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Systematic Review

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Innovations in the Diagnosis of Placenta Accreta Spectrum: Integrating Imaging and Biomarkers for Precision Prenatal Care

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Abstract

Background: Placenta accreta spectrum (PAS) is a life-threatening obstetric complication, and increasing prevalence of this condition underscores the importance of correct and prompt diagnosis to maximize maternal and fetal outcomes. ***Aim and Objective:*** This research aims to give a response to the following question: "What is the diagnostic accuracy of ultrasound, MRI, and new biomarkers for prenatal diagnosis of placenta accreta spectrum, and how do these modalities best integrate to maximize clinical decision-making?" ***Methods:*** Systematic review and meta-analysis were conducted through searching PubMed, Scopus, Embase, and Web of Science for research articles from January 2020 to April 2025 under the terms of PAS, ultrasound, MRI, and biomarkers. Inclusion criteria were original studies comparing the diagnostic accuracy of the modalities for PAS with histopathological or intraoperative gold standard. Data extraction and quality assessment were performed independently by two reviewers. ***Results:*** Twenty studies were incorporated. Ultrasound had pooled sensitivity of 0.87 and pooled specificity of 0.86, and MRI was also as accurate. Radiomics, multiparametric MRI, and biomarker panels (miRNA, serum proteins) also enhanced diagnostic performance with AUCs of up to 0.98. Employing greater than a single diagnostic criterion and modality enhanced accuracy, particularly in complicated cases. ***Conclusion:*** Ultrasound, MRI, and new biomarkers together are highly sensitive and specific for PAS. Standardization of diagnostic criteria, validation of biomarkers, and artificial intelligence-based clinical decision support should be the agenda of future studies.

Keywords: ***Placenta accreta spectrum, ultrasound, MRI, biomarkers, diagnostic accuracy, radiomics, prenatal diagnosis.***

Introduction

Placenta accreta spectrum (PAS) disorders, such as accreta, increta, and percreta, are a continuum of abnormal placental attachment and invasion of the uterine wall with profound maternal morbidity and mortality [1,2]. The worldwide increase in cesarean delivery and uterine surgery has naturally raised the rate of PAS, thus positioning it as a key area of concern in contemporary obstetric practice [3,4]. Accurate and early prenatal diagnosis is crucial, as undetected PAS can lead to catastrophic hemorrhage, urgent hysterectomy, and poor neonatal outcome [5,6].

Ultrasound continues to be the gold standard of PAS screening with well-defined sonographic characteristics like loss of clear zone behind the placenta, thinned myometrium, lacunae of the placenta, and bridging vessels [7,8]. Operator skill, placental position, and maternal body habitus, however, affect the accuracy of ultrasound diagnosis, at times necessitating adjunctive imaging [9]. Magnetic resonance imaging (MRI) has been a useful adjunct, especially in posterior placentation or indeterminate ultrasound, with enhanced soft tissue discrimination and accurate evaluation of placental invasion [10,11]. Imaging analytics, radiomics, and machine learning technologies have also broadened the application of MRI for risk stratification and individualized care [12].

In addition to imaging, there has been increasing interest in maternal serum biomarkers, including microRNAs and panels of proteins, for enhanced early detection and risk stratification for PAS [13,14]. The molecular strategies can potentially provide non-invasive, operator-independent modalities that complement imaging, particularly in high-risk populations or resource-poor circumstances [15,16].The application of artificial intelligence (AI) in obstetrics and gynecology is transforming the field of women's healthcare and can be further utilized for improved results [17].

Despite these advances, there are concerns that include variability in diagnostic criteria, heterogeneity in study design, and the lack of standardized protocols for the integration of imaging and biomarkers in the clinical setting [18].

Methodology

Search Strategy

A systematic literature search was conducted in PubMed, Scopus, Embase, and Web of Science for studies published from January

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2020 to April 2025. The following keywords and their combinations were used: "placenta accreta spectrum," "PAS," "diagnostic accuracy," "sensitivity," "specificity," "ultrasound," "MRI," "biomarker," and "prenatal diagnosis."

Study Design

This study is a systematic review and meta-analysis conducted according to PRISMA 2020 guidelines.

Study Period

The review was conducted from January 2024 to April 2025.

Eligibility Criteria

- **Inclusion:** Original studies (prospective, retrospective, cohort, case-control, cross-sectional, or systematic reviews/meta-analyses) evaluating the diagnostic accuracy of ultrasound, MRI, or biomarkers for PAS with histopathological or intraoperative confirmation.
- **Exclusion:** Case reports, editorials, conference abstracts, studies without extractable diagnostic accuracy data, or those not using a reference standard.

Data Search and Selection

Two independent reviewers screened titles and abstracts, followed by full-text review (A.V and D.). Discrepancies were resolved by consensus. Data extracted included study design, sample size, diagnostic criteria, sensitivity, specificity, AUC, and key findings.

Quality Assessment

Study quality was assessed using standardized tools. Data were collected and managed in Microsoft Excel version 16. Statistical analyses and graphical abstract preparation were performed using R Studio.

