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# Prospective evaluation of impact of post-Cesarean section uterine scarring in perinatal diagnosis of placenta accreta spectrum disorder

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**KEYWORDS:** Cesarean section; placenta increta; placenta percreta; placenta previa accreta; ultrasound imaging; uterine dehiscence

## CONTRIBUTION

*What are the novel findings of this work?*
Scarring of the lower uterine segment after multiple Cesarean deliveries is associated with structural abnormalities of the uterine contour on ultrasound and intraoperatively, often owing to a large area of dehiscence, independently of evidence of accreta placentation on histology, which can lead to the false-positive diagnosis of placenta percreta prenatally and intraoperatively.

*What are the clinical implications of this work?*
Prenatal ultrasound signs validated by standardized clinical and histopathological protocols, including detailed guided sampling for microscopic examination, allow for accurate perinatal diagnosis of placenta accreta spectrum and are essential for training, the development of new diagnostic protocols and tailored management.

## ABSTRACT

***Objective*** *Standardized ultrasound imaging and pathology protocols have recently been developed for the perinatal diagnosis of placenta accreta spectrum (PAS) disorders. The aim of this study was to evaluate prospectively the effectiveness of these standardized protocols in the prenatal diagnosis and postnatal examination of women presenting with a low-lying placenta or placenta previa and a history of multiple Cesarean deliveries (CDs).*

***Methods*** *This was a prospective cohort study of 84 consecutive women with a history of two or more prior CDs presenting with a singleton pregnancy and low-lying placenta/placenta previa at 32–37 weeks' gestation, who were referred for perinatal care and management between 15 January 2019 and 15 December 2020. All women were investigated using the standardized description of ultrasound signs of PAS proposed by the European Working Group on abnormally invasive placenta. In all cases, the ultrasound features were compared with intraoperative and histopathological findings. Areas of abnormal placental attachment were identified during the immediate postoperative gross examination and sampled for histological examination. The data of a subgroup of 32 women diagnosed antenatally as non-PAS who had complete placental separation at birth were compared with those of 39 cases diagnosed antenatally as having PAS disorder that was confirmed by histopathology at delivery.*

***Results*** *Of the 84 women included in the study, 42 (50.0%) were diagnosed prenatally as PAS and the remaining 42 (50.0%) as non-PAS on ultrasound examination. Intraoperatively, 66 (78.6%) women presented with a large or extended area of dehiscence and 52 (61.9%) with a dense tangled bed of vessels or multiple vessels running laterally and craniocaudally in the uterine serosa. A loss of clear zone was recorded on grayscale ultrasound imaging in all 84 cases, while there was no case with bladder-wall interruption or with a focal exophytic mass. Myometrial thinning (< 1 mm) in at least one area of the anterior uterine wall was found in 41 (97.6%) of the 42 cases diagnosed as non-PAS on ultrasound and 37 (88.1%) of the 42 diagnosed antenatally as PAS. Histological samples were available for all 48 hysterectomy specimens with abnormal placental attachment and for the three cases managed conservatively with focal myometrial resection and uterine reconstruction. Villous tissue*

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*was found directly attached to the superficial myometrium (placenta creta) in six of these cases and both creta villous tissue and deeply implanted villous tissue within the uterine wall (placenta increta) were found in the remaining 45 cases. There was no evidence of percreta placentation on histology in any of the PAS cases. Comparison of the main antenatal ultrasound signs and perioperative macroscopic findings between the two subgroups correctly diagnosed antenatally (32 non-PAS and 39 PAS) showed no significant difference with respect to the distribution of myometrial thinning and the presence of a placental bulge on ultrasound and of anterior uterine wall dehiscence intraoperatively. Compared with the non-PAS subgroup, the PAS subgroup showed significantly higher placental lacunae grade (*$P < 0.001$*) and more often hypervascularity of the uterovesical/subplacental area (*$P < 0.001$*), presence of bridging vessels (*$P = 0.027$*) and presence of lacunae feeder vessels (*$P < 0.001$*) on ultrasound examination, and increased vascularization of the anterior uterine wall intraoperatively (*$P < 0.001$*).*

***Conclusions*** *Remodeling of the lower uterine segment following CD scarring leads to structural abnormalities of the uterine contour on both ultrasound examination and intraoperatively, independently of the presence of accreta villous tissue on microscopic examination. These anatomical changes are often reported as diagnostic of placenta percreta, including cases with no histological evidence of PAS. Guided histological examination could improve the overall diagnosis of PAS and is essential to obtain evidence-based epidemiologic data.* © *2021 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

## INTRODUCTION

Scarring of the uterine wall after surgery is associated with permanent myofiber disarray, tissue edema, inflammation, elastosis and decrease in smooth muscle volume density[1–3]. Remodeling of the lower uterine segment after Cesarean delivery (CD) can lead to Cesarean scar defect, which can range from a small defect of the superficial myometrium to a deep defect or niche[4]. The incidence of Cesarean scar defect increases with the number of prior CDs and is influenced by the hysterotomy closure technique used and scar location[4–6]. After multiple lower-segment CDs, the anterior uterine wall becomes thinner and largely consists of fibrotic scar tissue[7–9].

