ORIGINAL ARTICLE

EXPLORING THE "PANNUS SIGN ": AN ULTRASONOGRAPHY FINDING FOR DETECTING PLACENTA ACCRETA SPECTRUM AND ITS ASSOCIATION WITH ADVERSE OUTCOMES: A PROSPECTIVE ANALYSIS AT AGA KHAN HOSPITAL, KARACHI

Asra Ahmad[1], Zainab Hussain[2], Faryal Bashir[3]

Authors' Affiliation
[1,2]Department of Radiology, Aga Khan University, Karachi
[3]Department of Radiology, Hayatabad Medical Complex, Peshawar

Corresponding Author
Zainab Hussain
Assistant Professor, Department of Radiology, Aga Khan University, Karachi
Email: zainab.hussain@aku.edu

ABSTRACT

Objective: To evaluate the utility of the sonographic "pannus sign" as an objective marker for identifying PAS in patients, its agreement with histopathology findings, and its association with adverse outcomes.

Material & Methods: A 39-months prospective chart review was conducted on patients diagnosed with PAS through ultrasound between March 2020 and June 2023. Demographic, clinical, and imaging data were extracted for analysis. A single researcher recorded the presence or absence of placental pannus on grayscale and color Doppler ultrasound images. The diagnosis of PAS was confirmed through post-cesarean biopsy reports. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using the chi-square test.

Results: The maternal mean age was 32.37±4.31 years, with 64.71% having a cesarean history. The placenta previa was present in 86.30% of the patients. Pannus sign (PS) was positive in 69.60% of the patients, and a diagnosis of a PAS was made in 91.20% via biopsy. PS had a sensitivity of 69.89%, a specificity of 33.33%, a PPV of 91.55%, NPV of 9.68%, and a diagnostic accuracy of 66.67%. Moreover, the relationship between PS and two common surgical procedures, hysterectomy (p=0.534) and bladder repair (p=0.487), revealed no significant link between the two.

Conclusion: The pannus sign has moderate sensitivity and specificity but a higher risk of false positives. A positive placental pannus on ultrasound was not associated with hysterectomy or the need for urinary tract repair.

Key Words: Histopathology, Pannus sign, Placenta, Ultrasonography.

This article may be cited as: Ahmad A, Hussain Z, Bashir F. Exploring the "pannus sign": an ultrasonography finding for detecting placenta accreta spectrum and its association with adverse outcomes: a prospective analysis at Aga Khan Hospital, Karachi. Ann Allied Health Sci. 2024;10(1):16-22.

INTRODUCTION

Placenta accreta spectrum (PAS) is a complex and prevalent obstetric complication caused by pathological placenta adhesion resulting from aberrant trophoblast invasion into the myometrium, which causes tissue extrusion, fibrinoid deposition, and extensive neovascularity.[1-3] The placenta's failure to detach naturally after birth can cause severe obstetric hemorrhage, which can be fatal and typically necessitates surgery.[1, 4, 5]

PAS refers to three basic subtypes: placenta accreta, increta, and percreta. Placenta accreta is a less severe disease in which placental villi attach to the myometrium without invasion. Placenta increta is an invasion of the myometrium, whereas placenta percreta is the most severe and life-threatening type, affecting the uterine serosa or adjacent structures.[2, 3, 6]

Pregnant women are likely to experience PAS due to a number of known causes. The main suspected cause of PAS disease is damage to the endometrial-myometrial interface which appears to precede development of PAS.[7] Placenta previa is a substantial independent risk factor, but a prior cesarean section is a common risk factor. [4, 8] PAS is linked to higher rates of death and morbidity in pregnant women, making it a key reason for hysterectomy. [1, 2, 5, 6]