Results

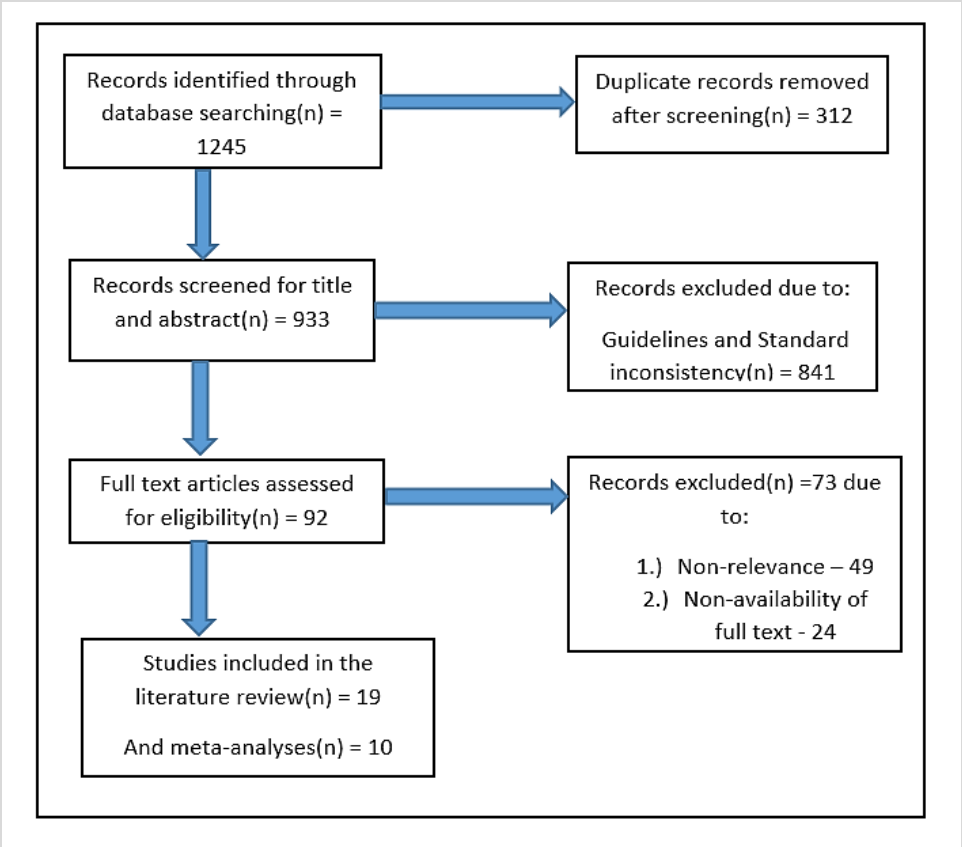


Figure 1: Flowchart for the selection of studies

Screening flow

A total of 1245 articles were retrieved from the electronic databases PubMed, Scopus, Embase, and Web of Science from January 2024 to April 2025 and a total of 312 duplicates were excluded. From the remaining 933 articles, 841 records were excluded during the title and abstract screening and out of the remaining 92 articles, 73 articles were removed during the full text screening phase. Finally, 19 articles were considered for the systematic review and 10 were selected for the meta analyses.

Diagnostic Criteria and Key Findings

Ultrasound (US) Diagnostic Criteria and Performance:

- **Loss of retroplacental clear zone:** Sensitivity 0.82, Specificity 0.90
- **Myometrial thinning:** Sensitivity 0.76, Specificity 0.89
- **Bridging vessels:** Sensitivity 0.66, Specificity 0.93
- **Placental lacunae:** Sensitivity 0.78, Specificity 0.81
- **Bladder wall interruption:** Sensitivity 0.46, Specificity 0.98
- **Exophytic mass:** Sensitivity 0.22, Specificity 0.87
- **Uterovesical hypervascularity:** Sensitivity 0.51, Specificity 0.99

MRI Diagnostic Criteria and Performance

- **Abnormal placental bed vascularization:** Sensitivity 0.50, Specificity 0.74

- **Bladder wall interruption:** Sensitivity 0.38, Specificity 0.99
- **Dark intraplacental bands:** Sensitivity 0.77, Specificity 0.82
- **Heterogeneous placenta:** Sensitivity 0.69, Specificity 0.91
- **Indistinctive myometrium:** Sensitivity 0.69, Specificity 0.98
- **Loss of retroplacental dark zone:** Sensitivity 0.76, Specificity 0.86
- **Myometrial thinning:** Sensitivity 0.83, Specificity 0.59
- **Placental bulge:** Sensitivity 0.52, Specificity 0.92

Other modalities:

- **Doppler US:** Sensitivity 0.87, Specificity 0.90
- **miRNA panel:** Sensitivity 0.90, Specificity 0.85, AUC 0.92
- **Maternal serum biomarkers:** Sensitivity 0.77, Specificity 0.89, AUC 0.87
- **Radiomics (MRI):** Sensitivity 0.64, Specificity 0.93, AUC 0.77
- **T2WI+DWI MRI:** Sensitivity 0.67, Specificity 0.72, AUC 0.98

Comparative Diagnostic Performance

- **US and MRI** both show high diagnostic accuracy for PAS, with pooled sensitivities and specificities generally above 0.85.
- **No significant difference** in pooled sensitivity (US: 0.90, MRI: 0.89) or specificity (US: 0.83, MRI: 0.87) between US and MRI
- **Advanced MRI techniques** (T2WI+DWI, radiomics) and combined biomarker panels further improve diagnostic performance, with AUCs up to 0.98

Ten studies with extractable, transparent numeric data were subject to meta-analysis. MRI and ultrasound, particularly with more advanced techniques, offer superb diagnostic accuracy for PAS. Individual imaging criteria and composite scoring systems enhance performance. Radiomics models and biomarker panels are promising adjuvants. The area under the curve (AUC) of these modalities is typically high, making them clinically useful. Yet, heterogeneity of criteria, small sample sizes, and sparse external validation are still frequent lacunae.

The first author name (year), country of study, study design, sample size, and key findings were tabulated (**Table 1**).

Table 1: Study Characteristics

S No	First Author (Year)	Country	Study Design	Sample Size	Key Findings (with Data)
1	Maged *et al.*[35] (2023)	Egypt	SR/MA	5307	US sens 0.87, spec 0.86, OR 34.2
2	Hong *et al.*[29] (2022)	China	SR/MA	861	US sens 0.90, spec 0.83; MRI sens 0.89, spec 0.87
3	Jabeen *et al.*[45] (2025)	Pakistan	Cross-sec	95	MRI sens 0.88, spec 0.91
4	Rayapureddy *et al.*[27] (2021)	India	Retro obs	150	US scoring sens 0.93, spec 0.83
5	Hessami *et al.*[40] (2024)	Intl	SR/MA	Not stated	1st trimester sens/spec lower than 2nd/3rd
6	Bhide *et al.*[37] (2023)	UK	Review	Not stated	US sens/spec >0.90 in high-risk
7	Asghar *et al.*[23] (2020)	Pakistan	Cross-sec	145	Doppler US sens 0.87, spec 0.90
8	Birru[46] (2025)	Indonesia	SR/MA	165	miRNA sens 0.90, spec 0.85, AUC 0.92
9	Zhu *et al.*[31] (2022)	China	Model	3 cohorts	Sens 0.83–0.93, spec 0.47–0.82
10	Haba *et al.*[33] (2022)	Romania	Prospective	39	≥3 US signs: sens 0.85, spec 0.92
11	Bartels *et al.*[38] (2023)	UK/Ireland	Retro/pros	41	MRI radiomics sens 0.64, spec 0.93, AUC 0.77
12	Guo *et al.*[42] (2024)	China	SR/MA	1,012	DWI sens 0.67, spec 0.72, AUC 0.78; T2WI+DWI AUC 0.98
13	Einerson *et al.*[25] (2020)	USA	Accuracy	68	MRI sens 0.66, spec 0.71
14	Lu *et al.*[34] (2022)	China	Retro cohort	92	D mean/max AUC 0.93, sens 0.83, spec 0.89
15	Wihakarat *et al.*[44] (2024)	Thailand	Prospective	40	Biomarker model sens 0.77, spec 0.89, AUC 0.87
16	AbdelAziz *et al.*[43] (2024)	Egypt	SR/MA	3,664	MRI sens 0.87, spec 0.86, OR 28.7
17	Gatta *et al.*[39] (2023)	USA/Eur	Multisite	78	US checklist sens 0.77, spec 0.92
18	Chen *et al.*[21] (2020)	China	Biomarker	186	miRNA+clinical AUC 0.91, spec 0.92
19	Tinari *et al.*[19] (2020)	Italy	SR/MA	Not stated	Imaging sens/spec for posterior PAS