There is mounting evidence that the development of the definitive placenta in the area of a prior CD can lead to a Cesarean scar pregnancy and subsequently to placenta accreta[10–12]. CD is considered the main predisposing factor for the development of both placenta previa and placenta accreta spectrum (PAS) in subsequent pregnancies[13–15]. These epidemiologic data suggest that the scar tissue of a Cesarean section stimulates the implantation of the blastocyst in the lower segment of the uterus, and may lead to the abnormal attachment of the placental tissue within and around the scar area[16].

Women with a history of CD presenting with an anterior low-lying placenta or placenta previa have the highest risk for PAS disorders[13–16]. Prenatal diagnosis of PAS decreases the risk of complications at delivery due to massive intrapartum hemorrhage[17,18]. In 2016, the European Working Group on abnormally invasive placenta (EW-AIP) proposed a standardized protocol for the ultrasound signs of PAS produced by Delphi concensus[19]. Most authors of population studies and of studies on prenatal imaging of PAS disorders do not report detailed data on the confirmation of the diagnosis at birth[20,21], and often refer to the clinical and histopathologic criteria reported by Irving and Hertig[22] in 1937, i.e. villous tissue directly attached to the superficial myometrium without interposing decidua. We have recently described a new methodological approach for the correlation of clinical and pathological data in women with invasive PAS[23], and an international expert panel has proposed reporting guidelines for the pathological diagnosis of PAS[24]. The aim of this study was to evaluate prospectively these standardized imaging and cilnicopathological protocols in the prenatal diagnosis and postnatal examination of women presenting with a low-lying placenta or placenta previa and a history of multiple CDs.

## METHODS

We conducted a prospective cohort study of 84 consecutive patients at high risk for PAS referred for perinatal care and management between 15 January 2019 and 15 December 2020 by an expert specialist multidisciplinary team at the Department of Obstetrics and Gynecology, University of Cairo, Egypt. All patients included in the study presented with a singleton pregnancy at 32–37 weeks' gestation, had a history of two or more prior CDs and were diagnosed prenatally with an anterior low-lying placenta or placenta previa and with ultrasound signs suggesting PAS. Women with a multiple pregnancy or women requiring emergency delivery before 32 weeks were excluded from the study group.

In all cases, detailed transabdominal and transvaginal (TVS) sonographic examinations of the placenta, uterus and pelvis were performed within 48 h before surgery using a GE Voluson E10 ultrasound system (GE Healthcare, Zipf, Austria). The placenta was recorded as 'low lying' when its edge was 0.5–2 cm from the internal os of the uterine cervix on TVS. When the placenta was < 0.5 cm from the internal os or completely covering it, it was defined as placenta previa (marginal or complete)[25]. Transabdominal ultrasound signs of PAS were recorded using the standardized description proposed by the EW-AIP[19] including: on grayscale ultrasound, loss of clear zone, myometrial thinning (Figure 1b), presence of placental lacunae (Figure 2b), bladder wall interruption, placental bulge and focal exophytic mass; and on color Doppler imaging (CDI), uterovesical hypervascularity;