Early detection of severe instances is crucial for effective planning and minimizing associated issues. Ultrasonography is commonly utilized in resource-limited nations to screen for numerous illnesses, including PAS, and is the most efficient diagnostic procedure worldwide. [8-10] Chalubinski et al.'s study on placental invasion prediction using prenatal ultrasound revealed sensitivity, specificity, PPV and NPV of 91.4%, 95.9%, 80.0%, and 98.4%, correspondingly.[8] Similarly, Lerner et al.'s study revealed that ultrasonography has 100% sensitivity and 94% specificity, with 83% and 100% predictive values for positive and negative outcomes.[10] In a recent review, an examination of its precision reveals sensitivity levels ranges from 77% to 93% and specificity ranging from 71% to 97%.[9]

Objective markers for severe forms of PAS, are crucial for antenatal detection.[11] A relatively recent observation in cases of PAS involves the occurrence of the placenta extending over the cervical os, exhibiting a resemblance to an abdominal pannus, which can be measured using ultrasound and this placental pannus has not been extensively evaluated locally for detection of PAS on ultrasound. This study explores the potential of this novel marker for identifying PAS on ultrasound, using biopsy results as the gold standard. The predictive ability of this newly proposed imaging sign should be tested in our population to determine if this imaging criterion, alone or in combination, can lead to a more reliable diagnosis.

MATERIAL AND METHODS

A prospective chart review was conducted over a period of 39 months from March 2020 to June 2023 at the Department of Radiology, Aga Khan University Hospital, Karachi, Pakistan. A consecutive recruitment of 102 patients diagnosed with PAS on ultrasound was finalized for analysis. The research included an analysis of sonographic measurements, demographic characteristics, clinical outcomes, and risk factors associated with placental invasion. Identified risk factors comprised the presence of complete or marginal placenta previa, APH, a history of uterine surgeries (including Cesarean section, dilatation and curettage, and myomectomy), advanced maternal age, and conception through in-vitro fertilization treatment. Primigravida women with concomitant illnesses and concurrent uterine and placental abnormalities were excluded from the study. A single radiologist precisely assessed grayscale images to identify placental pannus, utilizing commercially accessible real-time equipment equipped with standard 3.75-MHz sector transducers via transabdominal scanning. Comprehensive evaluation of placental invasion was conducted through two-dimensional grayscale, color, and power Doppler ultrasound imaging, with specific emphasis on scrutinizing the placenta and the retroplacental myometrial zone.

The pannus (PS) was recorded as positive when there was a placental bulge below the internal os line, with a positive PS indicating PAS. Diagnosis was confirmed by a post-cesarean histopathology report performed by an experienced pathologist. Ethical approval was obtained from the AKU Ethical Review Committee.

SPSS version 21® was used for data analysis. Associations among categorical variables were examined through the X^2 test or Fisher's exact test, depending on appropriateness, whereas numeric variables underwent analysis using the independent t-test or Mann-Whitney statistics. The ultrasonographic characteristic of placental pannus was evaluated for its sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR-), in relation to biopsy findings. Subsequently, diagnostic accuracy was computed with a significance level established at <0.05.

RESULTS

A total of n=102 patients were enrolled in the final analysis. The mean age of the enrolled women was 32.37±4.31 years. Past surgical history revealed that prior cesarean was observed in (n=99) patients. Gestational diabetes was present in approximately 21% of the patients. Antepartum haemorrhage (APH) was reported, showing a median volume of 3 Liters. The median gestational age was 35.0 (2.00) weeks.

