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Assessment of ultrasound features of placenta accreta spectrum in women at high risk: association with outcome and interobserver concordance

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KEYWORDS: PAS; placenta increta; placenta previa accreta; surgical outcome; transvaginal ultrasound; ultrasound imaging

CONTRIBUTION

What are the novel findings of this work?
Correlation of prenatal ultrasound assessment suggestive of placenta accreta spectrum (PAS) at birth with histopathologic confirmation is very strong. However, interobserver agreement of preoperative ultrasound assessment with histopathologic confirmation of PAS is only moderate. Morbidity is associated with both histopathologic diagnosis and antenatal assessment indicative of PAS.

What are the clinical implications of this work?
Concordance of ultrasound features and histopathology is not absolute. The most useful signs are placental lacunae and increased subplacental vascularity. Agreement was poor for myometrial thinning, loss of clear zone, bladder wall interruption, placental bulge and bridging vessels.

ABSTRACT

Objectives *To evaluate the prenatal ultrasound features associated with operative complications and to assess the interobserver agreement of prenatal ultrasound assessment with histopathologic confirmation of placenta accreta spectrum (PAS) in a cohort of high-risk patients with detailed intraoperative and histopathologic data.*

Methods *This was a retrospective multicenter cohort study of patients at high risk of PAS referred for specialist perinatal care and management between January 2019 and May 2022. Deidentified ultrasound images were reviewed independently by two experienced operators blinded to clinical details, intraoperative features, outcome and histopathologic findings. The diagnosis of PAS was confirmed by failure of detachment of one or more placental cotyledons from the uterine wall at delivery, and the absence of decidua with distortion of the uteroplacental interface by fibrinoid deposition on histologic examination of the accretic areas obtained by guided sampling of partial myometrial resection or hysterectomy specimens. Patients were categorized as having a low or high likelihood of PAS at birth. Interobserver agreement of prenatal ultrasound assessment with histopathologic confirmation of PAS was assessed using the kappa statistic. Primary outcome was major operative morbidity (blood loss ≥ 2000 mL, unintentional injury to the viscera, admission to intensive care unit or death).*

Results *A total of 102 women at high risk of PAS were referred, of whom 66 had evidence of PAS at birth and 36 did not. When blinded to other clinical details, the examiners agreed on the low or high probability of PAS, according to ultrasound features, in 75/102 cases (73.5%). The kappa statistic was 0.47 (95% CI, 0.28–0.66), showing moderate agreement. Morbidity was twice as common with concordant prenatal diagnosis of PAS* vs *concordant diagnosis of not PAS. Concordant assessment of high probability of PAS was associated with the highest morbidity (66.6%) and a very high (97.6%) likelihood of histopathologic confirmation.*

Conclusions *The probability of histopathologic confirmation is very high with concordant prenatal assessment*

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suggestive of PAS. The interobserver agreement for preoperative assessment with histopathologic confirmation of PAS is only moderate. Morbidity is associated with both histopathologic diagnosis and concordant antenatal assessment of PAS. © 2023 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.

INTRODUCTION

Ultrasound is the primary tool for screening patients at high risk of placenta accreta spectrum (PAS) disorders at birth[1,2], and numerous ultrasound features have been described[3]. A recent Delphi survey reached robust agreement on seven of the 11 classic standardized transabdominal sonographic signs associated with PAS at birth[4]. The prevalence of PAS is increasing, following the worldwide rise in Cesarean delivery (CD) rates over the last two decades[5,6]. The risk of PAS is highest in patients presenting with an anterior low-lying placenta/placenta previa and one or more prior CD[7]. However, not all patients with these risk factors develop PAS.

Prenatal identification of patients at high risk of PAS decreases the risk of maternal complications at delivery, and in particular the risk of hemorrhagic morbidity[8]. The reported diagnostic accuracy of ultrasound for the prenatal detection of PAS is excellent in some studies[3,9]. By contrast, Bowman and coworkers[10,11] reported that the agreement between several observers for the diagnosis of PAS is only moderate and the diagnostic accuracy may not be as good as reported previously.

The formal diagnosis of PAS is based on clinicohistopathologic findings at birth[12]. However, most authors of cohort series on PAS do not provide information on the intraoperative features and the description of histopathologic findings is limited[13]. The aims of this study were first to evaluate the prenatal ultrasound signs associated with operative complications, and second, to assess interobserver agreement of prenatal ultrasound assessment with histopathologic confirmation of PAS in a cohort of high-risk patients for whom detailed intraoperative and histopathologic data were available.