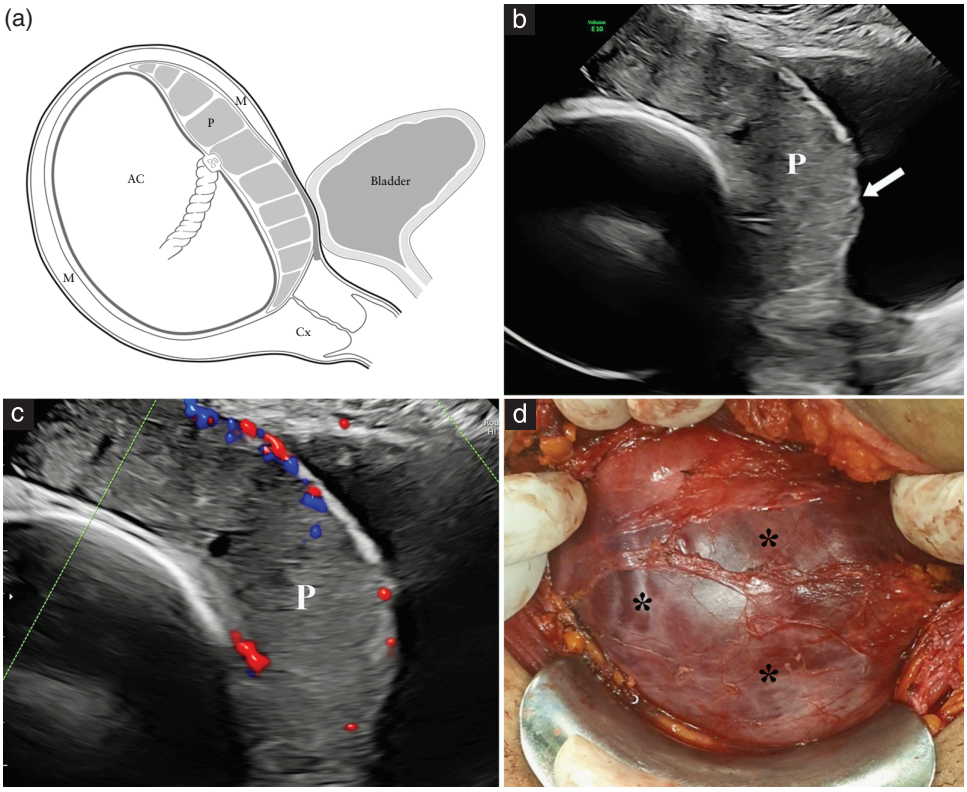


**Figure 1** Schematic representation (a) and sonographic (b,c) and intraoperative (d) images from a case of non-accreta placenta previa at 36 weeks' gestation. (a) Diagram showing a large area of dehiscence between the lower uterine segment and the bladder. (b) Longitudinal transabdominal view of the lower uterine segment, showing placenta previa and myometrial thinning of the uterobladder interface (arrow). (c) Color Doppler mapping showing normal uteroplacental vasculature. (d) Intraoperative image, showing an extended area of uterine dehiscence occupying the entire lower uterine segment anterior wall (*); underneath, most of the placenta is visible. AC, amniotic cavity; Cx, cervix; M, myometrium; P, placenta.

subplacental hypervascularity; bridging vessels and placental lacunae feeder vessels (Figure 2c). Placental lacunae were graded using the score proposed by Finberg and Williams[26]: Grade 0, no lacunae; Grade 1+, 1–3 lacunae; Grade 2+, 4–6 lacunae; and Grade 3+, > 6 lacunae. The minimal myometrial thickness was measured transabdominally with a full bladder at the level of the upper, middle and lower edges of the bladder–uterine wall junction. Myometrial thinning was recorded when the myometrial thickness was < 1 mm.

All patients were managed according to local protocols, including conservative surgical management, i.e. partial myometrial resection and uterine anterior wall repair when sufficient tissue was available for reconstruction after dissection of the lower segment[27] (Figure 3). Fetuses were delivered either through a horizontal incision at the upper edge of the placenta or through a vertical incision at the upper uterine segment. We used an image capture digital photographic protocol to record the macroscopic features during the different phases of the surgery and gross examination of the hysterectomy specimens, as described previously[23]. In brief, intraoperative photographs before and after delivery of the fetus were analyzed for the presence of anterior-wall uterine dehiscence with placental tissue seen through the uterine wall (Figure 1d) and the presence of abnormally increased vascularity (i.e. a dense tangled bed of vessels and multiple vessels running craniocaudally and laterally in the anterior perimetrium of the uterine serosa over the placental bed) (Figure 2d). The size of the uterine dehiscence was evaluated as a proportion of the anterior lower uterine segment and was recorded as focal if it was < 30%, large if it was 30–50% and extended if it involved > 50%. When hysterectomy was performed, the specimen was orientated anteriorly, measured and photographed and cut into slices 2–3 cm thick immediately after the surgical procedure by the surgical team. Areas of abnormal placental attachment that could not be digitally separated were identified and their size was recorded as a proportion of the placental basal plate (focal if < 10% or large if 10–30%). Between three and six samples were obtained from these areas, processed for histologic examination and stained with hematoxylin and eosin. The final PAS grading (placenta creta; placenta increta and placenta percreta) was defined using the International Federation of Gynecology and Obstetrics classification[28] and reporting guidelines for the pathology diagnosis of PAS[24].

Institutional Scientific and Research Ethical Committee approval (RSEC 021001) was obtained prior to the start of this study and all patients provided written consent for the use of the photographic images obtained before and after delivery. Baseline clinical data were collected using a standard clinical audit protocol and all data and images were fully anonymized for further analysis.