Pannus sign was observed to be positive in 69.60% of the patients, whereas on histopathology investigation diagnosis of a PAS was made in 91.20% of the patients. Hysterectomy was performed in n=87 patients, (88.00%), while bladder repair was performed in n=10 patients. Median hospital stay of the patients enrolled in this study was observed to be 05 days. (**Table 1)** Co-morbidities were found in 21.57% of the participants. Those who had ≥2 comorbids were 18.20%. Pregnancy induced hypertension was the most prevalent complication, found in approximately 7% of the patients. Hypothyroidism was the 2nd most common co-morbidity, comprising 4.5% of the patients. (**Figure 1)**

To better understand the characteristics of patients with and without PAS, a comparative analysis was conducted. The average age of patients with PAS (32.44±4.21 years) is only slightly higher than those without PAS (31.67±5.48 years), and this difference is not statistically significant (p = 0.609). Interestingly, both groups exhibit a notable proportion of individuals who underwent a previous cesarean section and present with placenta previa, with no discernible distinction between them (p = 1.000). Moreover, the presence of a history of myomectomy does not demonstrate a statistically significant difference between the two groups (p = 1.000). This data sheds light on potential similarities and differences between patients with and without PAS. There is a trend suggesting a higher prevalence of GDM in patients without PAS, but the difference is not statistically significant (p = 0.198). The amount of antepartum hemorrhage (liters) and its distribution do not differ significantly between the two groups (p = 0.767). The presence or absence of co-morbidities, as well as the distribution of patients with one or more co-morbidities, does not show a significant difference between the two groups (p = 1.000). (**Table 2)**

The focus on a significant signal called the "Pannus sign (PS)," detected through ultrasound is utilized to forecast the likelihood of the PAS condition, with histopathology considered the ultimate benchmark. Analysis of the overall study sample revealed sensitivity (SEN) of 69.89% for the Pannus sign, indicating the percentage of accurately identified positive cases of the condition. The specificity (SPE) of 33.33% represents the percentage of correct identification of negative cases, or those without the condition. The presence of a positive Pannus sign on an ultrasound may suggest a 70% probability that the individual is indeed affected by the PAS condition. However, its effectiveness in ruling out the condition is limited (33%). This is reflected in the PPV of 91.55%, indicating the likelihood of correctly predicting true positives. Nonetheless, the NPV of 9.68% denotes the probability of accurately identifying true negatives. A negative ultrasound result, indicating the absence of a Pannus sign, yields a high confidence level of 91% in ruling out the condition. The diagnostic accuracy (DA) of 66.67% represents the overall reliability of the diagnostic test **(Table 3)**.

In relation to the prior probability (before the test), the chance of having the PAS condition is around 91, However, even with a Positive Likelihood Ratio (which shows the increase in odds of having the condition with a positive test); the chances don not change significantly (1.05). This indicates that the test has minimal impact on the probability. Moving on to the posterior probability (after the test), we see that a positive result does increase the chances to about 92%. However, the confidence interval suggests that this increase is not precise, ranging from 87% to 95%. Simply put, a positive ultrasound result slightly raises the likelihood of having the condition, but with limited confidence. On the other hand, a negative result moderately decreases the odds of having the condition (0.90 Negative Likelihood Ratio). After the test, the chances of having the condition decrease to around 90%, with a confidence interval spanning from 78% to 96%. Essentially, a negative ultrasound result decreases the likelihood of having the condition, but with limited confidence once again.

A contingency table analysis exploring the relationship between PS and two common surgical procedures, hysterectomy (p=0.534) and bladder repair (p=0.487), revealed no significant link between the two. To explain it more clearly, both positive and negative Pannus signs had little impact on the outcomes of these surgeries. Furthermore, the median length of hospital stay showed no noticeable difference (p=0.331).

Table 1: Socio-demographic and clinical characteristics of the participants (n=102)

