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Original article

T2 Dark Bands on Placental MRI as a Potential Predictor of The Severity of Post-Partum Hemorrhage in Placenta Adhesion Disorders

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Abstract
Placenta adhesion disorders (PAD) are increasingly encountered in obstetric practice due to the increase in caesarean section deliveries and placenta previa rate. If a case is confronted unexpectedly, the result is massive blood loss, which cannot be managed optimally unless identified in the antenatal period. This study was conducted to assess the value of placental dark bands in T2 W images in predicting the severity of hemorrhage at delivery. Retrospective analysis of clinical data and magnetic resonance imaging (MRI) for 55 women who underwent pelvic MRI scans between February 2010 and October 2013 due to risk factors for placental adhesion. The frequency of delivery complications was higher in cases with T2 dark bands in comparison with that with no bands {blood loss (ml) median (25,75) 1500(500-3500) vs 550(400-1000), P=0.006; blood transfusion(ml) median (25,75) 1500(0-4200 vs 0(0,0), P=0.003; length of stay in hospital (days) median (25,75) 3(2-6) vs 2.5(2-3), P=0.02}. The median blood loss was higher in women with T2 multiple dark bands (3000 ml) compared to those with single dark bands (550 ml). Placenta previa (PP) was a cofactor for bleeding (PP present associated with blood loss mean ± SEM 2877.3± 525.6 vs 1441.9± 353.7 when PP absent, the difference in means [95%CI] 1435.4[-2692.5- -178.3] P=0.026). However, multiple bands are an independent factor for maternal bleeding as the amount of blood loss increases with the number of bands, irrespective of the presence or absence of PP. PAD is associated with severe blood loss and blood transfusion. T2 Dark bands have the potential ability to predict the severity of hemorrhage at delivery.
Keywords. MRI, Pad, Post-Partum Hemorrhage.

Introduction

Placenta adhesion disorders (PAD), also known as placenta accreta, invasive placenta, or morbidly adherent placenta, occur due to abnormalities that exist in the decidua basalis, leading the chorionic microvilli to invade the myometrium. According to the depth of invasion, PAD is divided into placenta accreta vera (the microvilli reach the myometrium without invasion), placenta increta (the microvilli partially invade the myometrium), and placenta percreta (the microvilli penetrate the myometrium and reach the serosal layer) [1]. In published evidence, the estimated incidence of PAD is reported as 1.7-3.4 per 10,000 deliveries [2, 3]. In a recent systematic review and meta-analysis, the prevalence of the condition was 9.3%, which increased when the dominant study [4] was excluded to 19.3%, which is thought to be representative of the realistic estimation of PAD in women who have risk factors in the third trimester [5].

Recognized risk factors for the condition include previous caesarean delivery (OR 14.41, 95%CI 5.63-36.85), placenta previa (PP) (OR 65.02, 95%CI 16.58-254.96), advanced maternal age (OR 1.15, 95%CI 1.06-1.24 for every one year, increase in age) and multiparity (2 or more OR 11.11, 95%CI 5.63-21.90) [2, 6]. In women with previous C-section and PP, the incidence was estimated to be 1 in every 20 women [2]. This emphasizes the significance of having a high index of suspicion for PAD when risk factors exist. PAD is associated with a major postpartum hemorrhage (PPH) at delivery, especially if the condition has not been previously recognized and an attempt is made to forcibly detach the placenta [7]. Other complications include hysterectomy, cystectomy, ureteric injury, fistula formation, re-operation, intensive care unit admission, infection, and maternal death [8,9].

Maternal complications associated with PAD may be significantly reduced if antenatal diagnosis is available to guide the delivery plan, time, and location. Accurate antepartum diagnosis enables the woman to be delivered in a unit staffed by a multidisciplinary team experienced in the management of PAD. The US has been reported to be able to detect or exclude PAD [5, 10, 11]. Color Doppler has been found to improve the US performance [5]. Nevertheless, the US ability is limited in certain cases, for example, when the placenta is posteriorly located or when maternal body mass index (BMI) is high [12, 13]. In these cases, MRI is a complementary diagnostic imaging technique. Recent work shows that the combination of both imaging techniques can improve the diagnostic accuracy of PAD [14]. Using both modalities also provides information for patient counseling and facilitates management decisions, especially if invasion of other organs has occurred, often the bladder and/or bowel. Accurate antepartum identification of the extent of other organ involvement and the position of the invasion are considered important factors affecting safe delivery and outcome [8]. Development of diagnostic techniques that have the capability to predict complications and assessment of their value and reliability should have priority in obstetric practice research. MRI has been

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used as a complementary diagnostic test for PAD. Nevertheless, its value as part of the management plan still needs to be fully investigated. Therefore, this study was conducted to assess both the correlation of T2 dark bands with the severity of PPH in PAD cases and the impact of antenatal diagnosis of PAD on peripartum management.

