

# Early prediction of placenta accreta spectrum by evaluation of risk factors and ultrasound

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## Abstract

**Introduction:** We explored the predictive utility of clinical risk factors and first-trimester pregnancy ultrasound signs for severe placenta accreta spectrum.

**Material and methods:** Patients with placenta accreta spectrum treated in our institution between March 1, 2017 and December 31, 2022 were analyzed. The patients were divided into those with mild and those with severe conditions. Univariate analysis was used to determine the clinical risk factors and first trimester ultrasound signs associated with severe placenta accreta spectrum. Receiver operating characteristic curves were drawn and the areas under the curves calculated.

**Results:** Univariate analysis revealed significant between-group differences between the groups in the number of cesarean sections, scar pregnancy, low gestational sac position, abnormal placental position, focal exophytic mass and abnormal placental lacunae in placental parenchyma ( $p < 0.05$ ). The number of cesarean sections and first trimester ultrasound signs predicted severe placenta accreta spectrum, with areas under the curves of 0.66 and 0.75. When the number of cesarean sections was combined with low gestational sac position, the placenta position and related ultrasound signs, the areas under the curves for predicting severe placenta accreta spectrum were 0.78, 0.73, and 0.89, respectively.

**Conclusions:** Clinical risk factors and first-trimester ultrasound signs predicted severe placental accreta spectrum and their combinations had even greater clinical utility.

**Key words:** clinical risk factors, first trimester, ultrasound, placenta accreta.

## Introduction

Placenta accreta spectrum (PAS) is a pathological condition characterized by infiltration of placental villi into the myometrium to various depths. PAS may cause uterine rupture, severe postpartum hemorrhage, and even maternal and fetal death [1]. According to the depth of placental implantation, PAS is divided into placenta accreta (PA), placenta increta (PI), and placenta percreta (PP) [2]. Of these, PA is most common, accounting for 50.7% of all PAS cases, but the risk is relatively low. The PA group was used as the “mild” group (control) in the present study. The incidences of PI and PP are lower (24.2% and 25.1%, respectively), but

PI and PP often trigger massive bleeding, hemorrhagic shock, and even a need for hysterectomy [3]. Thus, the PI and PP patients constituted the “severe” group in this study. Diagnosis of prenatal PAS includes evaluation of clinical risk factors (CRFs), ultrasonography (US), magnetic resonance imaging (MRI), and serological examinations [4]. US is currently preferred for evaluating the extent of PAS, with a sensitivity and specificity of 0.90 and 0.83, respectively [5]. In patients who have undergone previous cesarean deliveries, implantation of the gestational sac in the lower uterine segment, as revealed by US, early during the first trimester often indicates PAS. A cesarean scar pregnancy (CSP) markedly increases PAS risk [6]. A placental implantation scoring system that combines CRFs with US signs in the second and third trimesters is useful for assessing PA severity [7]. However, prediction during the first trimester would guide management of later pregnancy stages and reduce the incidence of adverse outcomes. This has received little attention.

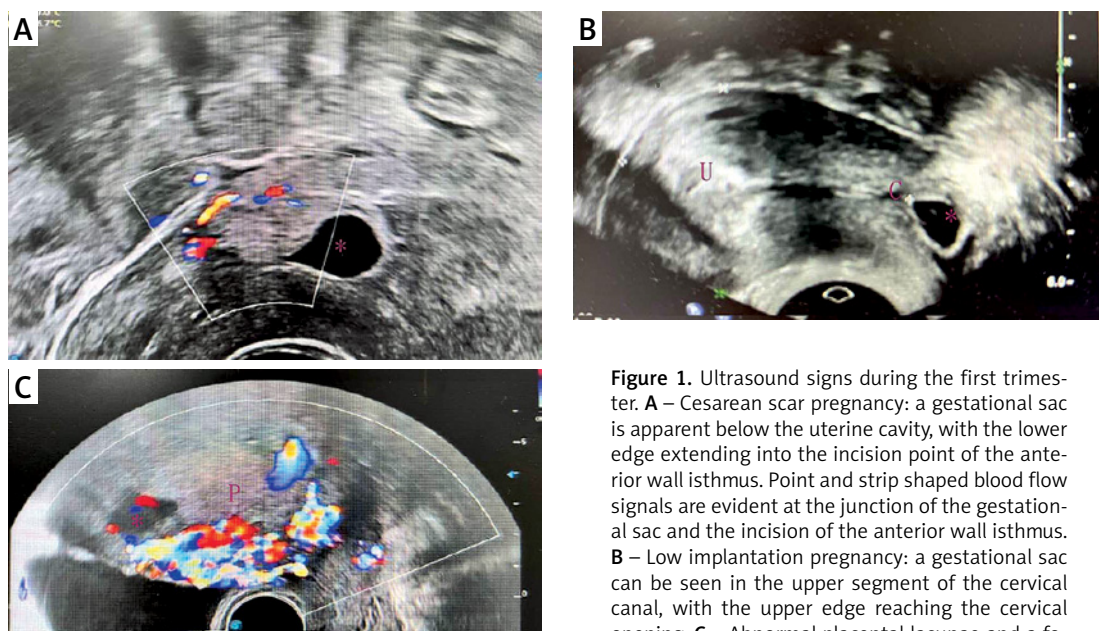
PAS is a dynamic condition, and placental implantation gradually worsens during pregnancy. Integration of US signs during all three trimesters would improve prediction of PAS and the associated adverse outcomes [8]. As CRFs or US signs may detect PAS during the first trimester, we systematically compared their utility in predicting severe PAS.