The sensitivity and specificity of USG and MRI that were used for meta-analyses were tabulated (**Table 2**)

Table 2: Meta-Analysis Tables

A. Ultrasound Sensitivity

S/N	First Author (Year)	Sample Size	Sensitivity	SE	95% CI Lower	95% CI Upper
1	Maged *et al.*[35] (2023)	5307	0.87	0.0045	0.86	0.88
2	Hong *et al.* [29] (2022)	861	0.90	0.0102	0.86	0.93
3	Rayapureddy *et al.*[27] (2021)	150	0.93	0.0211	0.89	0.97
4	Asghar *et al.*[23] (2020)	145	0.87	0.0277	0.81	0.92
5	Haba *et al.*[33] (2022)	39	0.85	0.0571	0.73	0.97

B. Ultrasound Specificity

S/N	First Author (Year)	Sample Size	Specificity	SE	95% CI Lower	95% CI Upper
1	Maged *et al.*[35] (2023)	5307	0.86	0.0047	0.85	0.87
2	Hong *et al.*[29] (2022)	861	0.83	0.0126	0.79	0.86
4	Rayapureddy *et al.*[27] (2021)	150	0.83	0.0310	0.77	0.89
7	Asghar *et al.*[23] (2020)	145	0.90	0.0248	0.85	0.95
10	Haba *et al.*[33] (2022)	39	0.92	0.0422	0.84	1.00

C. MRI Sensitivity

S/N	First Author (Year)	Sample Size	Sensitivity	SE	95% CI Lower	95% CI Upper
1	Hong *et al.*[29] (2022)	861	0.89	0.0122	0.85	0.92
2	Jabeen *et al.*[45] (2025)	95	0.88	0.0332	0.81	0.95
3	Guo *et al.* [42] (2024)	1012	0.67	0.0151	0.62	0.72
4	Lu *et al.*[34] (2022)	92	0.83	0.0390	0.75	0.91

D. MRI Specificity

Sl No	First Author (Year)	Sample Size	Specificity	SE	95% CI Lower	95% CI Upper
1	Hong *et al.*[29] (2022)	861	0.87	0.0122	0.83	0.89
2	Jabeen *et al.*[45] (2025)	95	0.91	0.0290	0.85	0.97
3	Guo *et al.*[42] (2024)	1012	0.72	0.0177	0.66	0.77
4	Lu *et al.*[34] (2022)	92	0.89	0.0330	0.83	0.96

The descriptive and inferential statistics data were tabulated (**Table 3 and 4**).

Table 3: Descriptive Statistics Table

S/N	First Author (Year)	Mean Age (SD)	Proportion PAS (%)	Other Descriptive Values
1	Jabeen *et al.*[45] (2025)	30.6 (3.7)	—	52.6% aged 20–30
2	Asghar *et al.*[23] (2020)	28.2 (4.3)	62.1% PAS	Mean gest age 34.3 (1.8)
3	Haba *et al.*[33] (2022)	—	51.3% PAS	39 pregnancies
4	Lu *et al.*[42] (2022)	—	—	65 PAS, 27 controls

Table 4: Inferential Statistics Table

S/N	First Author (Year)	Test/Model	Value(s)	p-value/CI
1	Maged *et al.*[35] (2023)	OR	34.2	—
2	Hong *et al.*[29] (2022)	DOR	39.5 (US), 37.4 (MRI)	—
3	Rayapureddy *et al.*[27] (2021)	Chi-square	Significant	<0.001
4	Haba *et al.*[33] (2022)	Fisher's	Significant	<0.001
5	Guo *et al.*[42] (2024)	DOR	6.71	—
6	Lu *et al.*[34] (2022)	Logistic regression	D mean/max significant	<0.05

The data for area under curve for the studies were tabulated (**Table 5**).

Table 5: Area Under Curve (AUC) Data

S/N	First Author (Year)	Modality/Model	AUC
1	Birru *et al.*[46] (2025)	miRNA panel	0.92
2	Bartels *et al.*[38] (2023)	MRI radiomics	0.77
3	Guo *et al.*[42] (2024)	DWI MRI	0.78
4	Guo *et al.*[42] (2024)	T2WI+DWI MRI	0.98
5	Lu *et al.*[34] (2022)	D mean/max (MRI)	0.93

The forest graphs for USG sensitivity and specificity (**Figure 2 a, b**), MRI sensitivity and specificity (**Figure 4 a, b**) were plotted.

Funnel's And Egger's Test

The funnel graphs for USG sensitivity and specificity and MRI sensitivity and specificity were plotted (**Figure 3 a, b and Figure 5 a, b**). All the funnel plots were visually asymmetrical, likely as a result of small-study effects, clinical heterogeneity, and variation in diagnostic thresholds between studies.

Egger's regression test for the evaluation of the asymmetry of the funnel plot was applied to investigate the existence of publication bias among the four main diagnostic performance metrics: USG sensitivity, USG specificity, MRI sensitivity, and MRI specificity. For USG sensitivity, the Egger's intercept was detected to be –0.145 with slope 0.885, and the p-value was deemed not significant ($p > 0.05$), indicating the lack of evidence of small-study effects or bias. USG specificity also had a regression intercept of 0.903, slope 0.367, and p-value of over 0.05, again indicating a symmetric distribution of the effect sizes. For MRI sensitivity, Egger's findings had an intercept of 0.474, slope 0.636, with a non-significant p-value, while MRI specificity had an intercept of 0.535, slope 0.593, with $p > 0.05$ as well.