MRI is a complementary diagnostic imaging technique. Recent work shows that the combination of both imaging techniques can improve the diagnostic accuracy of PAD [14]. Using both modalities also provide information for patient counseling and facilitates management decisions, especially if invasion of other organs has occurred, often the bladder and/or bowel. Accurate antepartum identification of the extent of other organ involvement and the position of the invasion are considered important factors affecting safe delivery and outcome [8]. Development of diagnostic techniques that have the capability to predict complications and assessment of their value and reliability should have priority in obstetric practice research. MRI has been used as a complementary diagnostic test of the PAD. Nevertheless, its value as part in the management plan still needs to be fully investigated. Therefore, this study was conducted to assess both; the correlation of T2 dark bands with the severity of PPH in PAD cases and the impact of antenatal diagnosis of PAD on peripartum management.

Methodology

Study and population

This was a retrospective analysis of the clinical data in one center and registered as a service evaluation at the hospital concerned. Ethical approval was not required. The records of 57 women who underwent pelvic MRI scans between February 2010 and October 2013 were reviewed. The MRI had been requested due to ultrasound features suggestive of abnormal placentation, an ambiguous US finding, or women at high risk of PAD. Two of the 57 cases were excluded because of unknown pregnancy outcome, leaving 55 cases for statistical analysis. The final diagnosis was confirmed by pathological and/ or surgical reports. The following complementary information was extracted from the case notes: demographic risk factors for PAD (maternal age, parity, previous caesarean section, placenta previa in current pregnancy), blood loss at delivery, volume of blood transfused, and duration of postpartum hospital stay.

US examination

The US was performed in the Feto-maternal medicine unit. A transabdominal approach was used for ultrasound (US) evaluation in all cases (Trans-abdominal US transducers 4-9MHz or 5-9MHz). US criteria used to detect invasion included prominent lacunae, abnormal colour doppler, loss of retroplacental clear space, and anomalies in the bladder myometrium interface.

MRI protocol

MR images were obtained by using a 1.5 Tesla MRI scanner (Seimes Avanto, Erlangen, Germany) using T1 W (sagittal) (TR/TE 700/32 ms, 180^{o} flip angle, field of view 350mm and 256x208 matrix, slice thickness 4mm); T2 W SSFSE (TR/TE 100/92 ms, 140^{o} flip angle, field of view 350mm and 512x512 matrix, slice thickness 5mm) (axial, coronal and sagittal) and Balanced GE sequences (TR/TE 6/2 ms, 61^{o} flip angle, field of view 350mm and 384x252 matrix, slice thickness 5mm) (axial and sagittal). Women entered the machine lying in their most comfortable position and feet first, to reduce claustrophobia. Body coils were used to acquire the images, and the entire uterus was covered in 3 orthogonal imaging planes. MR readers were not blind to US findings. The MR examination took between 20-30 minutes in all cases. No intravenous gadolinium was used.

Image analysis

Analysis of the images was achieved using the clinical picture archiving and communication system (PACS) and MRI workstation. In order to assess the diagnostic ability of each MRI criterion, re-reading of the MRI sequences was undertaken by an experienced radiologist. The MRI criteria selected were dark bands on T2 and their characteristics on balanced gradient echo sequences (BGE), uterine bulging, placental homogeneity, myometrial thickness, focal disruption of the myometrium, adjacent organ involvement, uterine wall thickness, loss of utero-placental interface, tenting of the bladder, and placental protrusion into the internal os. The MRI criteria used to diagnose PAD resulted in three groups of women. One group had entirely normal appearances of their placenta, one group had features typical of PAD, and the remaining group had one feature of invasion or a few features in a very localized area, but the remainder of the placenta was normal. These were evaluated separately as they were not typical for PAD. The pregnancy complications were compared accordingly.