### Material and methods

Consecutive pregnant patients with PAS who underwent US at our institution for suspicion of

PAS between March 1, 2017 and December 31, 2022 were analyzed retrospectively. The CRFs for PAS were retrieved from medical records and comprised maternal age, pregnancy method, body mass index, gravidity, parity, the number of abortions and cesarean sections (CSs), any history of uterine cavity procedures, uterine adhesions, uterine malformations, the relationship of the placenta to the uterine myometrium, and pathological examination results. US images taken at different gestational weeks were collected from women with a cesarean scar pregnancy (CSP), low implantation pregnancy, abnormally positioned or unusually thick placenta, focal exophytic mass (FEM), abnormal placental lacunae (PL), and myometrial thinning. The inclusion criteria were (i) PAS, (ii) all US examinations performed within the same week, and (iii) no other pregnancy complication. We excluded patients (i) with unavailable or incomplete US images, (ii) missing or incomplete clinical data, or (iii) severe comorbidities. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institution, and written consent was obtained before the study.

Transabdominal and transvaginal US examinations were performed by two trained physicians. Placental location, internal structure, and the relationship to nearby organs were evaluated (Figure 1). Color Doppler US was employed to assess blood flow at any suspected placental lacuna. The fetus and accessory structures were observed, as



**Figure 1.** Ultrasound signs during the first trimester. **A** – Cesarean scar pregnancy: a gestational sac is apparent below the uterine cavity, with the lower edge extending into the incision point of the anterior wall isthmus. Point and strip shaped blood flow signals are evident at the junction of the gestational sac and the incision of the anterior wall isthmus. **B** – Low implantation pregnancy: a gestational sac can be seen in the upper segment of the cervical canal, with the upper edge reaching the cervical opening. **C** – Abnormal placental lacunae and a focal exophytic mass. The boundaries between certain placental and muscle layers are unclear, and the posterior placental space is absent

\*gestational sac, U – corpus uteri, C – cervix, P – placenta.

were the US features postpartum. In case of disagreement, a third doctor with more experience was consulted. The CSP, low implantation, placental position, FEM, and PL statuses were incorporated into the regression model.

The guidelines state that clinical diagnosis of PAS during delivery is more valuable than pathological diagnosis. The clinical grades are level 1 (adhesive), abnormal adhesion of the placenta; level 2 (implantable), abnormal invasion of the placenta; and level 3 (penetrating), abnormal invasion of the placenta [4, 9]. All patients were scored based on their placental status during delivery.

### Statistical analysis

Measurements are expressed as the mean  $\pm$  standard deviation, and the *t*-test or  $\chi^2$  test was used to compare the value between the two groups. Numerical data are expressed as the frequency (%), and the  $\chi^2$  test or Fisher's exact test was used to compare these values between the two groups. Two-sided *p*-values < 0.05 were considered statistically significant. Receiver operating characteristic (ROC) curve analysis was used to calculate the areas under the curves (AUCs) for the accuracy of CRFs and US signs in predicting PAS. The Youden index (YI) was used to derive the optimal AUC values. All statistical analyses were performed using SPSS ver. 26.0.