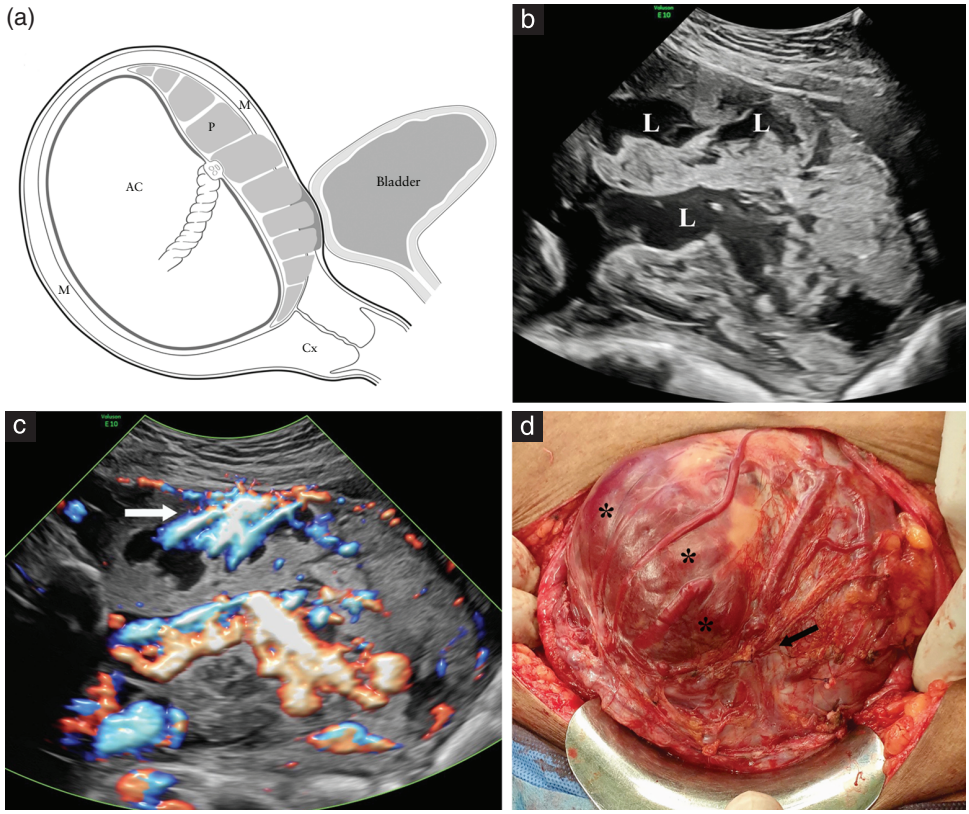


**Figure 2** Schematic representation (a) and sonographic (b,c) and intraoperative (d) images from a case of placenta previa increta at 34 weeks' gestation. (a) Diagram showing accreta villous tissue deeply implanted into the scar of a prior lower segment Cesarean section. (b) Longitudinal transabdominal view of the lower uterine segment, showing placenta previa with large lacunae (L). (c) Color Doppler image showing large feeder vessels (arrow). (d) Intraoperative image, showing an area of focal uterine dehiscence of the lower uterine segment anterior wall (*) and dense tangled bed of vessels and multiple vessels running craniocaudally and laterally in the anterior perimetrium. Note an area of adhesion involving the bladder (arrow). AC, amniotic cavity; Cx, cervix; M, myometrium; P, placenta.

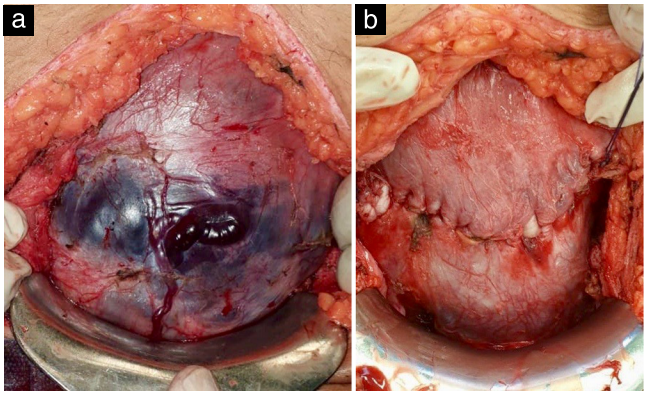


**Figure 3** Intraoperative images of a case of non-accreta placenta previa at 36 weeks' gestation, showing: (a) the anterior uterine wall with a large area of dehiscence covered by dilated vessels before hysterotomy; and (b) view after transverse lower segment hysterotomy and reconstruction of the lower uterine segment.

### Statistical analysis

StatGraphic-plus Version 3 data analysis and statistical software package (Manugistics, Rockville, MD, USA) was used to analyze the data. A standard Kurtosis analysis indicated that some demographic values were not normally distributed and the data are therefore presented as median (interquartile range). The data of a subgroup of 32 women diagnosed antenatally as non-PAS and who had complete placental separation at birth, were compared with those of 39 women diagnosed antenatally as having PAS disorder that was confirmed by histopathology at delivery. Categorical variables were compared between subgroups using the $\chi$-square test; $P < 0.05$ was considered to indicate statistical significance.