Statistical analysis

SPSS for Windows (version 21) and Excel were used in this study for statistical analysis. Based on the distribution of data, parametric or non-parametric tests were used to study the differences between and within the studied groups. Continuous data are summarized by the median (25th/75th centiles); categorical data by percentages. Continuous data is compared by the Mann-Whitney U-test, independent samples

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Kruskal-Wallis Test, or Student t Test; categorical data by the Chi-squared test. Missing data is documented but not otherwise considered. Graphical presentations are by clustered bar charts, dot plots, and mean plots. A P value of less than 0.05 was considered to be significant.

Results

Demographic characteristics of the study population

(Table 1) shows the differences between the PAD (invaded) group and the non-invaded group according to the final diagnosis, which is based on the histopathology and/or the surgical findings. All the tested parameters except one were not significantly different between groups. Gestational age at delivery was statistically lower in the invaded group with a mean ± SD of 36±2.16; the mean difference was 1.87 (P=0.007). Risk factors, including maternal age, parity, and history of previous C-section, did not show significant differences between groups. PP had a non-significant borderline difference between the invaded and non-invaded groups.

Table 1. Demographic characteristics of the study population.

Study Population Characteristics		Invaded	Not Invaded	P Value
Maternal Age	Mean±sd	32.3±5.42	32.8±5.76	>0.05[a]
Gestational Age At MRI	Median (25,75) Percentiles	33(30,35)	32(29,33)	>0.05[b]
Gestational Age At Delivery	Mean±sd	36±2.16	37.87±1.79	0.007[a]
Parity	0-1	3	22	0.200[c]
	2 Or More	8	22	
Pp (%)	Yes	54.5	25	0.058[c]
	No	45.5	75	
Previous Caesarean Section (%)	1 C-section	54.5	70.5	0.300[c]
	2 Or More	45.5	29.5	

[a]*Student t Test; SD standard deviation,* [b]*Independent samples Mann-Whitney, U Test,* [c]*Pearson Chi-square, PP placenta praevia.*

Table 2. Summarizes the average of blood loss in different categories of dark bands.

Categories Of Dark Bands	Mean ±SEM	Compare Different Groups		Difference In Means	95%ci	P Value (Sidak Adjustment for Multiple Comparisons)
None	1155.38± 390	None	Single	638.54	-2377.7- 1100.7	0.7
Single	1793.9 ±639.9	None	Multiple	2374	-4073.6- - 674.46	0.003
Multiple	3529.4± 561.9	Single	Multiple	1735.5	-384.9-3855.9	0.14

Association of MRI criteria and delivery complications

The group with PAD had higher blood loss; median (25,75) 4000(2500,4500) vs 550(400,875) P<0.001, blood transfusion; median (25,75) 7000(3450, 12000) P<0.001) and days in hospital; median (25,75) 10(5,12) vs 3(2,3) P<0.001) than normal cases according to the final diagnosis. The ten cases of PAD that were detected antenatally had intervention radiology techniques used in planned caesarean deliveries. Furthermore, the affected parents received comprehensive counseling regarding the complications of PAD.

The frequency of delivery complications was higher in cases with T2 dark bands than those with placenta without T2 dark bands on the MRI images; blood loss (ml), median (25,75) 1500(500-3500) vs 550(400-1000), P=0.006; blood transfusion (ml), median (25,75) 1500(0-4200 vs 0(0,0), P=0.003; length of stay in hospital (days), median (25,75) 3(2,6) vs 2.5(2,3), P=0.02}. In cases where the dark bands on T2 were hypointense on the BGE images (abnormal vascularity) had significantly higher delivery complications than cases did not had these criteria; blood loss (ml) median (25,75) 1500(500,4000) vs 600(400,1050), P=0.015; blood transfusion(ml) median (25,75) 1500(0,5700 vs 0(0,0), P=0.007; length of stay in hospital (days); median (25,75) 3(2.5,8.5) vs 2(2,3), P=0.02 (Figure 1).

Whilst (Table 2) shows that the difference in means of blood loss 1735.5ml between patients with single dark band (12) on T2 MRI and those with multiple dark bands (13) on T2 W is not statistically significant, the median blood loss was higher in women with multiple T2 dark bands (3000 ml) compared to those with single T2 dark bands (550 ml), (Table 3, Figure 2). On the other hand, (Figure 3A) indicates that cases with multiple bands are more likely to be invaded. PP was a cofactor for bleeding (PP) present (17) associated with blood loss mean ± SEM 2877.3 525.6 vs 1441.9±353.7 when PP absent (38) difference in means (95%CI) 1435.4 (-2692.5- -178.3); P=0.026. However, multiple bands are an independent factor for maternal bleeding as the amount of blood loss increases with the number of bands, irrespective of the presence or absence of

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PP (Table 4, Figure 3C). The nonparametric correlation coefficient also showed that the number of dark bands correlates significantly with the amount of blood loss and blood transfusions in this cohort, Spearman's correlation r=0.47 and r=0.53, respectively, (both significant at P=0.001).