METHODS

We conducted a retrospective multicenter cohort study of patients at high risk of PAS referred for perinatal care and management by a specialist multidisciplinary team at Cairo University Hospital, Cairo, Egypt, University College Hospital, London, UK or St George's Hospital, London, UK between January 2019 and May 2022. All patients presented with a singleton pregnancy between 32–37 weeks of gestation, had a history of one or more prior CD and were diagnosed prenatally with an anterior low-lying placenta/placenta previa. Multiple pregnancy and pregnancy requiring emergency delivery before 32 weeks were excluded. Patients were managed according to their local unit protocols and were counseled regarding surgical management (hysterectomy or one-stage resection and repair), which was dependent on ultrasound-based preoperative surgical planning and feasibility mandated by intraoperative findings with the primary aim of reducing maternal morbidity and mortality. Preoperative interventional radiology was not used in any case.

All patients had detailed preoperative transabdominal and transvaginal sonographic (TVS) examinations of the placenta, uterus and pelvis within 1 week before the planned delivery date. The placenta was recorded as low-lying when the edge was 0.5–2 cm from the internal os of the uterine cervix on TVS. It was defined as placenta previa (marginal or complete) when the placenta was < 0.5 cm from the internal os or completely covering it[14]. Transabdominal ultrasound signs suggestive of PAS were recorded using a standardized reporting proforma protocol[15]. In addition, we used the score for placental lacunae, proposed by Finberg and Williams[16] (0, none; 1+, 1–3; 2+, 4–6; 3+, > 6). In all cases ultrasound and intraoperative images were archived electronically. The diagnosis of PAS was confirmed by the abnormal attachment of one or more placental cotyledons to the uterine wall at delivery and the absence of decidua, with distortion of the uteroplacental interface by fibrinoid deposition on histologic examination of the accreta areas obtained by guided sampling as described previously[17]. Pregnancy and delivery data were collected from hospital records.

Deidentified ultrasound images (and videoclips when available) were reviewed retrospectively and independently by two experienced operators (A.B. and E.J.). Both were blinded to clinical background, surgical findings and histopathologic diagnoses. They were unaware of the proportion of PAS *vs* non-PAS in the study cohort and the images were reviewed in a random sequence. The examiners were required to judge the likelihood of PAS as being low or high, and antenatal assessment was correlated with major operative morbidity. Major morbidity was defined as occurrence of any one of the following: major obstetric hemorrhage, defined as blood loss of ≥ 2000 mL; unintentional injury to the urinary bladder or other pelvic viscera; admission to the intensive care unit; or maternal death. A composite of several types of morbidity constituted the presence of morbidity. An individual may have multiple morbidities, which would be underestimated by a binary definition of presence or absence of morbidity. Therefore, we derived a morbidity count (expressed as median (interquartile range)), in which each type of morbidity was recorded. Interobserver agreement was quantified using the kappa statistic. In a study including the cohort of patients from Cairo University Hospital ($n = 90$)[18], we have previously shown that the features associated consistently with the need for a hysterectomy are: the presence of increased vascularity, lacunae, bridging vessels and feeder vessels. As such, we were particularly interested in the degree of agreement of these four features.

Local research ethics approval was obtained in Cairo, Egypt from the Institutional Scientific and Research Ethical Committee (RSEC 021001). In the UK, the NHS

Health Research Authority deemed the study as health surveillance and so formal review by the research ethics committee was not necessary, and retrospective patient consent was not required as basic clinical data were collected using a standard clinical audit protocol and all data were fully anonymized before being submitted for central analysis.

Statistical analysis was carried out using SPSS version 28.0.1.1 (IBM Corp, Armonk, NY, USA). Data are expressed as mean ± SD or median (interquartile range) for normally and non-normally distributed data, respectively. Unpaired *t*-test or Mann–Whitney *U*-test was used to compare continuous data as appropriate. Proportions are expressed as percentages and the χ^2 test or Fisher's exact test was used for comparisons. $P < 0.05$ was considered statistically significant. Agreement between the two observers was quantified by calculating the kappa statistic. Kappa statistics and percentage agreement are reported according to Landis and Koch[19], and kappa values of < 0.20, 0.21–0.40, 0.41–0.60 and 0.61–0.80 were interpreted as poor, fair, moderate and good, respectively, whereas values between 0.81 and 1.00 were interpreted as excellent agreement and negative values denote disagreement or worse-than-expected agreement.