Variable		Descriptive statistics
Age (years) mean±SD		32.37±4.31
History of prior C-section, n (%)	Yes	99 (97.06)
	No	03 (2.94)
History of Myomectomy, n (%)	Yes	01 (0.98)
	No	101 (99.02)
Placenta previa, n (%)	Yes	88 (86.30)
	No	14 (13.70)
Gestational diabetes (GDM), n (%)	Yes	21 (20.60)
	No	81 (79.41)
Antepartum haemorrhage (APH) liters median(IQR)		3.0 (2.00)
Gestational age (weeks) median(IQR)		35.0 (2.00)
Hysterectomy, n (%)	Yes	87 (87.00)
	No	13 (13.00)
Urinary tract repair, n (%)	Yes	10 (9.80)
	No	92 (92.20)
Co-morbids, n (%)	Yes	22 (21.57)
	No	80 (78.43)
Number of co-morbids, n (%)	1	18 (81.80)
	≥2	4 (18.20)
Hospital stay(days) median(IQR)		05 (1.00)
Pannus measurement, n (%)	Positive	71 (69.61)
	Negative	31 (30.39)
Histopathology, n (%)	Positive	93 (91.18)
	Negative	9 (8.82)

SD, standard deviation; IQR, Interquartile range

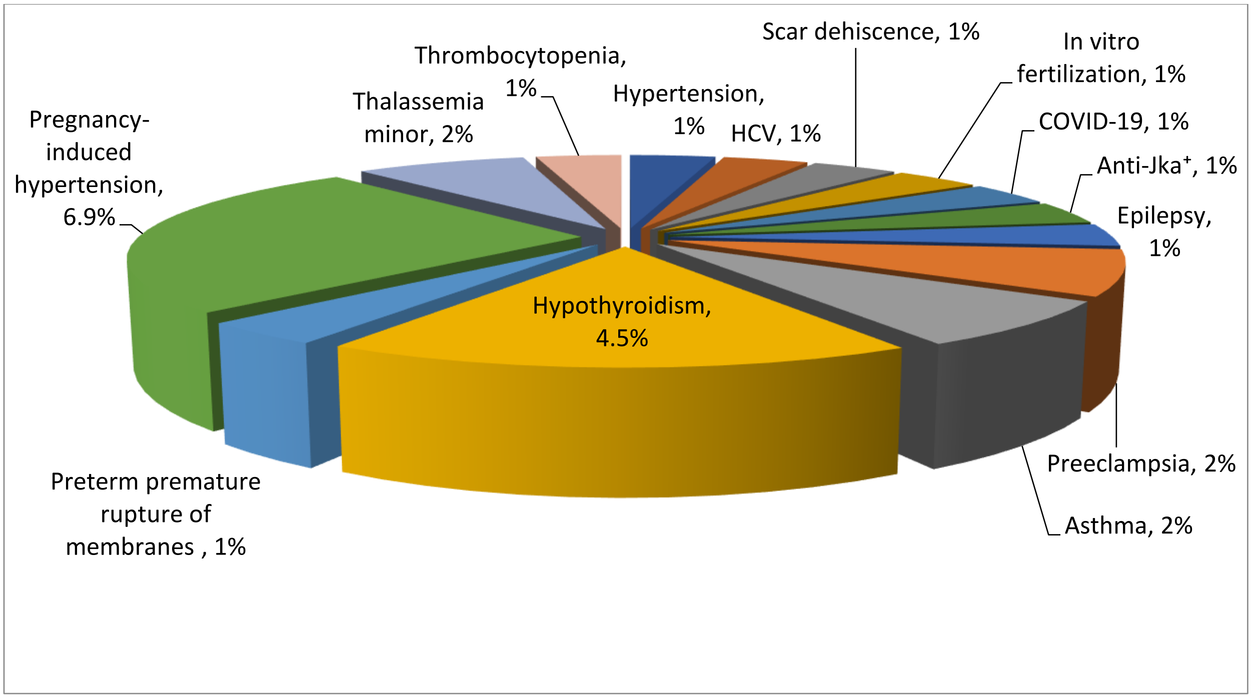

Figure 1: Co-morbids of the study sample

Table 2: Comparison of background characteristics of the study participants with and without Placenta accreta spectrum Disorders (n=102)