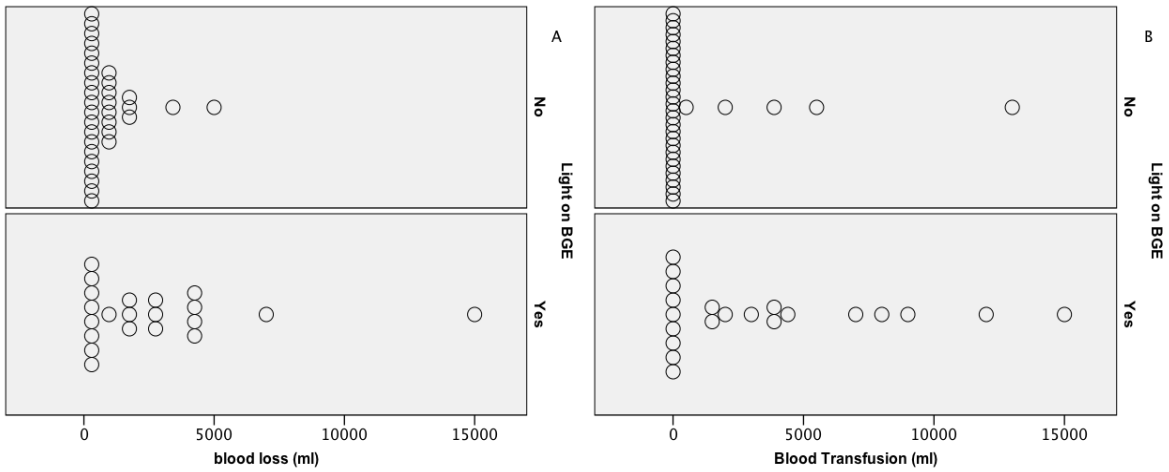

Figure 1. Shows the difference in blood loss (A) and blood transfusion (B) with the existence of the T2 dark bands that were light on the BGE.

Table 3. shows the difference in pregnancy complications in the different groups according to the number of T2 dark bands.

Complication	Number of dark bands on T2			P-value
	None	Single	Multiple	
Blood loss (ml)	550(400,1000)	550(462,750)	3000(1500,4250)	0.001
Blood transfusion (ml)	0(0,0)	0(0,0)	3750(1500,8000)	0.002
Length of stay in hospital (days)	2.5(2,3)	3(2,3)	6(3,12)	0.02

**Independent samples Kruskal-Wallis Test; Results presented in Median (25,75) percentile*

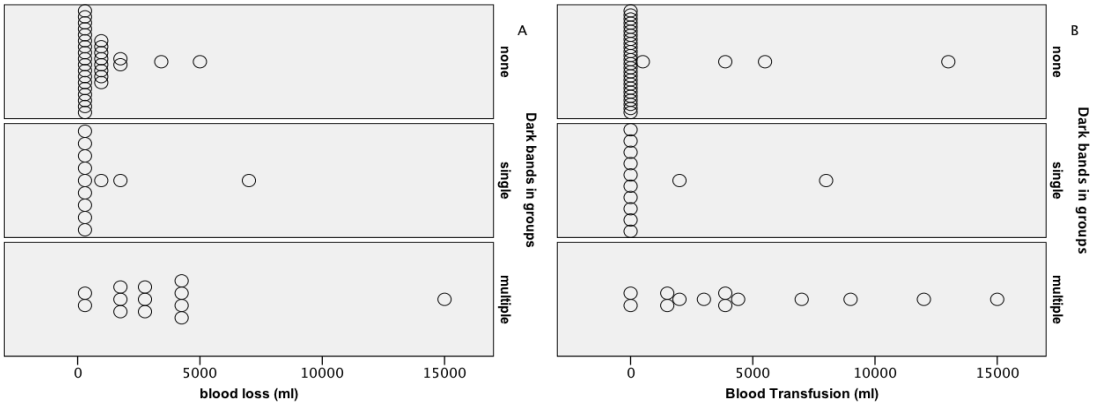

Figure 2. Shows the difference in blood loss (A) and blood transfusion (B) according to the presence of either single or multiple or the absence of T2 dark bands.

