Clinical Article

Development of a training program for the ultrasound screening of placenta accreta spectrum disorders

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Synopsis: A training program in detecting the ultrasound signs associated with placenta accreta spectrum using a standardised protocol improves the diagnostic accuracy.

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Abstract

Objective: Ultrasound diagnosis of placenta accreta spectrum (PAS) is not routinely taught during ultrasound training courses. We have prospectively evaluated the impact of a training program using a systematic protocol on ultrasound signs of PAS.

Methods: The intra and inter-observer variability rates and sensitivity, before and after additional training, of two research fellows with a prior basic training in obstetric ultrasound was tested using digitally recorded second-trimester ultrasound images of 52 cases of anterior placenta previa with (n=26) and without PAS (n=26).

Results: The highest level of interobserver degree of agreement for ultrasound signs was found for the absence of placental bulge and/or of focal exophytic mass on grey-scale imaging and the absence of subplacental hypervascularity, bridging vessels and lacunar feeder vessels on CDI. The level of agreement increased from 39% pre-training to 40% after-training and the numbers agreed by both graders as PAS increased from four to 20. There were no cases classified as inconclusive after-training. There was a significant ($P < 0.001$) change in sensitivity for both trainees after training.

Conclusions: Additional training in detecting the ultrasound signs associated with PAS using a standardised protocol improves the diagnostic accuracy of operators with only a basic obstetric ultrasound training.

KEYWORDS: Placenta accreta; placenta increta; placenta percreta; ultrasound; prenatal diagnosis; training.

1 | INTRODUCTION

When undiagnosed antenatally, placenta accreta spectrum (PAS) is often associated with massive obstetric haemorrhage due to attempts by the surgical operator at detaching the placenta from the uterine wall during delivery [1,2]. Prenatal diagnosis has been shown to lead to better maternal outcomes and has thus become essential in improving the management of PAS [3,4]. However, recent large prospective population studies have shown that PAS remains undiagnosed before birth in half [2] to two-third of the cases [5].

The first prenatal ultrasound description of placenta accreta was reported by Tabsh et al [6] in 1982 and in the following 25 years, 1078 cases including 38 case reports and 53 series of PAS diagnosed during pregnancy by expert operators have been reported in the international literature [7]. Placenta previa accreta has become the most common presentation of PAS [8] and the overall performance of ultrasound in diagnosing accreta placentation in patients presenting with low-lying/placenta previa in expert centres is excellent with a sensitivity of 88 to 97% and specificity of 90 to 97% [9].

In most countries around the world, screening for fetal abnormalities with ultrasound is now an integral part of routine antenatal care and many Western countries have specific prenatal ultrasound training courses for healthcare professionals. The majority of routine anomaly scanning around the world is still performed in the second trimester, between 18-22 weeks. Over the last two decades, an increasing number of fetal abnormalities have been detected between 11 and 14 weeks of gestation with detection rates of first-trimester fetal anomalies ranging from 32% in low-risk groups to more than 60% in

high-risk groups [10]. Of the factors examined for their impact on detection rate, the use of a standardized anatomical protocols has been shown to significantly improve the sensitivity of ultrasound examination for the detection of fetal anomalies in all subgroups [11].

Until recently there was no standardised protocol for the ultrasound diagnosis of PAS. Many 2-dimensional (2D) grey-scale and colour Doppler imaging (CDI) signs were reported in the literature with varying descriptions as to their sensitivity and specificity, confusing terminology and in many cases, a lack of confirmation of diagnosis at birth [7,11]. To improve consistency and allow appropriate comparison of different imaging markers, panels of experts have published consensus statements aiming to standardize the descriptions and minimum requirements for an ultrasound scan to diagnose PAS [12]. We have recently evaluated the incidence of each of these ultrasound signs in cases of PAS with detailed clinical and pathologic diagnosis and the proportion of agreement between experts and found that most of these signs are useful in the prenatal diagnosis of PAS [13]. The aim of the present study was to prospectively evaluate the impact of additional training and the use of a standardised examination protocol on the ultrasound diagnostic accuracy of PAS and how this training could be used for the ultrasound screening of women at risk of PAS in the general population.

2 | MATERIALS AND METHODS

Two newly appointed research fellows (LFDB and WA) at the Fetal medicine research institute (FMRI) with only a basic training in routine obstetric ultrasound reviewed the ultrasound images of 52 cases of placenta previa with (n=26) and without PAS (n=26). All prenatal ultrasound records were examined within the

research centre, basic clinical data were collected using a standard clinical audit protocol and all images were anonymised for data analysis This study was approved by the NHS Research Ethics committee (Reference 18/WM/0328).