### Results

A total of 150 patients who underwent US examinations at our institution during the same week were initially included. Of these patients,

15 were excluded for the following reasons: serious complications (*n* = 7), incomplete data (*n* = 4), and loss to follow-up (*n* = 4). Finally, 135 patients were enrolled.

By comparing the CRF and relevant examination data of the two groups (mild group, PA patients; severe group, PI and PP patients), the results showed that the principle CRFs for severe PAS were the number of CSs, CSP, low implantation pregnancy, abnormal placental position, FEM and PL (all *p* < 0.05) (Table I).

Logistic regression revealed that only abnormal placental position and PL were independently significant (Table II).

Only the number of CSs was a risk factor for severe PAS. The ROC curve for predicting severe PAS by CS revealed an AUC of 0.661, and the optimal critical value was 1, with a sensitivity of 52.30% and specificity of 79.60% (Figure 2).

The AUC obtained for each US sign ranked as follows: low implantation pregnancy (0.751), PL (0.698), CSP (0.686), abnormal placental position (0.655), and FEM (0.618) (Figure 3).

We combined the number of CSs with various US signs and generated ROC curves. The combination of the number of CSs with CSP (AUC = 0.677) or PL (AUC = 0.655) did not increase the accuracy of predicting severe PAS. When other first-trimester US signs (low implantation pregnancy, abnormal placental position and FEM) were combined with the number of CSs, the resulting AUCs for predicting severe PAS were larger than those of the US signs alone. The largest AUCs were found when low implantation pregnancy and abnormal placental position were combined with the num-

**Table I.** Risk factors in the two groups

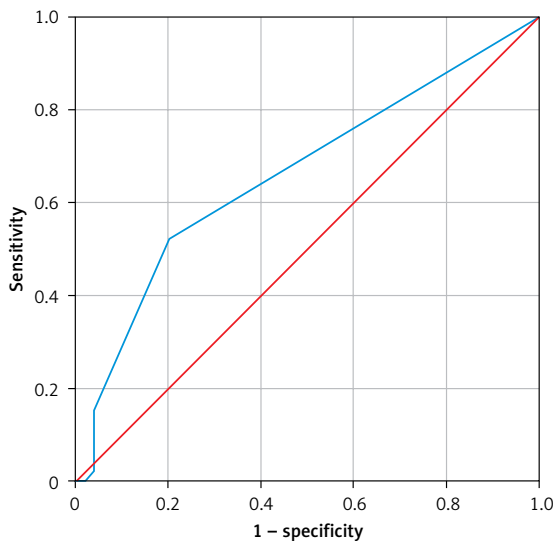
Parameter	Mild group ( <i>n</i> = 49)	Severe group ( <i>n</i> = 86)	<i>P</i> -value
Maternal age	33.24 $\pm$ 0.69	35.56 $\pm$ 0.45	0.54
Natural pregnancy	30 (61.2%)	62 (72%)	0.24
Bleeding	14 (28.50%)	34 (39.50%)	0.20
BMI	21.40 $\pm$ 0.42	21.94 $\pm$ 0.33	0.83
Uterine malformation	1 (2.00%)	2 (2.30%)	0.91
Gravidity	3.49 $\pm$ 0.27	4.19 $\pm$ 0.19	0.75
Parity	0.41 $\pm$ 0.11	0.92 $\pm$ 0.08	0.57
Abortion	2.04 $\pm$ 0.25	2.23 $\pm$ 0.18	0.77
Number of CSs	0.31 $\pm$ 0.11	0.7 $\pm$ 0.08	0.04
CSP	0	32 (37.20%)	0.00
Low implantation pregnancy	1 (2.00%)	45 (52.3%)	0.00
Abnormal placental position	27 (55.10%)	74 (86.00%)	0.00
Placental thickness	15.78 $\pm$ 0.46	16.88 $\pm$ 0.60	0.07
FEM	5 (10.20%)	29 (33.70%)	0.00
PL	1 (8.10%)	41 (47.60%)	0.00

BMI – body mass index, CS – cesarean section, CSP – cesarean scar pregnancy, FEM – focal exophytic mass, PL – abnormal placental lacunae.