Table 4. Blood loss associated with dark bands in the presence and absence of placenta previa.

Placenta previa	Dark bands in groups	Mean± SEM	95%CI	P value (Sidak adjustment for Multiple comparisons)
Absent	None	437.7±414.5	-394.5-1269.9	0.005
	Single	1076.2±586.6	-101.4-2253	
	Multiple	2811.7±654.8	1496.1-4126.3	
Present	None	1873.1±573.3	722.1-3024.0	
	Single	2511.6±819.1	867.3-4155.9	
	Multiple	4247.1±631.4	2979.6-5514.7	

SEM standard error of means, CI confidence interval.

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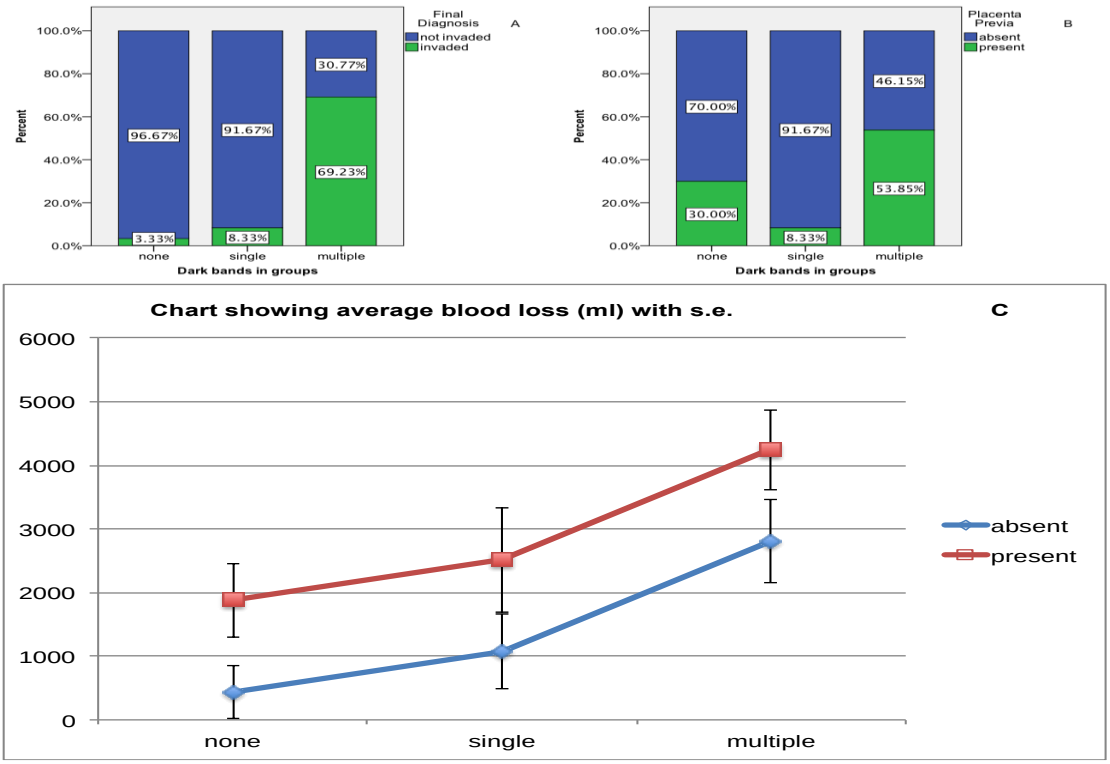

Figure 3. Demonstrates that T2 multiple dark bands are more in the PAD cases (A) than they are in the normal cases, however, only 53 % of cases with multiple bands have PP (B) and the means of blood loss is significantly different between cases no bands, single and multiple bands (C) even when adjusted for PP (present or absent). s.e. standard error.

According to the MRI classification of cases the atypical group (8) at delivery had higher median blood loss 1350(525,2900), blood transfusion 750(0,3500) and longer hospital stay 3(3,3.75) in comparison to normal (37) cases 500(400,700); 0(0,0); 2(2,3), but less than that of the PAD 10 cases 3000(2000,4500); 4400(3000,12000); 10(5,12) respectively (P<0.001) (Figure 4).