## RESULTS

During the study period there were 28 535 deliveries, of which 14 627 (51.3%) were CD, including 517 performed for placenta previa. Included in the cohort were 84 women with a history of two or more prior CDs who presented with an anteriorly located low-lying placenta or placenta previa. The maternal demographic characteristics, main ultrasound findings and PAS grading after histopathologic examination of the cohort are displayed in Table 1. Twenty patients were managed conservatively, including three cases presenting with a focal area of abnormal placental attachment who were managed by partial myometrial resection and uterine reconstruction. The antenatal ultrasound diagnosis and histopathological diagnosis of the cohort are presented in Figure 4.

### Intraoperative and histopathological findings

Intraoperative macroscopic examination found some degree of anterior uterine wall dehiscence in all cases, with 66/84 (78.6%) presenting with a large or extended area of dehiscence (Table 1). There were 52 (61.9%) cases with a dense tangled bed of vessels or multiple vessels running laterally and craniocaudally in the uterine serosa superficial to the placental insertion (Figure 2). Four women presented with a single dilated vessel running over the lower segment and were classified as having normal lower uterine segment vascularity.

Of the 64 patients who underwent hysterectomy, 16 had complete placental separation, of whom 15 were diagnosed as non-PAS and one as PAS on ultrasound (Figure 4). The immediate postoperative macroscopic examination of the 48 hysterectomy specimens with incomplete placental separation showed a focal accreta area in 29 (60.4%) cases and a large accreta area in 19 (39.6%) cases. Thirty-nine of these cases were diagnosed antenatally as PAS and nine as non-PAS. Microscopic examination showed evidence of accreta placentation in 51 (60.7%) of the 84 cases in the cohort, including the 48 cases who had hysterectomy with incomplete placental separation and the three cases who were managed conservatively with partial myometrial resection. Villous tissue was found directly attached to the superficial myometrium (placenta creta) in six of these cases and both creta villous tissue and deeply implanted villous tissue within the uterine wall (placenta increta) were found in the remaining 45 cases. There was no evidence of villous tissue invading the uterine serosa or beyond the uterine wall (placenta percreta) in any of the histological samples.

**Table 1** Maternal demographic characteristics, antenatal ultrasound (US) and intraoperative findings and histopathological outcome of 84 singleton pregnancies with anterior low-lying placenta or placenta previa

| *Variable* | *Value* |
|---|---|
| Maternal age (years) | 32.0 (28.5–34.0) |
| Gravidity | 4.0 (3.0–5.5) |
| Parity | 3.0 (2.0–4.0) |
| Number of prior CDs | 3.0 (2.0–4.0) |
| GA at delivery (weeks) | 36.2 (36.0–37.0) |
| Birth weight (g) | 2900 (2700–3120) |
| Placental location | |
| Low-lying | 8 (9.5) |
| Previa marginal | 13 (15.5) |
| Previa complete | 63 (75.0) |
| Antenatal US diagnosis | |
| PAS | 42 (50.0) |
| No PAS | 42 (50.0) |
| Intraoperative anterior uterine wall dehiscence | |
| Focal | 18 (21.4) |
| Large | 30 (35.7) |
| Extended | 36 (42.9) |
| Intraoperative anterior uterine wall vascularization | |
| Normal | 32 (38.1) |
| Increased | 52 (61.9) |
| Surgical outcome | |
| Cesarean hysterectomy | 64 (76.2) |
| Conservative management | 20 (23.8) |
| Histopathological diagnosis | |
| Placenta creta | 6 (7.1) |
| Placenta increta | 45 (53.6) |
| Dehiscence with no evidence of PAS | 33 (39.3) |

Data are presented as median (interquartile range) or *n* (%). CD, Cesarean delivery; GA, gestational age; PAS, placenta accreta spectrum.