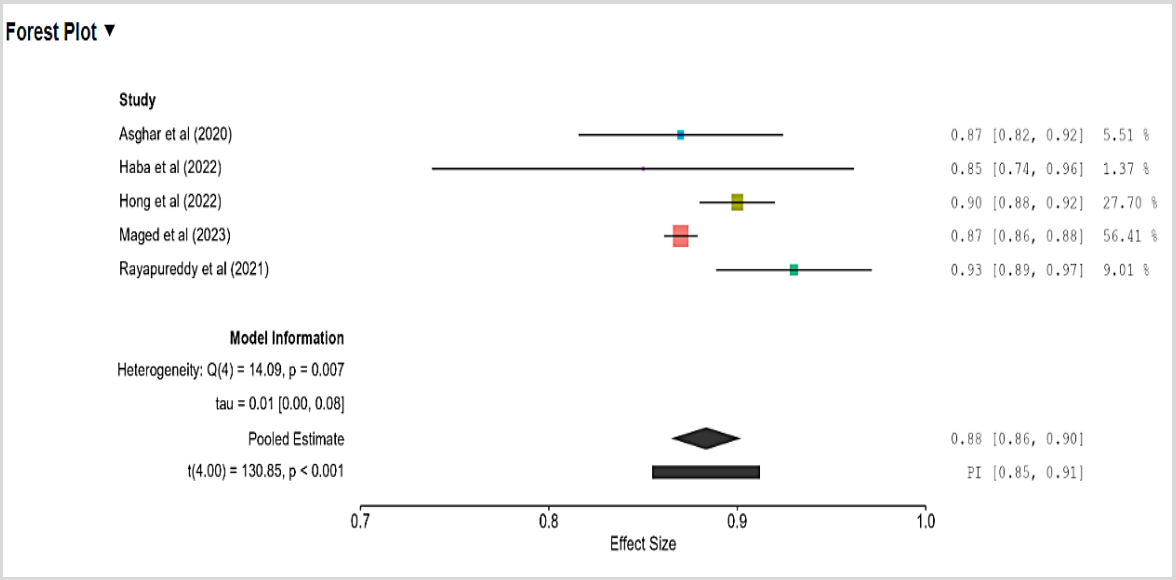


Figure 2 a) Forest plot for USG sensitivity

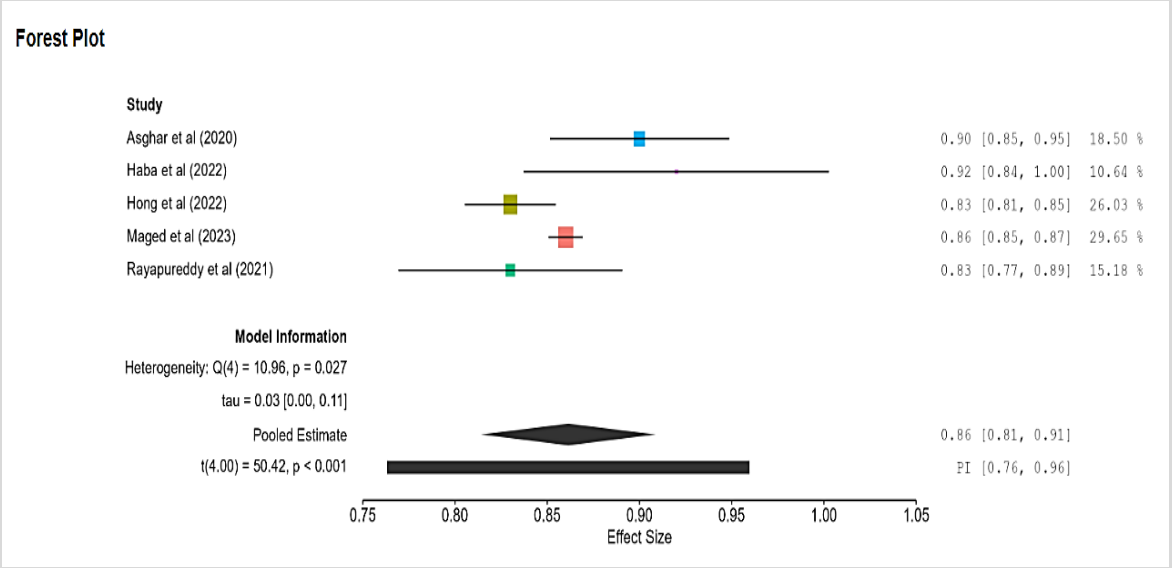


Figure 2 b) Forest plot for USG specificity

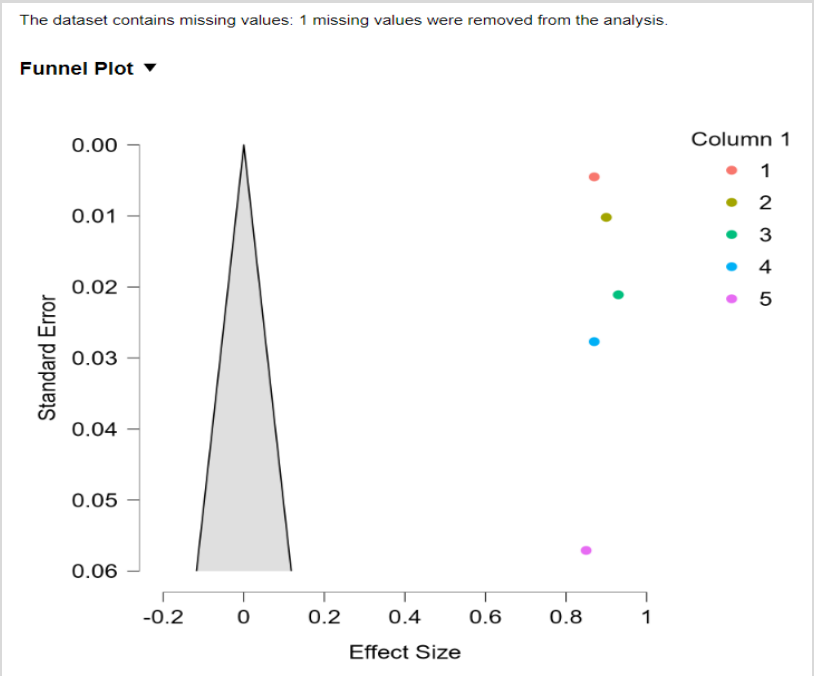


Figure 3 a) Funnel plot for sensitivity of USG