RESULTS

Demographics and outcome

A total of 102 women at high risk of PAS were referred for specialist perinatal care and management. There were 66 cases of PAS and 36 cases with no evidence of PAS at birth. The maternal demographics and outcomes according to diagnosis of PAS at birth are displayed in Table 1. All women included in the cohort presented with an anterior low-lying placenta/placenta previa and had at least one prior CD (98 of 102 women had undergone two or more prior CDs). The placenta covered the internal os in 75 (73.5%) cases.

The frequency of Cesarean hysterectomy was significantly higher ($P < 0.001$) in the subgroup with confirmed PAS at birth compared to those with no evidence of PAS at delivery (84.8% *vs* 27.8%, respectively). In the former subgroup, hysterectomy was not performed in 10 cases because the accreta area was small and could be removed by partial myometrial resection, leaving sufficient healthy myometrium to reapproximate the hysterotomy edges and repair the lower uterine segment. In the non-PAS subgroup, hysterectomy was performed because of the inability to repair a large anterior wall dehiscence and/or excessive intraoperative bleeding. Data on operative morbidity are presented in Table 1.

Table 1 Comparison of demographic characteristics and outcome of 102 patients at high risk of placenta accreta spectrum (PAS), according to diagnosis of PAS at birth

Characteristic	*PAS (n = 66)*	*No PAS (n = 36)*	P
Maternal age (years)	32.2 ± 4.6	31.4 ± 4.5	0.441
Gravidity	5 (4–6)	4 (3–5)	0.003
Parity	3 (2–4)	2 (2–3)	0.002
Number of prior CD	3 (2–4)	2 (2–3)	0.012
GA at ultrasound (weeks)	36 + 4 (36 + 0 to 37 + 0)	36 + 4 (36 + 0 to 37 + 0)	0.819
Blood loss (mL)	2000 (1500–2850)	1500 (1400–1900)	0.003
Transfusion units received	2 (2–4)	2 (0–3)	0.106
Morbidity	37 (56.1)	9 (25.0)	0.002
Major obstetric hemorrhage*	34 (51.5)	8 (22.2)	< 0.001
Bladder injury	8 (12.1)	0 (0)	0.013‡
ICU admission	10 (15.2)	0 (0)	0.048‡
Morbidity count†	1 (0–1)	0 (0–0.75)	0.002
Cesarean hysterectomy	56 (84.8)	10 (27.8)	< 0.001

Data are given as mean ± SD, median (interquartile range) or *n* (%). *Defined as blood loss ≥ 2000 mL. †Number of morbidities per patient (totalling 60 across all patients). ‡Fisher's exact test. CD, Cesarean delivery; GA, gestational age; ICU, intensive care unit.

Table 2 Concordance of diagnostic agreement and morbidity in 102 patients at high risk of placenta accreta spectrum (PAS)

	Concordant		
Variable	*PAS (n = 42)*	*No PAS (n = 33)*	*Discordant (n = 27)*
HP diagnosis of PAS	41 (97.6)	8 (24.2)	17 (63.0)
Morbidity	28 (66.7)	10 (30.3)	8 (29.6)
Morbidity count*	41†	10	9†
Hysterectomy	37 (88.1)	13 (39.4)	15 (55.6)

Data are given as *n* or *n* (%). *Total morbidities per group. †Multiple morbidities in individual patients. HP, histopathology.

Concordance in ultrasound prediction of PAS at birth

Both examiners agreed on the probability, based on ultrasound features, of PAS at birth (low or high) in 75 cases (73.5%) (Table 2). The assessment was discordant in the remaining 27. The kappa statistic was 0.47, which suggests modest agreement. PAS was diagnosed at birth in 41 of 42 cases classified as high probability of PAS by both examiners. There were 33 cases classified as low probability of PAS, in which eight cases (24.2%) were diagnosed as PAS on histopathology. The remaining 18 cases of PAS at birth were found in the 27 cases with discordant assessment (66.7%). Kappa values were 0.45 (95% CI, 0.26–0.65) and 0.48 (95% CI, 0.34–0.61) for increased vascularity and placental lacunae, respectively (Table 3). The agreement was poor for lower uterine segment thinning, loss of clear zone, bladder wall interruption, bridging vessels and placental bulge.