For each case, the trainees were given access to 15-20 2D grey-scale and CDI digitally recorded images per case obtained between 20 and 28 weeks of gestation by both transabdominal and transvaginal sonography (TVS) using standard ultrasound equipment (GE Voluson® 730, GE Medical System, Zipf, Austria) and a standard protocol [13]. They reviewed the images before and after additional specific training. For the review of ultrasound images, they used ultrasound signs from the standardized descriptions [12] including for grey scale imaging: loss of clear zone, myometrial thinning, the presence of placental lacunae; bladder wall interruption; placental bulge and focal exophytic mass and for CDI: utero-vesical hypervascularity; subplacental hypervascularity; bridging vessels and lacunae feeder vessels. They were instructed to identify at least 2 ultrasound markers to make a diagnosis of PAS. They were blind to the clinical diagnosis at birth and to the examination results of each other.

Six weeks after their first examination, the research fellow independently repeated their examination, following an expert tuition session modelled on the online training modules for the diagnosis of fetal abnormalities from the fetal medicine foundation (www.fetalmedicine.org).

Statistical analysis

Stata/IC version 15.0 (StataCorp LLC, TX, USA) was used to analyse the data. Because the distributions were skewed, continuous data are presented as medians and interquartile ranges (IQR). Because of the uneven distribution of values amongst cells some of the kappa values are unstable as indicated by negative values despite

high agreement and we have used the percentage agreement as previously described [15,16]. A binomial test of significance was conducted to assess whether there was evidence of higher agreement in the third than the second trimester. A Chi-square test was conducted to compare sensitivity pre and post training. A P value <0.05 was considered significant.

3 | RESULTS

The PAS study group included 10 cases of placenta creta (Adherenta), 10 cases of placenta increta and six cases of placenta percreta confirmed clinically at delivery and by subsequent detailed histopathological examination by a perinatal pathologist. All PAS cases were managed by primary peri-partum hysterectomy. In all cases, the placenta was mainly anterior reaching or covering the internal cervical os on transvaginal ultrasound at mid-gestation and confirmed at 32-34 weeks of gestation. The non-accreta study group included 26 cases of anterior placenta previa classified using the same ultrasound criteria. All women in both groups, had an obstetric history of 1 or more prior caesarean deliveries (median 2; IQR 1 to 2) and were all delivered by caesarean sections. All cases in the PAS group had a planned caesarean-hysterectomy. All the ultrasound images reviewed by the trainees were from obtained during the mid-pregnancy (median 21 weeks; IQR 20 to 22) detailed fetal anatomy scan using the same ultrasound equipment (GE Voluson® 730, GE Medical System, Zipf, Austria).

The results of the independent examination by the trainees before and after the additional training are presented in Table 1. The highest level of interobserver degree of agreement for ultrasound signs was found for the absence of placental

bulge and/or of focal exophytic mass on grey-scale imaging and the absence of subplacental hypervascularity, bridging vessels and lacunar feeder vessels on CDI. in the degree of agreement for the presence of myometrial thinning, placental lacunae, utero-vesical and subplacental hypervascularity. After training, both trainees agreed in all cases, that there was placental bulge and/or of focal exophytic mass on grey-scale imaging.

Table 2 displays the overall classification made by the trainees before and after training. The % of agreement increased from 39 pre-training to 40 after-training and the numbers agreed by both graders as PAS increased from four to 20. There were no cases classified as inconclusive after-training as compared to 4 graded inconclusive from grader 1 pre-training and 1 graded inconclusive pre-training from grader 2. Before training trainee 1 had 0 false positives and 18 false negatives cases and trainee 2 had 3 false positives and 21 false negatives cases. After-training, trainee 1 had six false positives and five false negatives cases and trainee 2 had six false positives and seven false negatives cases. For both trainees, there was a statistically significant ($P< 0.001$) change in sensitivity after training (Table 3).

4 | DISCUSSION

Our study is the first to evaluate the impact of a specialist training for the prenatal diagnosis modelled on existing training modules for the diagnosis of fetal anomalies. We found that an additional training in detecting the ultrasound signs associated with PAS using a standardised protocol improves significantly the diagnostic sensitivity of operators with only a basic obstetric ultrasound training.