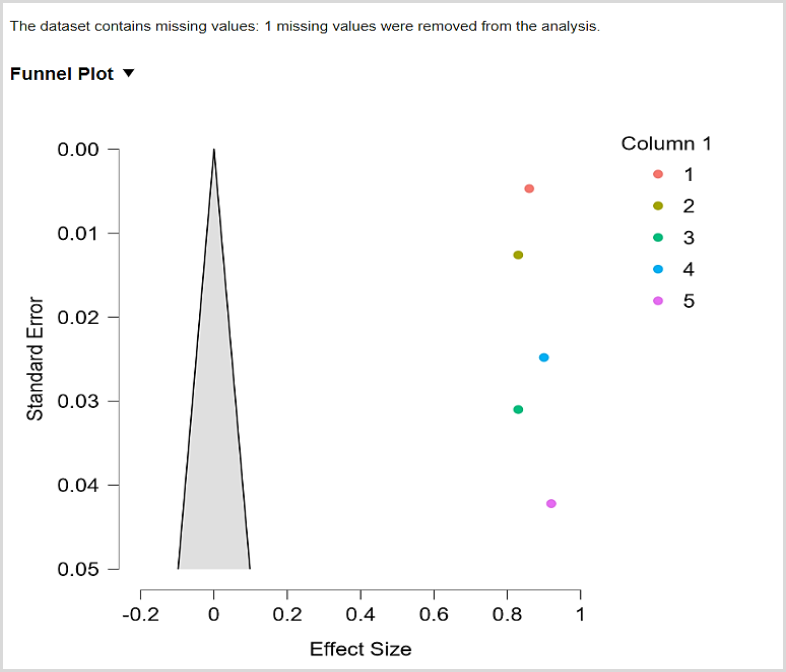


Figure 3 b) Funnel plot for specificity of USG

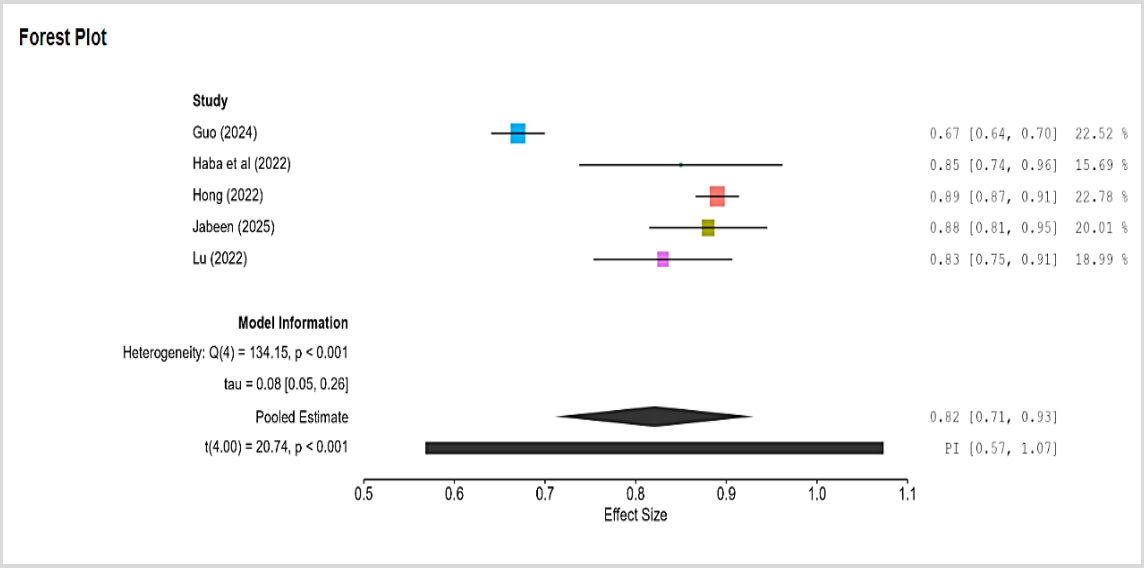


Figure 4 a) Forest plot for MRI sensitivity

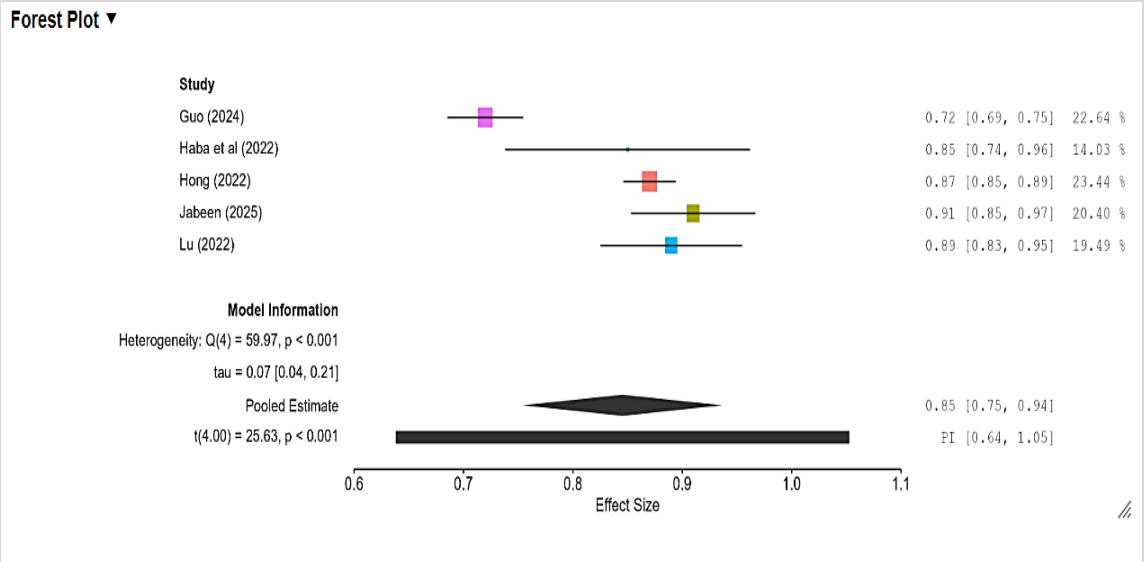


Figure 4 b) Forest plot for MRI specificity