**Table II.** Results of multivariate logistic regression analysis of the two groups

Parameter	B	S.E.	Wald	P-value	OR	95% CI
Maternal age	0.035	0.067	0.274	0.601	1.036	0.908–1.182
Natural pregnancy	0.098	0.607	0.026	0.871	1.103	0.336–3.625
Bleeding	0.394	0.58	0.462	0.497	1.483	0.476–4.622
BMI	0.086	0.089	0.94	0.332	1.09	0.916–1.298
Uterine malformation	-0.305	2.457	0.015	0.901	0.737	0.006–90.954
Gravidity	2.052	1.622	1.6	0.206	7.784	0.324–187.103
Parity	-1.971	1.728	1.3	0.254	0.139	0.005–4.124
Abortion	-2.08	1.615	1.659	0.198	0.125	0.005–2.959
Number of CSs	0.294	0.613	0.23	0.632	1.341	0.404–4.458
CSP	1.744	0.678	6.62	0.597	5.718	0.515–21.58
Low implantation pregnancy	-0.115	0.094	1.484	0.223	0.891	0.741–1.073
Abnormal placental position	1.808	0.641	7.966	0.005	6.097	1.737–21.395
Placental thickness	-0.108	0.093	1.345	0.246	0.898	0.749–1.077
FEM	-1.984	1.217	2.657	0.103	0.137	0.013–1.494
PL	2.825	0.868	10.593	0.001	16.869	3.077–92.48

BMI – body mass index, CS – cesarean section, CSP – cesarean scar pregnancy, FEM – focal exophytic mass, PL – abnormal placental lacunae.

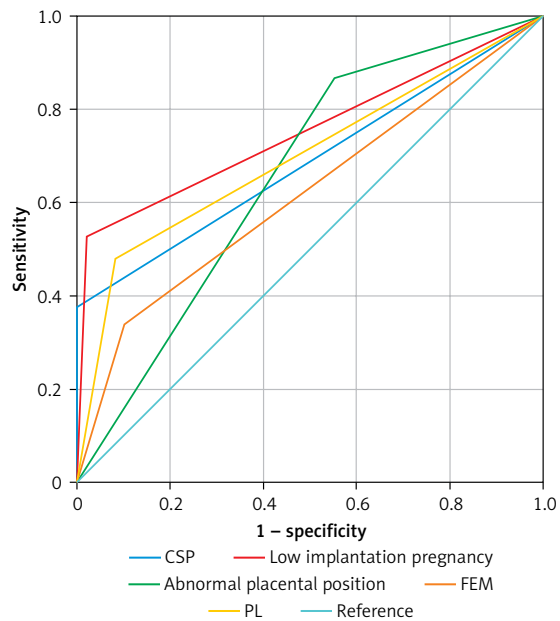


**Figure 2.** Receiver operating characteristic (ROC) curve showing the accuracy of the number of cesarean sections for predicting severe placenta accreta (area under the curve (AUC) = 0.661)

ber of CSs (AUCs = 0.779 and 0.727, respectively) (Figure 4).

Although the number of abortions was not significant, the guidelines consider that a history of abortion is a risk factor for PAS; we thus included this in the ROC analysis. Addition of the number of abortions to the US signs improved the accuracy of predicting severe PAS (Table III).

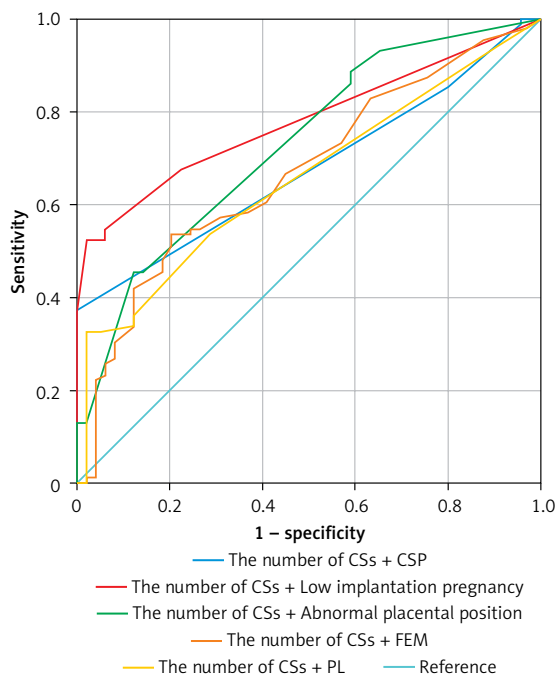
The combinations of the number of CSs, the number of abortions, the number of CSs and abortions with relevant US signs improved the predictive accuracy, with AUCs of 0.886, 0.891, and 0.888, respectively (Figure 5).