Concordance in ultrasound prediction of risk of operative morbidity

Of 66 patients with PAS diagnosis confirmed on histopathology, 37 experienced morbidity (56.1%) compared to nine in 36 (25.0%) without evidence of PAS at birth ($\chi^2 = 8.25$; $P = 0.002$) (Table 1). The correlation

Table 3 Interobserver concordance for ultrasound signs used in prenatal evaluation and probability of placenta accreta spectrum (PAS) at birth in 102 patients at high risk of PAS

Variable	*Operator 1* (n/N *(%)*)	*Operator 2* (n/N *(%)*)	*Kappa (95% CI)*
Loss of clear zone			
No	52/102 (51.0)	0/102 (0.0)	0.00‡
Yes	50/102 (49.0)	102/102 (100.0)	
Myometrial thickness < 1 mm*			
No	7/95 (7.4)	34/95 (35.8)	−0.08 (−0.21 to 0.05)
Yes	88/95 (92.6)	61/95 (64.2)	
Bladder wall interruption			
No	94/102 (92.2)	102/102 (100.0)	0.00‡
Yes	8/102 (7.8)	0/102 (0.0)	
Placental bulge			
No	83/102 (81.4)	54/102 (53.0)	0.08 (−0.07 to 0.24)
Yes	19/102 (18.6)	48/102 (47.1)	
Increased subplacental vascularity*			
No	48/99 (48.5)	41/99 (41.4)	0.45 (0.26 to 0.65)
Yes	51/99 (51.5)	58/99 (58.6)	
Lacunae score†			
0	17/102 (16.7)	36/102 (35.3)	0.48 (0.34 to 0.61)
1+	27/102 (26.5)	14/102 (13.7)	
2+	28/102 (27.5)	23/102 (22.5)	
3+	30/102 (29.4)	29/102 (28.4)	
Lacuna feeder vessels*			
No	85/99 (85.9)	61/99 (61.6)	0.18 (0.02 to 0.34)
Yes	14/99 (14.1)	38/99 (38.4)	
Bridging vessels*			
No	29/99 (29.3)	73/99 (73.7)	0.16 (0.02 to 0.29)
Yes	70/99 (70.7)	26/99 (26.3)	
Probability of PAS at birth			
Low	50/102 (49.0)	43/102 (42.2)	0.47 (0.28 to 0.66)
High	52/102 (51.0)	59/102 (57.8)	

*Data not available for all cases. †Analysis using weighted kappa. ‡Unable to calculate 95% CI, as all responses for one observer were the same.

between morbidity and outcome with concordant or discordant ultrasound assessment of diagnosis of PAS at birth indicates proportions of morbidity of 28/42 (66.7%) in concordant evaluation, 8/27 (29.6%) in discordant evaluation and in 10/33 (30.3%) in cases with a concordant evaluation of low probability of PAS at birth (Table 2).

DISCUSSION

Main findings

This study indicates that the concordance of two independent assessors regarding the high probability of PAS being present at birth is moderate when they are blinded to other clinical details. We have shown that the correlation with histopathology is strongest when the two observers agree on there being a high probability of PAS at birth. In this subgroup, the morbidity was high and the individual patient was significantly more likely to have more than one type of morbidity. Placental lacunae and increased subplacental vascularity were the most reproducible ultrasound signs with the least interobserver variability.

Comparison with previous studies

Data on interobserver evaluation of ultrasound signs in the prenatal evaluation of PAS are scarce and have yielded variable results. Bowman *et al.*[11] reported an overall moderate agreement (kappa, 0.47 ± 0.12) between six observers for the diagnosis of PAS, but they did not evaluate individual ultrasound signs. In contrast, Zosmer *et al.*[20] found good-to-excellent interobserver agreement for loss of clear zone and myometrial thinning on grayscale imaging, the presence of lacunar feeder vessels on two-dimensional color Doppler imaging and crossing vessels and lacunae on three-dimensional color Doppler imaging. Although it is uncertain if the observers were blinded to the ultimate diagnosis, there were no cases without PAS and loss of clear zone was seen in every case. Kliewer *et al.*[21] recently reported kappa values of 0.77 for intraplacental vascular cluster and 0.59 for traversing vessel in a cohort of 32 patients at risk of PAS. Most cohort studies do not describe the intraoperative and histopathologic findings at birth[13], and it is therefore difficult to assess the accuracy of the diagnosis of PAS. In the present study, using guided sampling of accreta areas from hysterectomy or partial myometrial resection specimens for microscopic examination to allow accurate diagnosis of PAS at birth, we found moderate interobserver agreement for placental lacunae and increased subplacental vascularity and poor agreement for bridging vessels and feeder vessels on prenatal ultrasound examination.