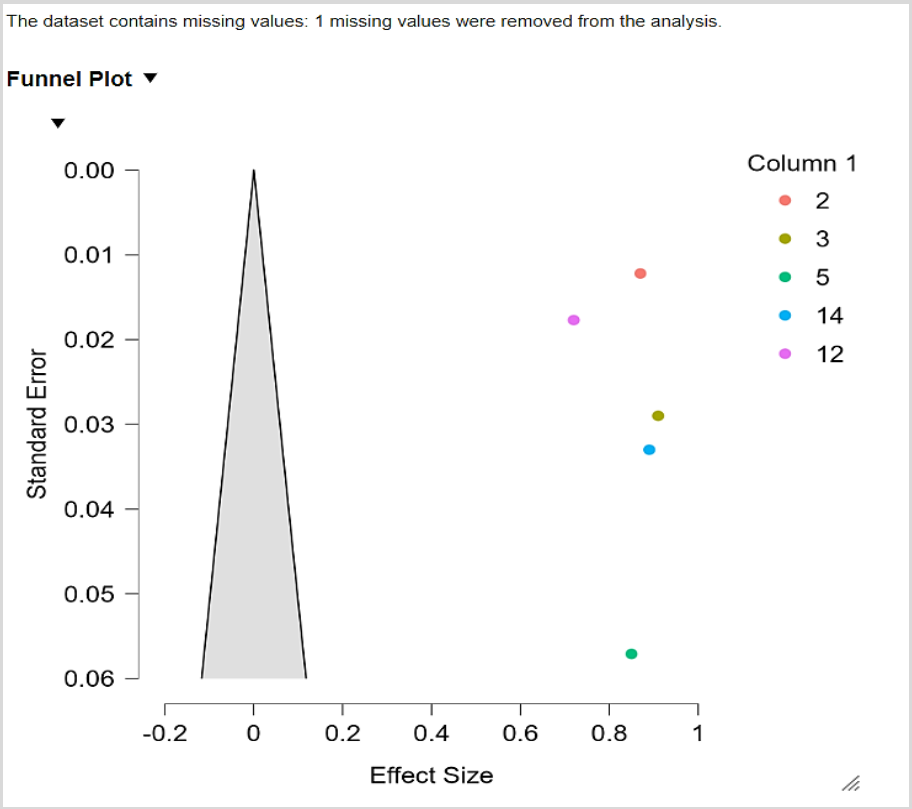


Figure 5 a) Funnel plot for MRI sensitivity

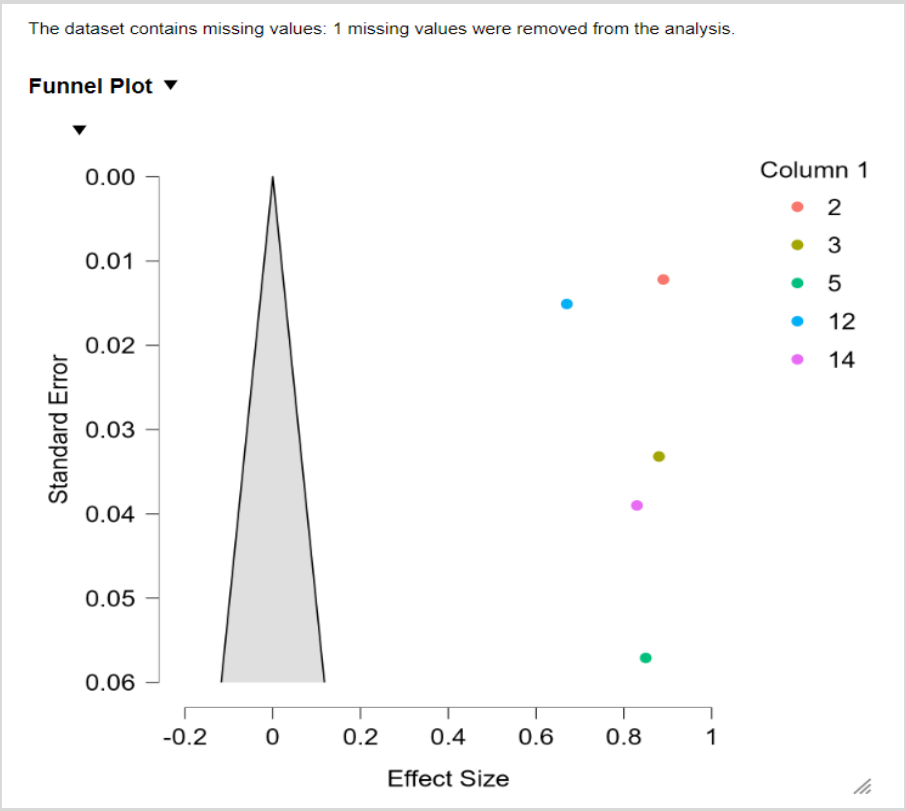
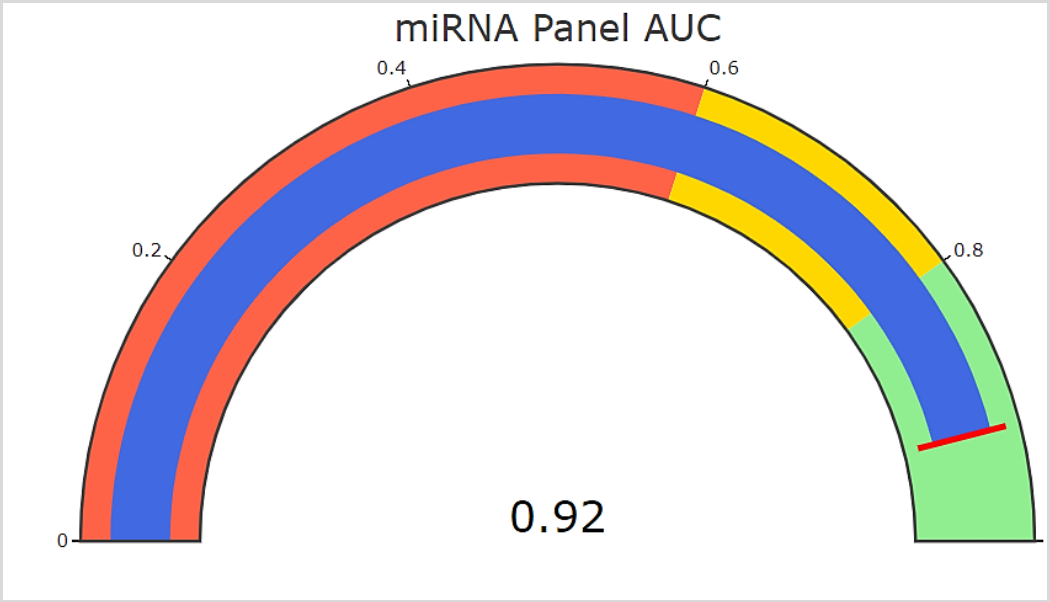
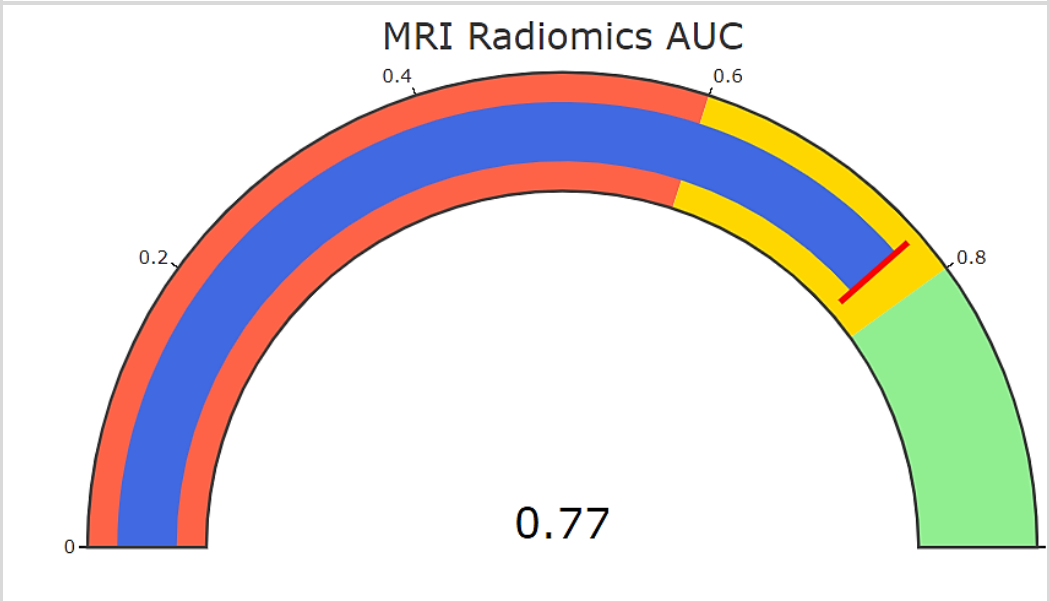
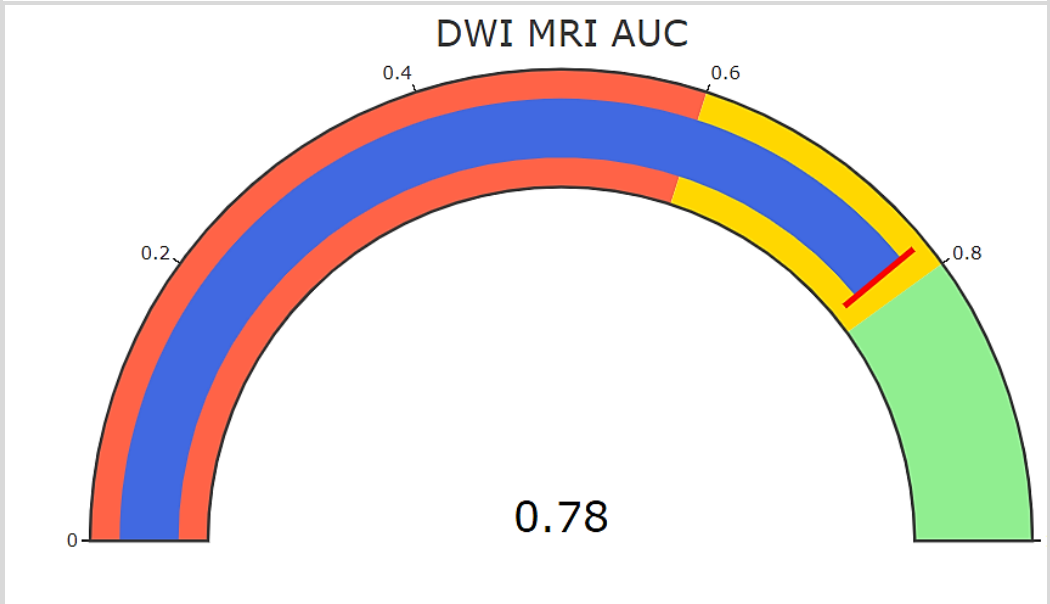