**Figure 3.** Receiver operating characteristic (ROC) curves showing the accuracy of ultrasound signs for predicting severe placenta accreta (area under the curve (AUC) for low implantation pregnancy, abnormal placental lacunae (PL), cesarean scar pregnancy (CSP), abnormal placental position (PL), and focal exophytic mass (FEM): 0.751, 0.698, 0.686, 0.655, 0.618, respectively)

### Discussion

In this case-control study, we found significantly higher numbers of CSs, CSP, low gestational sac positions, abnormal placental position, PL and FEM in the severe PAS group. Both CRFs and first trimester US signs predicted severe PAS, with



**Figure 4.** Receiver operating characteristic (ROC) curves showing the accuracy of combining the number of cesarean sections with ultrasound signs for predicting severe placenta accreta (area under the curve (AUC) for number of cesarean sections (CSs) + low implantation pregnancy, number of CSs + abnormal placental position, number of CSs + cesarean scar pregnancy (CSP), number of CSs + focal exophytic mass (FEM), number of CSs + abnormal placental lacunae (PL): 0.779, 0.727, 0.677, 0.669 and 0.655, respectively)

AUCs of 0.661 and 0.75, respectively. The combination of CRFs and US signs enhanced predictive accuracy, with an AUC of 0.89.

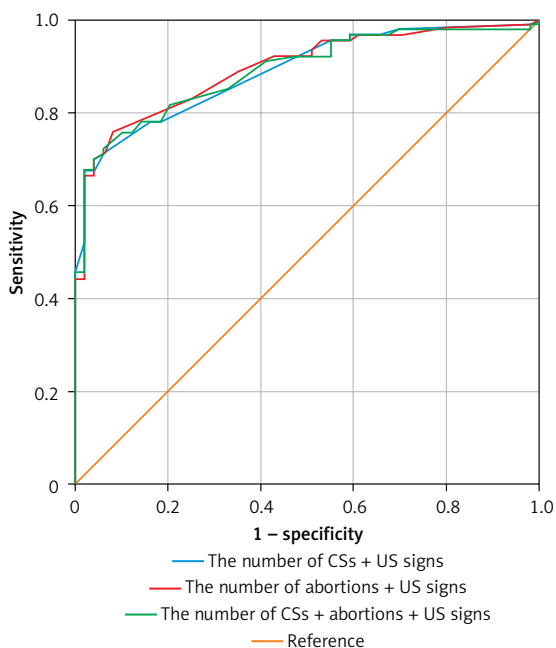
Early identification of high-risk patients, especially PI and PP patients, is essential for appropriate management. Placenta previa and scarred uterus are independent risk factors for PAS. Other risk factors include a history of uterine surgery, smoking during pregnancy, uterine lesions or structural abnormalities, *in vitro* fertilization and embryo transfer (IVF-ET), and a twin pregnancy [10, 11]. PAS diagnosis relies on intra- and post-operative features [12]. US is the recommended diagnostic tool, but its accuracy is rather low [13]. CRFs are somewhat predictive of PAS. The AUC of US findings alone for predicting PAS was only 0.69; addition of the CRFs to the US findings increased the AUC to 0.83 [14]. As CRFs and US examination are commonly used to diagnose PAS, we explored the utility of CRFs and first-trimester US signs for predicting severe PAS.

All our patients had PAS. On univariate analysis, only the number of CSs (among the CRFs) differed significantly ( $p < 0.05$ ) between the two groups. A history of CS, placenta previa, *in vitro* fertilization, and minor surgical procedures such as uter-

**Table III.** Prediction of severe placenta accreta by the combination of number of abortions and ultrasound signs

	AUC	P-value
Number of abortions + CSP	0.72	< 0.001
Number of abortions + low implantation pregnancy	0.77	< 0.001
Number of abortions + abnormal placental position	0.672	0.001
Number of abortions + FEM	0.661	0.002
Number of abortions + PL	0.71	< 0.001

CSP – cesarean scar pregnancy, FEM – focal exophytic mass, PL – abnormal placental lacunae.