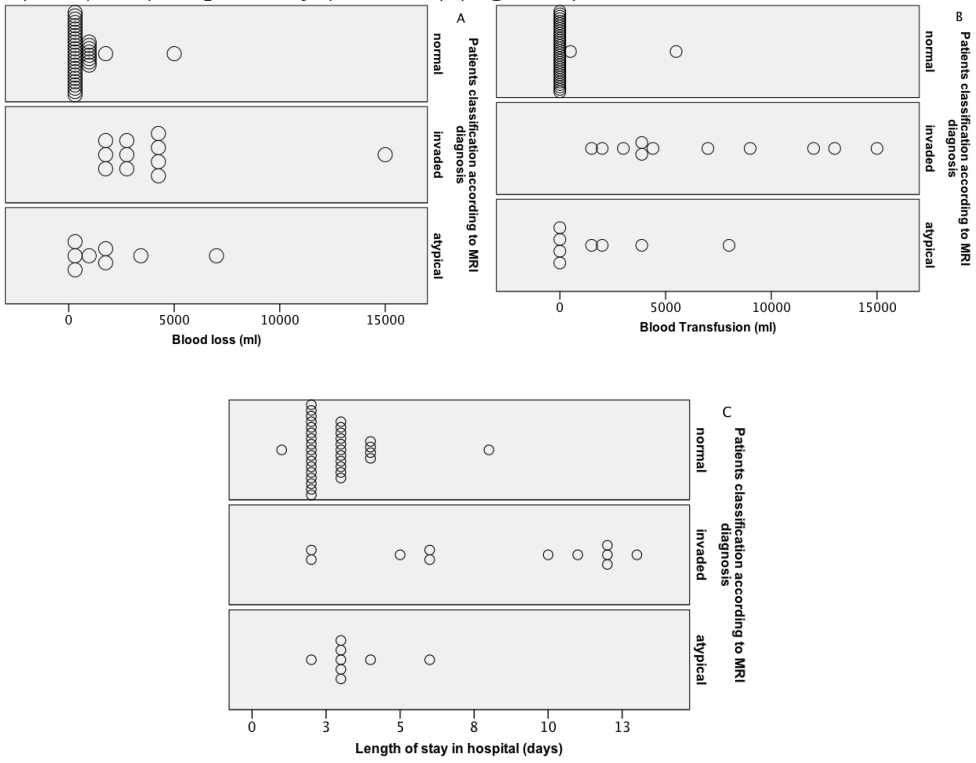

Figure 4. The three groups of patients based on MRI diagnosis. The graphs show the difference in blood loss (A), the difference in blood transfusion (B) the difference in the length of stay in hospital (C) in the three groups.

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Discussion

PAD is associated with severe complications at delivery. In the current study, we found that the amount of blood lost at delivery escalates with the number of dark bands on T2 W MRI images. Dark bands on T2 W images correlate with the frequency of blood loss irrespective of the presence or absence of PP. Patients with atypical features on MRI had increased blood loss. Placental adhesion disorder is a relatively rare complication of pregnancy, but it is increasing in frequency. It is associated with life-threatening complications resulting in substantial maternal morbidity and mortality. Risk factor assessment is crucial to prompt early antenatal investigation. Recognized risk factors include previous caesarean section and placenta praevia in the current pregnancy. The lower uterine segment normally has a small amount of decidua tissue, which may explain the significant association between low-lying placentas and PAD [15]. In a recent prospective large cohort that included 205 cases of PAD, a previous caesarean section is reported to increase the risk of invasion significantly from seven-fold when only one prior C/S exists to 56-fold in patients with 3 or more previous caesarean deliveries [3]. Probably because of our small cohort, this was not the case in the current study. All the examined risk factors did not significantly increase the risk of invasion in our cohort. PP has a non-significant borderline difference between the invaded and non-invaded groups. Using a larger sample size may increase the difference between groups and improve its significance in increasing the risk of invasion.