Variable		Placental invasion: Normal placenta	Placental invasion: Placenta Accrete	p-value
Age (years) mean±SD		31.67±5.48	32.44±4.21	0.609
History of prior c- section, n (%)	Yes	9(100.0)	90(96.77)	1.000
	No	0(0.00)	3(3.23)	
Placenta previa, n (%)	Yes	7(70.00)	81(88.04)	0.138
	No	3(30.00)	11(11.96)	
History of myomectomy, n (%)	Yes	00(0.00)	1(1.08)	1.000
	No	9(100.0)	92(98.92)	
Gestational diabetes (GDM), n (%)	Yes	00(0.00)	21(22.58)	0.198
	No	9(100.0)	72(77.42)	
APH (liters) median(IQR)		2.90(1.25)	3.00(2.00)	0.767
Gestational age (weeks) median(IQR)		35.0(2.00)	35.0(2.00)	0.969
Co-morbids, n (%)	Yes	2(22.22)	20(21.51)	1.000
	No	7(77.78)	73(78.49)	
Number of co-morbids, n (%)	1	2(100.0)	16(80.00)	1.000
	≥2	0(0.00)	4(20.00)	

Table 3: Ultrasound diagnostic utility using histopathology report as a gold standard

Ultrasound pannus sign	Final diagnosis on histopathology: Negative	Final diagnosis on histopathology: Positive	SEN, [95% CI]	SPE, 95% CI	PPV, 95% CI	NPV, 95% CI	DA, 95% CI
Positive	6	65	69.89	33.33	91.55	9.68	66.67
Negative	3	28	[59.3-78.7]	[9.0-69.0]	[81.8-96.5]	[2.53-26.90]	[56.6-75.6]

SEN; Sensitivity, SPE; Specificity, PPV; Positive Predictive Value, NPV; Negative Predictive Value

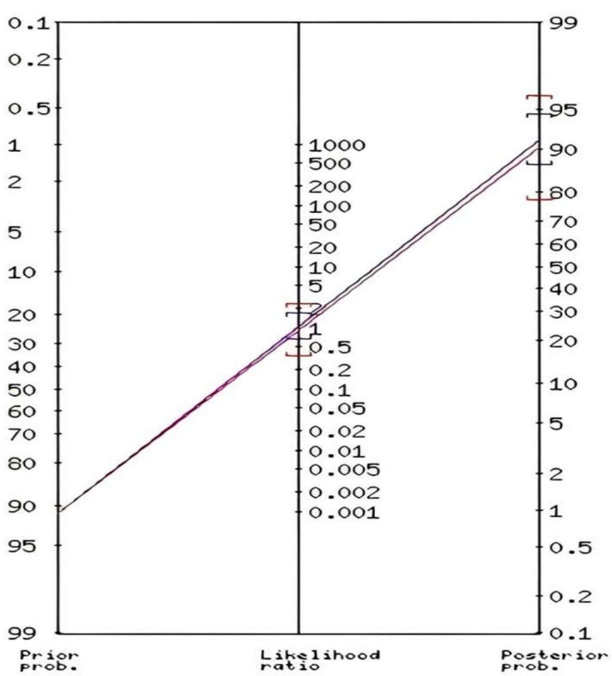

Figure 2: Nomogram of Likelihood ratio, prior and posterior probability Positive test

DISCUSSION

Placenta accreta spectrum (PAS) is a complex obstetric condition associated with significant maternal morbidity and mortality. When placental villi infiltrate the myometrium, it can result in anomalous adhesion between the placenta and the myometrium. [1-3]

Early and efficient antenatal detection of severe forms of PAS, such as percreta, is crucial for optimizing patient management throughout pregnancy, devising appropriate delivery strategies, and enhancing the prognosis for both the mother and baby in high-risk PAS cases. [1-3, 5, 6] In a resource poor country like ours, ultrasound is an indispensable tool used for widespread screening of various conditions PAS being one of them.