**Figure 5.** Receiver operating characteristic (ROC) curves showing the accuracy of combining clinical risk factor with ultrasound signs for predicting severe placenta accreta (area under the curves (AUCs) for number of abortions + ultrasound (US) signs, number of cesarean sections (CSs) + US signs, and number of abortions and CSs + US signs: 0.891, 0.886, and 0.888)

ine curettage are risk factors for PAS [15–17]. Our CRF data agree with earlier observations that the number of prior CSs is a risk factor for PAS. We did not identify some factors reported by others; this may be because our control group comprised PA patients, whereas the control groups of other groups had no PAS. Also, we focused on risk factors for severe PAS in this study, while other studies examined risk factors for both mild and severe PAS. Earlier studies evaluated women with placenta previa with or without a CS history only during their second or third trimester [18], whereas we enrolled all women with or without a CS history. In general, a prior CS is closely associated with severe PAS [14, 18].

In terms of first-trimester US signs, a low implantation pregnancy, abnormal placental position, PL and FEM status correlated significantly with severe PAS (all  $p < 0.05$ ). The results suggest that both CRFs and first-trimester US signs are predictive of severe PAS.

On multivariate analysis, abnormal placental position and PL were the only independent factors that significantly predicted severe PAS, as was also true for women in their second and third trimesters [19]. Our results suggest that placenta previa and PL, representing severe PAS, in the placental parenchyma are the most important US signs predicting PAS. This is consistent with the results of other studies that used scoring systems employing a combination of CRFs and US signs in the second and third trimester to evaluate PAS severity [20]. One study found that first-trimester US signs were good predictors of PAS [21]. We combined these US signs with CRFs to identify patients at high risk of PAS, which guided management of later pregnancy stages. CRFs and US are commonly used for prenatal PAS diagnosis. We found that severe PAS was predicted more accurately by the combination of CRFs with first-trimester US signs than by CRFs or US signs alone. On univariate analysis, the rates of CSP and low gestational sac position were significantly higher in the severe group (37.2% and 52.3%) than in the mild group (0% and 2%), suggesting that these factors predict the development of severe PAS in late pregnancy, consistent with previous research [22, 23]. CSP and a low implantation pregnancy revealed by first trimester US have been employed to diagnose PAS [24]. Recent studies used different scoring systems, including a combination of CRF and US signs, to better predict PAS [25]. Abu Hashim *et al.* [26] found that combined CRFs and US PAS-related examinations in the second and third trimesters improved predictive accuracy compared with US alone. In our study, the AUC of CRF (the number of CSs) alone for predicting severe PAS was only 0.661, with low sensitivity and specificity. In terms of first-trimester US signs, the AUCs of low implantation pregnancy, PL, CSP, abnormal placental position, and FEM were 0.751, 0.698, 0.686, 0.655, and 0.618, respectively.

In terms of predictions afforded by the CRFs and first-trimester US signs, the combination of the CS number with low implantation pregnancy status was the most accurate, followed by the combination of CS number with placental position. The number of abortions is a risk factor for PAS [27, 28]. Although that number did not differ between the two groups, abortion may damage the endometrium and thus trigger PAS. Therefore, we considered abortion as a CRF. The AUC of the abortion number combined with a low implantation pregnancy was 0.77. CRFs combined

with several first-trimester US signs yielded an AUC of 0.891, and thus was highly predictive of severe PAS.

Our work had certain limitations. First, we focused on CS history and the number of abortions, which are known risk factors for severe PAS. The prior history of CS was a result of our study compared with mild PAS. Our results may tend to reflect the risk factors and early prediction of severe PAS. Second, this was a retrospective study with a limited sample size. Multi-center randomized controlled trials are needed. Third, we explored the predictive utility of only maternal age, CS number and a history of uterine cavity operation. Other risk factors including multiple pregnancies and smoking during pregnancy were not evaluated; such CRFs may enhance PAS prediction.

In conclusion, our study suggests that CRFs and first trimester US data are predictive of PAS. Predicting PAS would improve pregnancy management and outcomes.

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## Ethical approval

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Medical Ethics Committee of the Xiangya Hospital Central South University (202304083).

## Conflict of interest

The authors declare no conflict of interest.

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