Lim et al. found a significant correlation between the volume of T2 dark bands and the depth of invasion in PAD cases (accreta, increta, percreta ($P<0.001$) [16]. Derman et al. found that all PAD cases had abnormal thick intraplacental bands on the T2 and the BGE images, and that the most bizarre intraplacental bands were present in the percreta cases [14]. Although these two studies included a small sample size, the findings are of high clinical significance. Interestingly, when we studied the relationship between pregnancy complications and T2 dark bands, there were significant associations between the existence of T2 dark bands and dark bands that become white in BGE and the amount of blood lost, blood transfusion, and length of stay in hospital. Furthermore, we observed that there is a dose-response relationship between the number of dark thick bands and blood loss. These clinical findings correlate with the radiological findings of Lim et al (2009) and Derman et al (2011) [14,16]. Therefore, T2 multiple thick dark bands might have the potential to be considered as a reliable predictor of the severity of PPH in cases with PAD. Although (Table 2) shows that the difference in means of blood loss, 1735.5ml, between patients with a single T2 dark band and those with multiple T2 dark bands is not statistically significant. From a clinical point of view, losing more than 1000ml of blood in the first 24 hours of delivery is considered a major PPH. We found that PP contributed to the reported complications; however, multiple dark bands were an independent cause for the amount of blood lost and transfused. This is an important clinical finding indicating its potential to be a useful predictor of the severity of PPH.

A recent study compared vascular architecture at the placenta-maternal interface of normal patients with that of those with placenta increta. They found that the size and spatial organization of the vascular architecture in the subplacental myometrium in cases with increta is different from that in normal pregnancy being larger and sparser. This might explain the life-threatening hemorrhage when placental separation is established after fetal delivery [17]. Wright et al. (2011) examined the predictors of severe PPH in a retrospective review that included 77 patients who experienced hysterectomy at delivery for pathologically confirmed PAD [18]. None of the examined factors, which included: maternal age, gravidity, parity, number of previous C-sections, depth of placental invasion, and history of antenatal or blood transfusion, associated significantly with massive PPH [18].

In the current study, the maternal blood loss in the PAD group that was diagnosed antenatally (mean 4400ml; range 1500-15000ml) was similar to that reported by Tikkanen et al (2011), and was significantly ($p=0.012$) lower than that of the false negative group in their institution (7800ml; range 2500-17000ml) [19]. Wong et al. also reported less blood loss in the antenatally diagnosed PAD group than in the intra-partum diagnosed cases (average 1400ml vs 3600ml, $P=0.003$) [20]. In addition, Fitzpatrick et al. and Pilloni et al. also found that antenatal diagnosis of PAD was associated with less blood loss (median 2750ml vs 6100ml; $P=0.008$ and 1300ml vs 3000ml, $P<0.048$) [21, 22], respectively. In our institution, the only case that was diagnosed intra-partum was the only case that did not have prophylactic interventional radiology used during the surgery, and had 7000ml blood loss and 8000ml blood transfused. Although this case was accreta, where the maternal hemorrhage is expected to be lower than that associated with increata and percreta, and hysterectomy can be avoided, it was the only case that underwent urgent hysterectomy after an unplanned vaginal delivery.

All cases suspected of having invasion on antenatal evaluation, either by US or MRI or both, had a blood transfusion. This data is in accordance with that reported by McLean et al (2011) [23]. (Figure 4) shows blood loss, blood transfusion, and the length of stay in hospital in the invaded and non-invaded and atypical groups according to the MRI classification in the re-evaluation of the images. We observed the third group that includes the cases with abnormal features on MRI scan (Figure 5), but not typical for invasion and unconfirmed clinically. There were significant differences in the median between the three groups in all the tested parameters (Table 4). The surgical report in the majority of them stated that the placenta was fragmented and was delivered in pieces, and they required significant cord traction or manual removal,

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which might suggest undiagnosed accreta. In our study, a direct statistical comparison between the maternal outcome of patients with antenatal and those with intra-partum diagnosis of PAD is difficult because we had only one case with intra-partum diagnosis. However, antenatal diagnosis is associated with better maternal outcomes as it tailors the management.