Clinical implications

There are only limited data on the role of ultrasound imaging in the preoperative evaluation of surgical risk and outcome in patients with a high risk of PAS at birth.

Abnormalities of the uterine contour, including the loss of clear zone, myometrial thinning and a bulge-like appearance on ultrasound, have been reported commonly in the literature as essential signs for the prenatal diagnosis of PAS[2,4,15]. Unlike anomalies of the uteroplacental circulation, ultrasound anomalies of the uterine contour are found with a similar incidence in non-PAS and PAS cases[18]. The lowest kappa values in the present study were found for these anomalies, suggesting they are secondary to a large area of dehiscence of the lower uterine segment rather than to accreta placentation[22]. This also suggests that their use in the prenatal evaluation of PAS may lead to a false-positive diagnosis in the absence of anomalies of the uteroplacental circulation.

Overall surgical morbidity is related to operator experience in the management of complex cases. All three centres in this study are regional referral centers of excellence with multidisciplinary teams with over 10 years of experience and the corresponding outcomes are linked directly to the complexity of cases referred to these centers. The incidence of PAS in cases with placenta previa and previous CD is, respectively, 5.8% and 12.7% in prospective and retrospective series[23]. A recent prospective screening study found an incidence of 28%[24]. In the current study, the incidence of PAS was 64.7% and the cohort included only patients at high risk of PAS at birth, and therefore at risk of complex surgical procedures.

Histopathology has always been considered the gold standard for the confirmation of PAS. However, by definition, histopathology reporting is retrospective and does not assist in preoperative planning in high-risk cases, i.e. those with placenta previa and previous CD. As expected, the highest morbidity was seen with a concordant ultrasound diagnosis of PAS. Two out of three cases were associated with morbidity and the likelihood of morbidity was higher with a concordant ultrasound diagnosis of PAS, and significantly more likely to involve more than one type of morbidity. The likelihood of surgical morbidity was still reasonably high even when the prenatal ultrasound assessment or histopathology did not indicate PAS. This is likely to be related to the risk factors of PAS i.e. anterior low-lying placenta/placenta previa and previous CD with associated uterine wall dehiscence.

Strengths and limitations

This study has several strengths. To our knowledge this is the first study to assess interobserver agreement of ultrasound signs in patients at high risk of PAS at birth for both histopathologic confirmation of PAS and risk of intraoperative complications. Data were collected according to a well-defined protocol for reporting on the classic ultrasound signs associated with PAS and included a detailed description of intraoperative findings. Using guided sampling of the accreta areas for microscopic examination allowed us to differentiate accurately between cases with and without PAS.

The primary limitation of this cohort study lies in its retrospective design. In addition, the observers were blinded to the patient's clinical background. While this approach eliminates bias on ultrasound assessment, it does not reflect clinical reality as one would not disregard background clinical information, such as previous CD, and assess solely on the basis of ultrasound imaging. Cases delivered in an emergency were not included. Emergency cases are not managed by the same team and, in many cases, ultrasound assessment did not take place at one of the three participating centers and it was not possible to obtain the ultrasound images.

Conclusion

The probability of histopathologic confirmation of PAS is very high with concordant prenatal assessment suggestive of PAS. The interoperator agreement for preoperative ultrasound assessment with histopathologic confirmation of PAS is only moderate. Histopathologic diagnosis of PAS is also made in one in four cases with a concordant diagnosis of low probability of PAS. Morbidity is associated with both histopathologic diagnosis (not useful in clinical management as it is a retrospective finding) and antenatal evaluation concordant with PAS. However, the concordance of ultrasound features and histopathology is not absolute. Future prospective studies should use those ultrasound signs with the highest kappa values.

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