Numerous studies have explored the link between placenta previa and past cesarean section and the risk of developing PAS condition. [4, 8, 12] The risk of PAS escalates in tandem with the presence of scar tissue, as evidenced by the association between risk and prior cesarean deliveries. Our study cohort comprised exclusively high-risk pregnancy, characterized by a history of placenta previa in 88 cases (86.30%), and the majority, 99 cases (97.10%), had undergone at least one C-section previously. Currently, the prenatal diagnosis of PAS mostly relies on imaging examinations coupled with an assessment of relevant high-risk factors, with ultrasonography retaining precedence in PAS diagnosis.[13]

The pannus sign occurs when there is insufficient remaining myometrium to keep the uterus structurally intact, resulting in an overhanging protrusion beyond the internal os. This is a recent discovery with limited research on its diagnostic accuracy for PAS. Our study found that the "pannus sign" has good sensitivity but limited specificity as a marker for PAS. Sensitivity was measured at 69%. This sensitivity implies that the "pannus sign" is useful in detecting PAS cases. However, the specificity of the "pannus sign" was significantly lower at 33.3%. This implies that the sign may generate some false positives and lead to unneeded interventions or greater concern for patients. However, the moderate sensitivity of the pannus sign suggests that it is an excellent rule-in test. In our investigation, the "pannus sign" had a PPV of 91.55%, indicating a high possibility of correctly identifying percreta. A positive "pannus sign" indicates a high risk of percreta. The PPV emphasizes the need for confirmation through additional diagnostics and clinical assessment. However, the NPV for pannus sign was only around 9.68%, indicating a low certainty of the absence of PAS even without the sign. In the context of resource-poor countries, the low NPV of the pannus sign is less concerning. This is because ultrasound is widely available and relatively inexpensive even in most resource-poor countries. Therefore, even if the NPV of the pannus sign is low, it is still a cost-effective way to screen for placenta percreta in high-risk populations. MRI is frequently used in clinical settings to confirm cases of PAS, particularly in patients deemed high-risk or those exhibiting strong suspicion of PAS following initial ultrasonography. Prior research studies[14, 15] have highlighted MRI as the preferred modality for assessing PAS in individuals with placenta previa, given its high accuracy in determining the severity of PAS. In a study conducted by Karin A. Fox, [14] it was found that among the 164 women examined, a positive (+) value was observed in 90 cases, while 30 cases showed a negative (-) value on US. Magnetic resonance imaging (MR) agreed with US findings in all cases except for four, demonstrating a concordance rate of 91% with a mean difference of 7.4 mm. The sensitivity and specificity of the diagnostic methods were calculated as 82.7% (95% CI, 72.5-89.6%) and 37.7% (95% CI, 25.1-77.5%), respectively. The PPV and NPV were determined to be 68.9% and 57%, respectively. These findings shed light on the performance characteristics of the imaging modalities in question, providing valuable insights into their reliability and accuracy in the context of the study population.

The cross-tabulation of Pannus sign on ultrasound with hysterectomy and bladder repair revealed no statistically significant association. Both positive and negative Pannus signs were found to have similar outcomes concerning the need for hysterectomy and urinary tract repair. Additionally, there was no significant difference in the median length of hospitalization. The presence or absence of Pannus sign did not show a significant impact on these specific outcomes, suggesting that Pannus sign may not be a strong predictor for hysterectomy, bladder repair, or hospital stay length in this context. In a similar study that used MRI as the gold standard, a positive Pannus sign detected on ultrasound correlated with the necessity for hysterectomy and urinary tract repair. However, when observed on MRI, it was only associated with the need for hysterectomy. [14]

This study stands out due to its focus on the placental pannus—a rarely locally investigated sign for PAS. The findings bear significant implications, especially in resource-poor settings. However, the study has some limitations, notably the absence of specific placental invasion diagnoses like accreta, increta, and percreta on ultrasound. The focus on the presence or absence of placental pannus, rather than specific types, may limit reliability compared to exact biopsy diagnoses. Additionally, the association of placental pannus with severe forms of PAS, as highlighted in literature, emphasizes the need to concentrate on this sign in severe PAS rather than across all types in future studies.