### Comparison of ultrasound and delivery findings

Of the 84 women included in the study, 42 (50.0%) were diagnosed as having PAS and the remaining 42 (50.0%) as non-PAS on antenatal ultrasound examination. Loss of clear zone was recorded on grayscale ultrasound imaging (Figure 1b) in all 84 cases. There was no case with bladder wall interruption or with a focal exophytic mass. Myometrial thinning (< 1 mm) in at least one area of the anterior uterine wall was found in 41/42 (97.6%) cases diagnosed antenatally on ultrasound as non-PAS and 37/42 (88.1%) diagnosed as PAS. A placental bulge was observed in 16 and 18 of the antenatally diagnosed non-PAS and PAS cases, respectively. Placental lacunae were reported in 16 (38.1%) of the non-PAS cases on ultrasound, including 14 cases classified as Grade 1+ and two as Grade 2+. All 42 cases diagnosed as having PAS on antenatal ultrasound showed placental lacunae, including one classified as Grade 1+, 14 cases with Grade 2+ and 27 with Grade 3+ placental lacunae (Figure 2b). On CDI, an increase in uterovesical/subplacental vascularity was observed in eight (19.0%) of the non-PAS cases and in 41 (97.6%) of the PAS cases (Figure 2c). Lacunae feeder vessels were found in four (9.5%) and 37 (88.1%) of the ultrasound-diagnosed non-PAS and PAS cases, respectively. Four (9.5%) non-PAS and 13 (31.0%) PAS cases presented with bridging vessels on CDI.

In 10 out of the 42 cases diagnosed as non-PAS on antenatal ultrasound, including nine cases managed by hysterectomy and one by partial myometrial resection, the histologic examination showed creta villous tissue in four cases and both creta and increta villous tissue in six. Among the 42 cases diagnosed antenatally as PAS, there were two cases with creta villous tissue but with no deeply implanted villous tissue and one case with complete placental separation. The overall performance of the EW-AIP ultrasound imaging protocol for the antenatal detection of PAS in our cohort was as follows: sensitivity, 80.39% (95% CI, 67.47–90.37%); specificity, 96.97% (95% CI, 84.24–99.92%); positive likelihood ratio, 26.53 (95% CI, 3.85–184.48); negative likelihood ratio, 0.20 (95% CI, 0.11–0.35) and diagnostic accuracy, 86.9% (95% CI, 78.02–93.36%).

Table 2 displays and compares the main ultrasound signs and perioperative macroscopic findings in the 32 cases diagnosed antenatally as non-PAS with no evidence of PAS at delivery and the 39 cases diagnosed antenatally as PAS with abnormally deep villous attachment (increta) confirmed by histopathology. There was no significant difference between the non-PAS and PAS subgroups

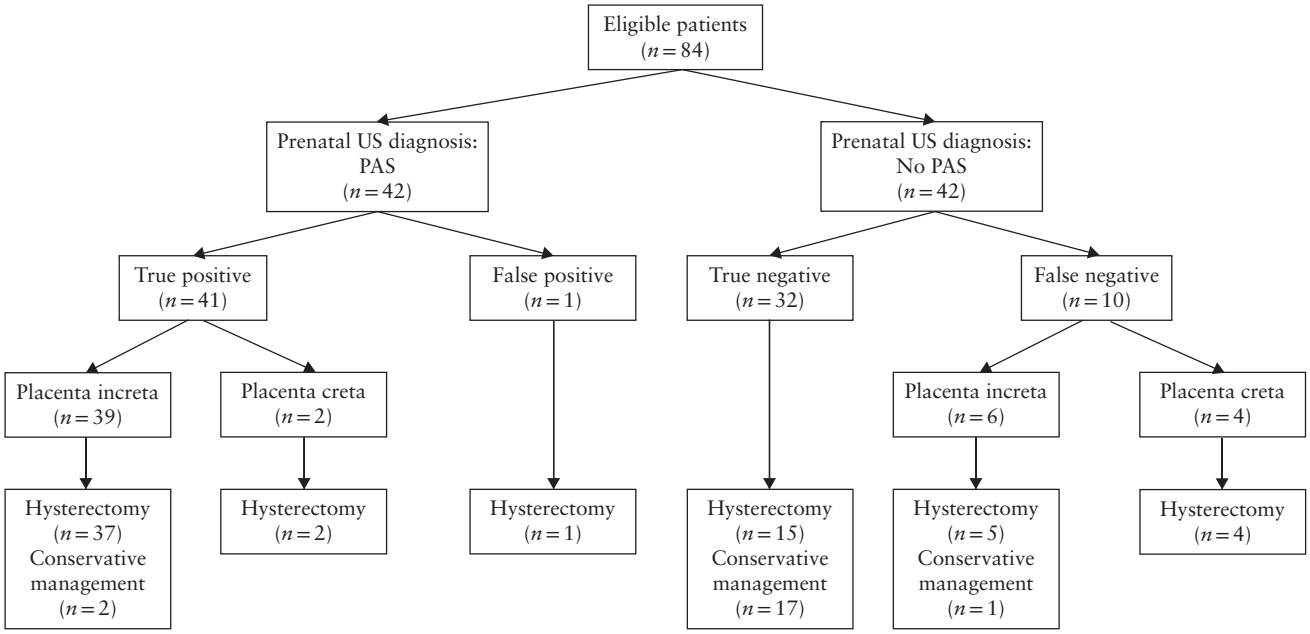


**Figure 4** Flowchart showing antenatal diagnosis on ultrasound (US) and histopathological diagnosis and management in 84 women with anterior low-lying placenta or placenta previa and a history of two or more Cesarean deliveries, included in the study. PAS, placenta accreta spectrum.