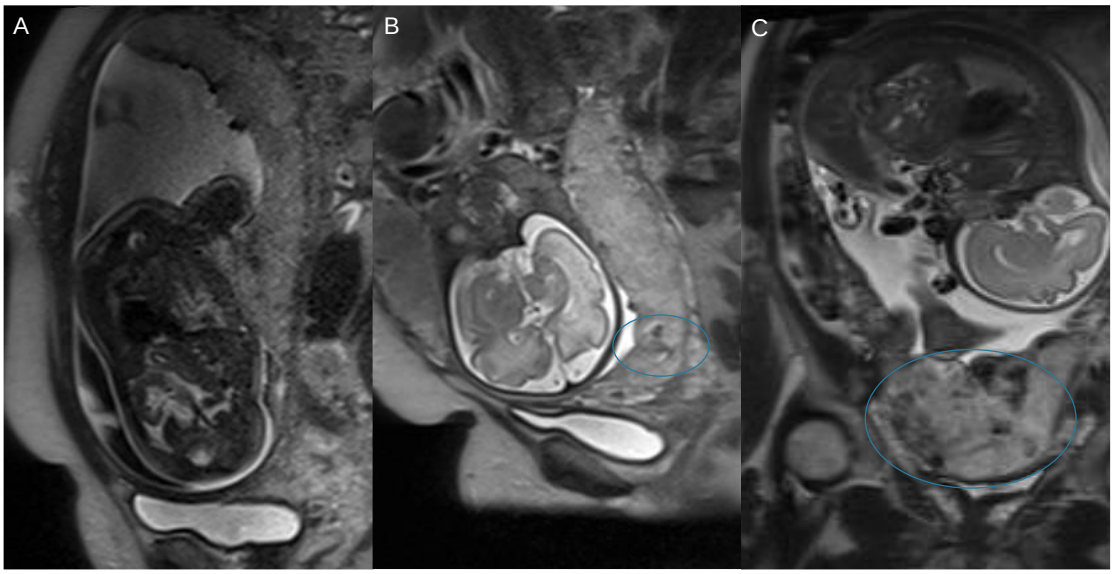

Figure 5. MRI images of normal (A) homogenous placenta, atypical placenta (B) with a single dark band, and the rest of the placenta normal and invaded placenta (C) with multiple dark bands and marked heterogeneity.

Management choices for PAD vary from conservative approaches to radical management, and the decision depends on numerous factors, including early diagnosis, level of invasion, available expertise, and patient preference [24]. Therefore, patient counseling is crucial in the antenatal period. These patients should have their delivery planned in a center where the required surgical expertise is available as part of a multidisciplinary team. Planned caesarean hysterectomy with no placental detachment is considered the optimal management approach [25, 26]. It has been reported that this is associated with reduced blood loss, transfusion, and postoperative complications in comparison to other management approaches [20, 25]. This would explain the difference in the average amount of blood loss between our antenatally diagnosed group and Wong's antenatally diagnosed group of PAD, who had elective placental separation in only 2 cases. Pan et al also reported a significant difference in the average of blood lost between attempted placental removal hysterectomy (6750ml) and non-attempted placental removal hysterectomy (2062.5ml) ($P<0.05$), which was facilitated by antenatal diagnosis [27], whereas placental separation has been tried in all our PAD cases.

In the current study, all PAD cases had hysterectomy except one, in which MRI overestimated the depth of invasion of accreta as percreta; however, in surgery, it was possible to manually remove the placenta, and the patient lost 2000 ml of blood, and the same amount of blood was transfused into the patient. Recent data from China emphasized that the obstetric hysterectomy rate, as indicated by PAD, was 20% in the period 2004-2010 and increased to 77.8% from 2011 through 2014, whereas the rate of obstetric hysterectomy indicated by uterine atony in the same two periods reduced from 50% to 11% [27]. Hysterectomy is a massive complication of PAD, especially in primigravida. The associated fetal and maternal mortality rates with PAD have been forecasted to reach 9-19% and 6-7% respectively, [28]. However, a systematic review, which assessed uncontrolled postpartum bleeding that led to emergency postpartum hysterectomy, included only studies conducted in developed countries, and reported the maternal morbidity and mortality rate as 56% and 2.6% [29]. Accurate antenatal diagnosis and planned delivery would save life and fertility, which is paramount for the future quality of life of affected women.

Our study was a retrospective observational analytical cohort, and the design has some inherent limitations that cannot be avoided. Incomplete data was the major issue we encountered. Therefore, there is a risk of bias because we had to rely on incomplete information. However, the missed data exists in both subgroups; therefore, the risk is balanced all over the study sample. However, the current study is the first to correlate radiological findings from MRI to clinical results and report the potential value of T2 dark bands in the prediction of the severity of PPH.

Conclusion

Antenatal diagnosis of PAD allows multidisciplinary team management of the delivery in a controlled environment, optimizing maternal and neonatal outcomes. Multiple thick dark bands on T2 sequences

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appear to be useful predictors of the severity of PPH. In addition, the atypical group of patients who have neither PAD nor normal placentation requires additional support at caesarean section delivery because they may represent the accreta form. These have few or localized features characteristic of PAD on the MR images. A large prospective multicenter study is required to confirm the findings reported here and provide information for national guidelines for the diagnosis and management of PAD.

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Conflicts of Interest
The authors declare no conflicts of interest.

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