A recent prospective longitudinal study including women with placenta previa and at least one prior cesarean delivery or uterine surgery showed that using three ultrasound signs improved the detection rate for placenta percreta with a sensitivity of 100% (95% CI 92.6-100) and a specificity of 77.2% (95% CI 69.9-83.4) [17]. This study and the cohort studies included in recent systematic reviews were published by expert teams and these data cannot be applied to the general population of women who are provided with a regular mid-trimester fetal anatomy scan by non-expert ultrasonographers. The data of the present study show that additional training modelled on existing teaching module developed to improve the knowledge of sonographers in the diagnosis of fetal anomalies, are associated with a significant improvement in the diagnostic sensitivity of both trainees (Table 3).

In the present study, we have used the standardized descriptions of the ultrasound markers associated with PAS and the corresponding reporting protocol proposed recently by the European Working Group on Abnormally Invasive Placenta (EW-AIP) and the AIP international expert group [12,13]. Using the same descriptions, we have previously reclassified the ultrasound findings of cases reports and cohort studies on the ultrasound prenatal diagnosis of PAS [7]. We found that in the 72 cases that provided detailed correlations between ultrasound findings and PAS grading a loss of clear zone (62.1%) and the presence of bridging vessels (71.4%) were the most common ultrasound signs found in cases of placenta creta or adherenta whereas a loss of clear zone (84.6%) and subplacental hypervascularity (60%) and placental lacunae (82.4%) and subplacental hypervascularity (54.5%) were the most common ultrasound signs found placenta accreta and placenta percreta, respectively. No ultrasound sign or a combination of ultrasound signs were specific of the depth of accreta placentation. The detection of these signs with

transabdominal ultrasound varies with maternal bladder filling, direct pressure of the ultrasound probes, myometrial contractions and gestational age [11,18]. TVS can circumvent some of these issues and is essential to locate the edge of the placenta in cases of placenta previa accreta but its use is only reported by less than half of authors of expert cohort studies [9]. For each case, we provided the trainees with images obtained with both transabdominal ultrasound and TVS suggesting that both ultrasound techniques should be included in a training program.

The impact of invasive placentation is mainly at the level of the deep uterine circulation and transformation of the radial and arcuate arteries and the development of neo-vascularisation lead to major anatomical changes under the placental bed and in the placental cotyledon above the accreta area [11]. The corresponding signs i.e. loss of clear zone, intraplacental lacunae and lacunar feeder vessels were the most commonly identified sings in this study and in previous studies [7]. We recently found that these signs are associated with highest level of interobserver degree of agreement between experts [14]. In the present study, there was a complete agreement between the trainee for the absence of placental bulge and/or of focal exophytic mass on grey-scale imaging post-training. These signs are almost exclusively seen in the most invasive and extended cases of PAS [7] and when review by expert were only found in 2 cases out of 23 cases during the third trimester examination [14]. By contrast, myometrial thinning is a consequence of prior caesarean scar [11] and not a consequence of accreta placentation. Although it has been commonly reported in observational studies [7] and this sign is associated with a high level of interobserver of agreement between experts in both the second and third trimester [14], the trainees agreed on the absence of myometrial thinning in 32 out of 52 cases before and after training. The findings of the present study suggest

that the development of a protocol for screening PAS during routine mid-trimester scans would require a simplified version of the list of ultrasound signs reported by experts.

In the UK, most routine prenatal ultrasound examinations are performed by ultrasonographers with no medical training and thus less likely to be aware of the risk factors associated with the development of PAS. The risk of both placenta previa and PAS is higher in women with a history of caesarean delivery [8,19-21]. The incidence of placenta previa accreta increases with the numbers of prior caesarean deliveries from 4.1% in women with one prior caesarean to 13.3% in women with $\geq$2 previous caesarean sections [9]. These risks are independent of other maternal characteristics, such as parity, body mass index, tobacco use, and coexisting hypertension or diabetes [8]. Caesarean deliveries are not the only cause of PAS [22,23] but following the exponential rise in rate of caesarean section in many countries around the world, placenta previa accreta has become the most common presenting type of PAS, found in more than 95% of the cases [9]. Thus, ultrasound operators should be made aware that women with a previous history of caesarean deliveries, presenting with a low-lying placenta or placenta praevia in the second trimester of pregnancy have become the largest group of women with the highest risk of PAS.