**Table 2** Antenatal ultrasound and intraoperative findings in 32 women diagnosed on antenatal ultrasound as not having placental accreta spectrum (PAS) disorder who had complete placental separation at birth and in 39 women diagnosed antenatally with PAS disorder in whom presence of placenta increta was confirmed by histopathology at delivery

| *Variable* | *No PAS (n = 32)* | *PAS (n = 39)* | $\chi^2$ | P |
|---|---|---|---|---|
| Myometrial thinning (< 1 mm) | | | | |
| Lower edge | 12 (37.5) | 19 (48.7) | | 0.342 |
| Middle | 28 (87.5) | 27 (69.2) | | 0.067 |
| Upper edge | 15 (46.9) | 13 (33.3) | | 0.703 |
| All three levels | 6 (18.8) | 8 (20.5) | | 0.852 |
| Placental lacunae grade | | | 71.001 | < 0.001 |
| Grade 0 (none) | 26 (81.3) | 0 (0.0) | | |
| Grade 1+ (1–3 lacunae) | 6 (18.8) | 0 (0.0) | | |
| Grade 2+ (4–6 lacunae) | 0 (0.0) | 13 (33.3) | | |
| Grade 3+ (> 6 lacunae) | 0 (0.0) | 26 (66.7) | | |
| Placental bulge | | | 2.017 | 0.155 |
| Yes | 8 (25.0) | 16 (41.0) | | |
| No | 24 (75.0) | 23 (59.0) | | |
| Uterovesical/subplacental hypervascularity | | | 49.257 | < 0.001 |
| Yes | 5 (15.6) | 38 (97.4) | | |
| No | 27 (84.4) | 1 (2.6) | | |
| Bridging vessels | | | 4.828 | 0.027 |
| Yes | 3 (9.4) | 12 (30.8) | | |
| No | 29 (90.6) | 27 (69.2) | | |
| Lacunae feeder vessels | | | 22.042 | < 0.001 |
| Yes | 3 (9.4) | 25 (64.1) | | |
| No | 29 (90.6) | 14 (35.9) | | |
| Intraoperative anterior uterine wall dehiscence | | | 2.584 | 0.274 |
| Focal | 9 (28.1) | 7 (17.9) | | |
| Large | 14 (43.8) | 14 (35.9) | | |
| Extended | 9 (28.1) | 18 (46.2) | | |
| Intraoperative anterior uterine wall vascularization | | | 25.912 | < 0.001 |
| Normal | 22 (68.8) | 4 (10.3) | | |
| Increased | 10 (31.3) | 35 (89.7) | | |

Data are presented as *n* (%).

with respect to median maternal age, gravidity, parity, number of prior CDs, gestational age at delivery and birth weight. There was no significant difference between the subgroups in the distribution of myometrial thinning and the presence of a placental bulge on ultrasound examination and of anterior uterine wall dehiscence intraoperatively. The distribution of placental lacunae grade was significantly different ($P < 0.001$) between the two subgroups, with only six cases in the non-PAS subgroup presenting with Grade 1+ whereas all the cases in the PAS subgroup were found to have Grade 2+ or 3+. In the PAS compared with the non-PAS subgroup, there was a significantly higher number of cases showing hypervascularity of the uterovesical/subplacental area ($P < 0.001$), presence of bridging vessels ($P = 0.027$) and lacunae feeder vessels ($P < 0.001$) on ultrasound examination and increased gross vascularization of the anterior uterine wall intraoperatively ($P < 0.001$).

## DISCUSSION

The findings of our study indicate that the lower uterine segment in women with prior multiple CDs presenting with an anterior low-lying placenta/placenta previa shows extended remodeling due to scarring on both ultrasound examination and intraoperatively, independently of the presence of accreta villous tissue on microscopic examination.

### Comparison with other studies

A recent special report of the Society for Maternal–Fetal Medicine stated that the main second- and third-trimester sonographic markers of PAS are placental lacunae, abnormal uteroplacental interface, abnormal uterine contour, exophytic mass and bridging vessel[29]. Abnormalities of the uterine contour, including loss of the clear zone, myometrial thinning and a bulge-like appearance, on ultrasound have been commonly reported in the literature as essential signs for the prenatal diagnosis of PAS[19,30–34]. These changes become more pronounced in the third trimester when the lower uterine segment is further stretched by the combined effect of fetal presentation and Braxton–Hicks uterine contractions[8,9]. We found no difference in the distribution of these signs between the non-PAS and the PAS subgroups. All the patients in the present cohort had two or more prior CDs and over 70% presented with large or extended dehiscence of the lower uterine segment (Table 1). These findings support the concept that abnormalities of the uterine contour are secondary to scarring and remodeling of the anterior wall of the lower uterine segment as a result of CD rather than to accreta placentation.