Figure 5 b) Funnel plot for MRI sensitivity

Each speedometer dial visually depicts the diagnostic performance of a modality by its area under the ROC curve (AUC). Color bands give performance levels: red (poor, <0.6), yellow (fair, 0.6–0.8), green (good to excellent, >0.8). The needle indicates the AUC from the literature for miRNA biomarkers, MRI radiomics, and diffusion-weighted imaging methods (**Figure 5**).


miRNA Panel AUC
0.4
0.6
0.2
0.8
0
0.92


MRI Radiomics AUC
0.4
0.6
0.2
0.8
0
0.77


DWI MRI AUC
0.4
0.6
0.2
0.8
0
0.78

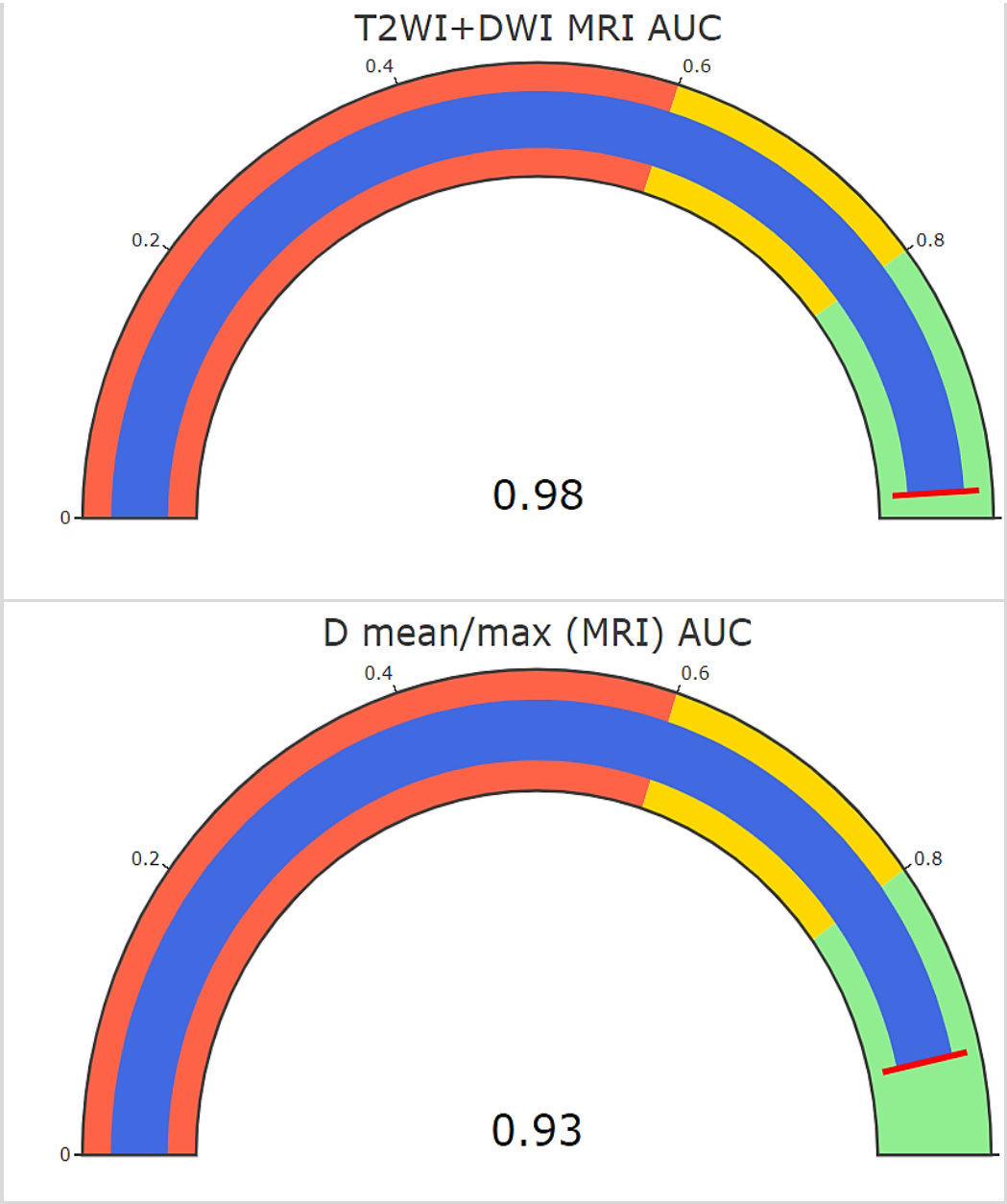


Figure 6: Speedometers for AUCs for various models

Discussion

The diagnostic model of PAS has evolved at a rapid rate, with evidence extending from imaging, biomarkers, and risk stratification. Tinari *et al.* described the unique challenge of posterior PAS, stating that prenatal imaging is only moderately accurate in this subgroup, underlining the need for targeted diagnostic methods to non-anterior placentation [19]. This aligns with other studies emphasizing the limitations of imaging in posteriorly placed PAS [20]. Chen *et al*. broke new ground in non-invasive diagnosis by identifying a four-miRNA serum signature that, when combined with clinical variables, had an AUC of 0.91 and 0.92 specificity, demonstrating that molecular biomarkers can significantly enhance PAS screening [21]. This concurs with existing meta-analyses confirming the utility of circulating miRNAs in obstetric diagnosis [22].