Our study is limited by the number of trainees involved and the present data need to be evaluated on a larger scale. Strengths of the present study included the use standardized ultrasound signs and reporting protocol for the pre- and post-training diagnostic evaluations. The increase in sensitivity of two research fellows with only a prior basic training in general obstetric ultrasound indicates that like for

fetal structural defects, the prenatal detecting of PAS can be improved using a similar training strategy. The results of well-conducted prospective cohort studies [24,25] have shown that the sensitivity and specificity of grey-scale imaging alone in diagnosing placenta previa accreta are high when performed by experience operators, suggesting that colour-Doppler imaging and three-dimensional ultrasound may not be essential to the screening of accreta placentation. These findings and our data indicate that operators in low-resource countries with access to basic ultrasound equipment only can be trained remotely using on-line training programs to diagnose PAS prenatally and thus improve the management and outcome of this complex obstetric complication.

In conclusion, the vast majority of women at high-risk of PAS will have a routine mid-trimester fetal anatomy scan in a local hospital by ultrasonographers with no or limited experience at examining the placenta. High reproducibility and low interobserver variability of ultrasound imaging of PAS are essential to implement a screening program for women at high risk of PAS. Unlike MRI, ultrasound imaging is operator-dependent and thus the additional training based on ultrasound signs with excellent or good interobserver agreement should improve the diagnostic accuracy of ultrasound in women with PAS.

Author contributions

EJ and NZ designed the study and developed the training protocol. ID coordinated the data collection and supervised the trainees LBDS and WA. CB and EB carried out the statistical analysis. EJ and ID drafted the manuscript. EJ is the guarantor of the study. All authors in the critical discussion and approved the final version of the manuscript for publication.

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Conflict of interest

The authors have no conflicts of interest to declare.

Table 1: Interobserver agreement for the ultrasound signs used in the diagnosis of PAS in the second trimester before and after training.

Ultrasound signs	**Pre-training agreement (%)**	**Post-training agreement (%)**
<u>Grey-scale Parameters</u>		
1.Loss of clear zone	67.3	67.3
2.Myometrial thinning	71.1	86.5
3.Placental lacunae	88.5	65.4
4.Bladder wall interruption	86.5	88.5
5.Placental bulge	94.2	100
6.Focal exophytic mass	94.2	100
<u>CDI Parameters</u>		
7.Utero-vesical HV	63.5	75.0
8.Subplacental HV	71.1	80.8
9.Bridging vessels	86.5	80.8
10.Lacunae feeder vessels	75.0	73.1

CDI= Colour Doppler Imaging; HV= hypervascularity.

Table 2: Overall classification made by the trainees before and after training.

Variable	Placenta previa	PAS	Inconclusive
Pre-training			
Placenta previa	35	4	4
PAS	4	4	0
Inconclusive	1	0	0
Post-training			
Placenta previa	20	5	-
PAS	7	20	-

Table 3: Accuracy for PAS diagnosis before and after training for both trainees.

Variable	Pre-training % (95% CI)	Post-training % (95% CI)
Trainee 1		
Sensitivity (SN)[*]	30.8 (14.3 to 51.8)	80.8 (60.6 to 93.4)
Specificity (SP)	100.0 (86.8 to 100.0)	76.9 (56.4 to 91.0)
Positive Predicted Value (PPV)	100.0 (63.1 to 100.0)	77.8 (57.7 to 91.4)
Negative Predicted Value (NPV)	59.1 (43.2 to73.7)	80.0 (59.3 to 93.2)
Positive Likelihood Ratio (PLR)	-------	3.50 (1.69 to 7.24)
Negative Likelihood Ratio (NLR)	0.69 (0.54 to 0.89)	0.25 (0.11 to 0.57)
Trainee 2		
Sensitivity (SN)[#]	19.2 (6.6 to 39.4)	73.1 (52.2 to 88.4)
Specificity (SP)	88.5 (69.8 to 97.6)	76.9 (56.4 to 91.0)
Positive Predicted Value (PPV)	62.5 (24.5 to 91.5)	76.0 (54.9 to 90.6)
Negative Predicted Value (NPV)	52.3 (36.7 to 67.5)	74.1 (53.7 to 88.9)
Positive Likelihood Ratio (PLR)	1.67 (0.44 to 6.26)	3.17 (1.51 to 6.63)
Negative Likelihood Ratio (NLR)	0.91 (0.72 to 1.15)	0.35 (0.18 to 0.68)

Comparison in SN. [*]Trainee 1 X^2 15.94; df=2; P= 0.00034 and [#]Trainee 2 X^2 14.05; df=2; P= 0.00088

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