The main structural changes associated with PAS occur at the level of the uteroplacental circulation[8,9,32]. In the present study, some of these changes, although less pronounced, were also found in non-PAS cases (Table 2), suggesting that previa placentation in a lower uterine segment remodeled by multiple Cesarean scars can also impact the development of uteroplacental circulation. These changes may depend on the residual myometrial thickness and the proportion of the definitive placenta developing within the scar area. Several authors have proposed scoring systems to assist in the ultrasound diagnosis of PAS in women at high risk[35–38]. The main ultrasound criteria used in these studies were the loss of the retroplacental clear space[35–38], interruption or irregularity of the bladder–uterine interface[35,36,38], the number of placental lacunae[35–38], hypervascularity of the retroplacental space[37,38] and the presence of bridging vessels[35]. Using these scores, all the patients in the present study, including those with no microscopic evidence of PAS, would have been classified as high risk on ultrasound owing mainly to abnormalities of the uterine contour, limiting their value in women with a history of multiple CDs.

### Clinical implications

Recent systematic reviews and meta-analyses of the epidemiology of PAS have found that the reported prevalence of PAS in the general obstetric population and its incidence in women presenting with a low-lying placenta/placenta previa and a prior CD are highly variable[20,21]. The large heterogeneity between cohort studies is due to the lack of use of a standardized protocol for prenatal ultrasound imaging for both PAS and placental location and for confirmation of the diagnosis at birth[20,21]. In particular, none of the studies included in the two systematic reviews reported on the intraoperative findings and, even though half of them stated that they obtained histopathological confirmation of the diagnosis, the majority provided no details and those that did referred to the histological criteria described by Irving and Hertig in 1937 for superficial PAS[22]. The depth of abnormal villous attachment undoubtedly correlates with outcome but was reported in less than half of the studies included in both systematic reviews, undermining the role of prenatal imaging in the management of PAS. Within this context, the surface of abnormal villous attachment is also likely to have an impact on outcome and should be reported in future studies.

New clinical classification systems for PAS have been proposed recently to compare prenatal imaging findings with the degree of placental abnormal attachment at vaginal birth and/or Cesarean section[38–40]. Clinical classification systems are prone to confirmation bias, with the surgeon more likely to confirm what has been reported on prenatal imaging and pathologists basing their diagnosis on the surgeon's intraoperative findings. Most hysterectomy specimens arrive at the laboratory distorted by attempts by the surgeon to remove the placenta[23,41] and/or extensive surgical dissection of the lower segment[7,42], further limiting the accuracy of the clinicopathological correlation. Not surprisingly, the widest range in the incidence of the different grades of PAS is found in placenta previa percreta, with some studies reporting over 50% of cases diagnosed as such[21]. In many

studies, placenta percreta is described intraoperatively as placental tissue having invaded through the serosa with or without a clear surgical plane between the bladder and the uterus, with multiple adhesions and increased vascularity of the lower segment[40,41]. In the present study, we found no histological evidence for percreta placentation, but had we used the above intraoperative criteria, > 50% of our cases, both PAS (Figure 2) and non-PAS (Figures 1 and 3), would have also been classified as percreta. These findings suggest that areas of dehiscence of the lower uterine segment in patients with a history of prior CDs presenting with placenta previa can be easily mistaken intraoperatively as placenta percreta, which could explain the wide variation in the incidence of this placentation anomaly reported in the clinical literature.

### Strengths and limitations

Our study has several strengths. It is the first study of which we are aware that has sought to evaluate prospectively standardized ultrasound signs for the prenatal diagnosis of PAS and compare them with detailed histopathological findings at birth. We also used a standardized protocol for the recording of gross intraoperative features and immediate postoperative dissection of all hysterectomy specimens, limiting ascertainment bias. The single-institution study design and the fact that Egypt has one of the highest fertility and CD rates in the world may limit the generalizability of our results[43].

### Conclusions

With the increasing rate of CD worldwide, accurate prenatal diagnosis of PAS is crucial. Systematic documentation of the intraoperative findings and the use of guided sampling for histological examination allowed us to accurately stratify our cases for the depth and extent of abnormal villous attachment and to differentiate between the anatomical changes due to scarring *vs* those associated with PAS. This approach could improve the overall diagnosis of PAS, and is essential to obtain evidence-based epidemiologic data and for the development of new diagnostic protocols and tailored management strategies.

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