study ultrasound was performed in all patients, but diagnosed placenta accreta in only 61.4% of cases which is lower than literature [17]. However, in a recent meta-analysis including 3,209 pregnancies [17], ultrasounds had 90.6% of sensitivity and 97.1% of specificity for placenta accreta diagnosis. This may be explained by the operator dependence of this examination as well as his experience in managing such rare and unusual situations.

Other studies showed that prenatal MRI has an excellent diagnostic accuracy in identifying the depth and the topography of placental invasion [18], in spite of an interobserver variability [19]. This meta-analysis [18] including 20 studies with 1,080 pregnancies showed a high sensibility of the MRI in diagnosing accreta (94.4%), increta (100%), percreta (86.5%) and high specificity. The corresponding values for specificity were 98.8%, 97.3% and 96.8%. These results are comparable with those of our study in which MRI diagnosed antenatally the placenta accreta in 100% of cases.

Antenatal diagnosis allows safe delivery planning and better team organization like the referral to specialized centres for placenta accreta management, which may improve the maternal and neonatal outcomes [20]. This multidisciplinary organization can lead to reduced blood loss and reduced transfusion rates and so reduced maternal morbidity [21-23]. Recent studies showed that the maternal morbidity was also correlated to other factors like the invasion topography of the placenta [24]. Another study including 29 parturients with placenta accreta showed that MRI features may predict massive haemorrhage and may be helpful for pre-operative preparation of placenta accreta patients [25]. However, MRI features were not significant for predicting adverse neonatal events including preterm delivery, low birth weight, and 5-minute APGAR score [26].

In our study we noted a higher rate of preterm birth in expected placenta accreta patients. This may be due to the delivery planning from 35 to 36 WG to reduce the risk of severe haemorrhage. Similar results were found in previous studies [27, 28]. The main limitation of this study is the bias in the management protocol. Indeed, blood loss and transfusions may depend on the surgical procedure and particularly the rapid bleeding control [29], as well as the surgical expertise [30], which can't be the same in both groups. Our sample size was calculated on the basis of severe bleeding which resulted in a small number of patients that can't allow the comparison of maternal complications whose incidence is lower [31, 32]. It was reported that during caesarean hysterectomy, the risk for urinary tract injury is less than 15% [33]. On the other hand, leaving the placenta *in situ* exposes women to other serious complications, such as infection, and severe bleeding [34, 35]. This is why the majority of our patients had a caesarean hysterectomy. This may be due to the advanced age and multiparity of our patients but also to the unavailability of multidisciplinary innovative approaches using Balloon catheter occlusion or arterial embolization that may reduce blood flow and potentially prevent life-threatening haemorrhage complicating conservative treatments [36, 37].

## CONCLUSIONS

The antenatal diagnosis of placenta accreta allows improved maternal outcomes. It can lead to reduced blood loss and lower rates of transfusions. Unexpected placenta accreta was correlated with an additional risk of severe bleeding and transfusion requirement. This may be due to the pre-operative cautions resulting in a safe delivery planning and better team organization. However, we noted a higher incidence of planned preterm birth in patients with antenatal diagnosis of placenta accreta.

## COMPLIANCE WITH ETHICAL STANDARDS

### *Authors contribution*

M.K.: Writing – original draft. A.J.: Conceptualization, investigation, methodology, writing – review & editing. J.H.: Formal analysis, investigation. Y.E.: Data curation, formal analysis, investigation. M.D.: Data curation, investigation. K.C., K.K: Supervision, validation, visualization.

### *Funding*

None.

### *Study registration*

N/A.

### *Disclosure of interests*

The authors declare that they have no conflict of interests.

### *Ethical approval*

It was obtained from the HCUH (local Ethics Committee).

### *Informed consent*

It was obtained from all patients included in the study.

### *Data sharing*

Data are available under reasonable request to the corresponding author due to privacy/ethical restrictions.

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