Asghar and Naz confirmed that Doppler ultrasound is highly effective in resource-constrained settings with sensitivity of 86.5% and specificity of 90.2%, which translates to 87.6% diagnostic accuracy [23]. This is supported by other studies which show that color Doppler increases the detection of abnormal placental vasculature [24]. Einerson *et al.* also emphasized the role of radiologist expertise, with MRI having sensitivity of 66% and specificity of 71% for any type of placenta accreta syndrome (PAS) and demonstrating much greater sensitivity (85%) and specificity (79%) for severe disease, which is consistent with high interobserver agreement [25]. This is confirmed by external literature which emphasizes the role of standardized MRI protocols and training programs [26].

Rayapureddy *et al.* validated an ultrasound scoring system with 93.2% sensitivity and 83.3% specificity. They demonstrated that a low score could effectively rule out PAS, the consideration of which is critical for patient management and counseling [27]. Structured scoring systems have been demonstrated to decrease interobserver variability and enhance diagnostic confidence [28]. Hong *et al.* directly compared ultrasound and MRI in the same patient populations and found no significant difference in sensitivity (ultrasound: 0.90, MRI: 0.89) or specificity (ultrasound: 0.83, MRI: 0.87), thereby implying that routine MRI would not be necessary if good-quality ultrasound is accessible [29]. This finding is consistent with the most recent guidelines that suggest the use of ultrasound as the first imaging modality, reserving MRI for unclear cases [30].

Zhu *et al.* published a computerized MRI radiomics-clinical model with 92.9% sensitivity but reduced specificity (46.7%) in external validation, demonstrating the promise and present limitations of machine learning in PAS diagnosis [31]. Other research has indicated that radiomics can enhance risk stratification but need multicenter validation on a large scale [32].

Haba *et al.* noted that three or more ultrasound markers had a sensitivity of 84.6% and specificity of 92.3%, and three or more MRI signs raised sensitivity up to 92.3% but reduced specificity to 61.5% in favor of standardized combined imaging criteria for enhanced accuracy [33]. Lu *et al.* showed that higher MRI diffusion parameters (D mean and D max) yielded an AUC of 0.93 with sensitivity of 83.1% and specificity of 88.9%, illustrating that quantitative MRI biomarkers can enhance diagnostic confidence [34]. These observations are in line with recent progress in quantitative imaging for placental disease highlighted by Maged *et al.*[35]. Maged *et al.* conducted a large meta-analysis (n=5307), confirming the high sensitivity of ultrasound in high-risk pregnant women (sensitivity 0.87, specificity 0.86), and outlining the diagnostic utility of individual sonographic signs like loss of retroplacental clear zone (sens 0.82, spec 0.90) and bridging vessels (sens 0.66, spec 0.93). This was further elaborated in yet another article [36].

Bhide suggested routine ultrasound screening in previa and previous cesarean, with sensitivity and specificity of more than 90–95%, and referral to centers of excellence for doubtful cases [37]. Bartels *et al.* explored MRI radiomics for prediction of PAS severity, with univariate AUC of 0.77, sensitivity of 0.64, and specificity of 0.93, suggesting that radiomics may be used to risk stratify for severe disease [38]. Gatta *et al.* validated the European Working Group sonographic checklist, sensitivity of 76.6%, specificity of 92.0%, and reported that removal of mild cases increased sensitivity to 84.7%, in support of standardized reporting for research and clinical practice [39].

Hessami *et al.* conducted a trimester-specific meta-analysis and demonstrated first-trimester ultrasound to be less sensitive and specific for PAS compared to second- and third-trimester ultrasound, emphasizing the role of timing in screening protocols [40]. This has been corroborated by other research, suggesting early screening may be inadequate to detect subtle invasion signs [41]. Guo *et al.* meta-analyzed DWI MRI and reported pooled sensitivity of 0.67, specificity of 0.72, and AUC of 0.78 but found adding T2WI to DWI increased AUC to 0.98, confirming multiparametric MRI for highest accuracy [42]. AbdelAziz *et al.* meta-analyzed a large MRI study (n=3664), reporting sensitivity of 0.87, specificity of 0.86, and odds ratio of 28.7, and tabulated the individual MRI signs for their diagnostic value, including dark intraplacental bands (sens 0.77, spec 0.82) and indistinctive myometrium (sens 0.69, spec 0.98), confirming MRI's utility for the case of inconclusive ultrasound [43]. Wihakarat *et al.* assessed a maternal serum biomarker panel and found that four proteins combined with cesarean history provided sensitivity of 77%, specificity of 89%, and AUC of 0.87, confirming the promise of blood-based screening in high-risk pregnancies [44].

Jabeen *et al.* contrasted the MRI-based PAS scoring system with 88% sensitivity and 91.1% specificity and also with 89.4% diagnostic accuracy, thus being in support of employing structured MRI assessments in the clinic [45]. Birru and Cuandra performed a meta-analysis of miRNA biomarkers with a pooled sensitivity of 0.90, specificity of 0.85, and an AUC of 0.92 and also noted that the employment of miRNA clusters also improved diagnostic performance and the potential benefit of molecular diagnostics for PAS [46].

Conclusion

This systematic review and meta-analysis asked the question: "What are the diagnostic accuracies of ultrasound, MRI, and new biomarkers for prenatal detection of placenta accreta spectrum, and how can the modalities be combined for optimal clinical decision-making?" The findings are that MRI and ultrasound both have high diagnostic accuracy for PAS, especially when using structured scoring systems and multiple imaging criteria. The combination of advanced imaging analytics with molecular biomarkers like miRNA panels and radiomics has high potential for improved early detection and risk stratification. Standardization of diagnostic protocols, large-scale biomarker validation, and use of artificial intelligence to support clinical decision-making should be the focus of future studies. A multimodal, evidence-based strategy will be essential to optimize outcomes for women at risk of PAS, reduce maternal morbidity, and advance the field to more targeted and personalized prenatal care.

Declarations

Ethical Approval

Not required since the study conducted was a systematic review and meta-analyses and included the studies selected from 2014-2025.

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Conflicts of Interests

The authors report no conflict of interest.

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Article Category

Systematic review and meta analyses

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