CONCLUSION

The Pannus sign exhibits a moderate level of sensitivity but shows lower specificity, making it proficient in detecting actual positive cases while presenting a higher likelihood of false positives. Both positive and negative Pannus signs yield comparable outcomes concerning hysterectomy and the necessity for urinary tract repair. Future research should explore its reproducibility and its role in conjunction with other markers for PAS diagnosis, potentially enhancing the accuracy of antenatal detection and improving clinical outcomes.

REFERENCES

1. Morlando M, Collins S. Placenta Accreta Spectrum Disorders: Challenges, Risks, and Management Strategies. Int J Womens Health. 2020;12:1033-1045.
2. Bartels HC, Postle JD, Downey P, et al. Placenta Accreta Spectrum: A Review of Pathology, Molecular Biology, and Biomarkers. Dis Markers. 2018;2018:1507674.doi: 10.1155/2018/1507674
3. Arakaza AZou L, Zhu J. Placenta Accreta Spectrum Diagnosis Challenges and Controversies in Current Obstetrics: A Review. Int J Womens Health. 2023;15:635-654.
4. Adu-Bredu TK, Rijken MJ, Nieto-Calvache AJ, et al. A simple guide to ultrasound screening for placenta accreta spectrum for improving detection and optimizing management in resource limited settings. Int J Gynecol Obstet. 2023;160(3):732-741.
5. Jamali AH, Sherwani A, Sheikh A, et al. Diagnostic Accuracy of Ultrasound in Morbidly Adherent Placenta Keeping Histopathology as Gold Standard. Pak J Med Health Sci. 2023;17(05):600-603.
6. Liu X, Wang Y, Wu Y, et al. What we know about placenta accreta spectrum (PAS). Eur J Obstet Gynecol Reprod Biol 2021;259:81-89.
7. Jauniaux ECollins S, Burton GJ. Placenta accreta spectrum: pathophysiology and evidence-based anatomy for prenatal ultrasound imaging. Am J Obstet Gynecol. 2018;218(1):75-87.
8. Chalubinski KM, Pils S, Klein K, et al. Prenatal sonography can predict degree of placental invasion. Ultrasound Obstet Gynecol. 2013;42(5):518-524.
9. Hayes EAyida G, Crocker A. The morbidly adherent placenta: diagnosis and management options. Curr Opin Obstet Gynecol. 2011;23(6):448-453.
10. Lerner JPDeane S, Timor-Tritsch IE. Characterization of placenta accreta using transvaginal sonography and color Doppler imaging. Ultrasound Obstet Gynecol. 1995;5(3):198-201.
11. Jauniaux E, Ayres-de-Campos D, Langhoff-Roos J, et al. FIGO classification for the clinical diagnosis of placenta accreta spectrum disorders. Int J Gynecol Obstet. 2019;146(1):20-24.
12. Ye C, Ling L, Li S, et al. Comparisons of the diagnostic accuracy of the ultrasonic sign-score method and MRI for PA, PI and PP in high-risk gravid women: a retrospective study. Ann Transl Med. 2023;11(2):81.
13. Solheim KN, Esakoff TF, Little SE, et al. The effect of cesarean delivery rates on the future incidence of placenta previa, placenta accreta, and maternal mortality. J Matern Fetal Neonatal Med. 2011;24(11):1341-1346.
14. Romeo V, Verde F, Sarno L, et al. Prediction of placenta accreta spectrum in patients with placenta previa using clinical risk factors, ultrasound and magnetic resonance imaging findings. Radiologia medica. 2021;126(9):1216-1225.
15. Fox KA, Castillo J, Shetty T, et al. 1104: Pannus sign on ultrasound and MRI predicts placenta percreta. Am J Obstet Gynecol. 2020;222(1):S680.