ORIGINAL RESEARCH ARTICLE

Predictive value of doppler ultrasound blood flow indicators and placental growth factors in patients with severe preeclampsia

DOI: 10.29063/ajrh2025/v29i5.12

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Abstract

This study aimed to improve the diagnostic efficacy of severe preeclampsia (SP) and enhance fetal outcomes by investigating the predictive value (PV) of 3D energy Doppler ultrasound flow parameters and maternal peripheral blood placental growth factor (PLGF). Clinical data were obtained from 105 SP patients and 100 normal controls (NC). Ultrasound was used to measure blood flow parameters such as the systolic/diastolic velocity ratio (S/D), resistance index (RI), and pulsatility index (PI) in the uterine, umbilical, and middle cerebral arteries (MCA). Additionally, PLGF levels were assessed. Receiver operating characteristic (ROC) curves were used to evaluate the PV of these ultrasound parameters and PLGF levels. The results revealed significantly higher maternal blood pressure and lower fetal parameters, such as amniotic fluid index and fetal weight, in the SP group compared to the NC group ($P<0.05$). The combination of ultrasound blood flow parameters and PLGF levels showed the best predictive performance for SP, with sensitivity of 91.43%, specificity of 90.00%, and an AUC of 0.896. These findings suggest that combining ultrasound and PLGF measurements offers a reliable method for predicting severe preeclampsia. *(Afr J Reprod Health 2025; 29 [5]: 136-145).*

Keywords: severe preeclampsia; 3D energy Doppler ultrasound; arterial blood flow parameters; placental growth factor

Résumé

Cette étude visait à améliorer l'efficacité diagnostique de la prééclampsie sévère (PS) et l'issue fœtale en étudiant la valeur prédictive (VP) des paramètres de débit échographiques Doppler 3D et du facteur de croissance placentaire périphérique (FGP) maternel. Les données cliniques ont été recueillies auprès de 105 patientes PS et de 100 témoins normaux (TC). L'échographie a permis de mesurer des paramètres de débit sanguin tels que le rapport des vitesses systolique/diastolique (RV/D), l'indice de résistance (IR) et l'indice de pulsatilité (IP) dans les artères utérines, ombilicales et cérébrales moyennes (ACM). De plus, les taux de FGP ont été évalués. Les courbes ROC (Receiver Operating Characteristics) ont été utilisées pour évaluer la VP de ces paramètres échographiques et des taux de FGP. Les résultats ont révélé une pression artérielle maternelle significativement plus élevée et des paramètres fœtaux significativement plus faibles, tels que l'indice de liquide amniotique et le poids fœtal, dans le groupe PS par rapport au groupe TC ($P < 0,05$). La combinaison des paramètres échographiques du débit sanguin et des taux de PLGF a montré la meilleure performance prédictive pour la SP, avec une sensibilité de 91,43 %, une spécificité de 90,00 % et une ASC de 0,896. Ces résultats suggèrent que la combinaison des mesures échographiques et PLGF offre une méthode fiable pour prédire la prééclampsie sévère. *(Afr J Reprod Health 2025; 29 [5]: 136-145).*

Mots-clés: : prééclampsie sévère ; échographie Doppler 3D ; paramètres du débit sanguin artériel ; facteur de croissance placentaire

Introduction

Preeclampsia is characterized by the onset of hypertension in pregnant women with normal blood pressure prior to pregnancy, typically after 20 weeks of gestation, and is accompanied by one or more end-organ dysfunctions[1]. Globally, the incidence of preeclampsia is approximately 3-5%, making it a common pregnancy complication and a leading cause of maternal mortality[2]. Statistics show that about 15% of preterm births are also attributable to preeclampsia[3]. Preeclampsia causes vasospasm in the small blood vessels, leading to reduced blood flow (BF) to multiple organs and systems, and triggers various complications. Preeclampsia can also lead to uterine atony, increasing the risk of postpartum hemorrhage, thereby posing a threat to the mother's life[4]. Preeclampsia may impair placental function to some extent, resulting in fetal growth restriction,

intrauterine distress, placental abruption, or even fetal death[5]. Severe preeclampsia (SP) is a more critical form of the disease, characterized by sustained hypertension during pregnancy accompanied by proteinuria. Given its severity, early prediction of SP is crucial for reducing the incidence of adverse pregnancy outcomes.

Color Doppler ultrasound imaging is a critical tool for predicting high-risk pregnancies and preeclampsia during prenatal care. It not only provides clear visualization of uterine morphological changes but also enables the assessment of alterations in intrauterine hemodynamic parameters[6]. In preeclampsia, widespread placental underdevelopment and fibrosis of the uteroplacental arteries lead to arterial narrowing, with failure in the remodeling of the uterine spiral arteries. This results in reduced blood flow to the placenta, inadequate placental perfusion, and, ultimately, impaired fetal growth and development in utero[7]. Maternal uterine arteries (UtA), fetal umbilical arteries (UA), and fetal middle cerebral arteries (MCA) are critical vessels in the uteroplacental-fetal circulation. Changes in their hemodynamic parameters have become significant indicators for predicting preeclampsia and perinatal outcomes[8,9]. Placental growth factor (PLGF) is an angiogenic factor secreted by trophoblast cells in the placenta. PLGF primarily exerts its biological functions by specifically binding to its receptor VEGFR-1/Flt-1, which uniquely regulates the function of trophoblast and endothelial cells, promoting neovascularization[10] Studies noted that several weeks prior to the clinical onset of preeclampsia, PLGF level in the maternal serum is notably reduced [11]. Therefore, measuring the PLGF levels in maternal blood can help identify the oxygen supply stress on trophoblast cells, allowing for the prediction of preeclampsia. However, the combined use of ultrasound BF parameters (BFPs) and PLGF for predicting SP still requires further evidence to support its clinical value.

Therefore, this study analyzed changes in 3D energy Doppler ultrasound BFPs and peripheral blood PLGF levels in obstetric patients with SP, while simultaneously evaluating the PV of these indicators for SP. The aim was to provide reference data for the clinical management of SP and to improve maternal and fetal outcomes.

Methods

General information

Retrospective clinical data were collected from 105 patients with SP and 100 normal controls (NC) who received treatment at Xi'an International Medical Center Hospital between January 2023 and January 2024. The participants were categorized into SP and NC groups based on their disease status. Inclusion criteria for SP group were: (1) those meeting the diagnostic criteria for SP [12], with onset before 34 weeks of gestation; (2) singleton pregnancy; (3) no other obstetric complications; (4) no other major organ dysfunction or endocrine abnormalities; (5) complete clinical data; (6) informed consent signed by the patient and their family. Exclusion criteria were: (1) multiple pregnancies; (2) premature rupture of membranes, intrauterine infection, fetal congenital diseases, etc.; (3) concomitant hypertension, diabetes, or other pregnancy-related complications or comorbidities.

Ultrasound BF index examination

Relevant BFPs were examined employing the Voluson E8 real-time 3D color Doppler ultrasound diagnostic system (General Electric Company, USA). A convex array volume probe (RAB 4-8-D) or a convex array probe (C1-5) was utilized, with probe frequencies set at 3–8 MHz or 2–5 MHz, respectively. All measurements were performed by the same associate chief physician in the ultrasound department. Each parameter was measured three times to generate an average value.

The patient was placed in a supine or lateral position, and after calm breathing to obtain stable and satisfactory BF spectrum images, the BFPs were measured employing the instrument's built-in analysis package. This included the systolic/diastolic velocity ratio (S/D), resistance index (RI), and pulsatility index (PI) for the maternal uterine artery (UtA), fetal umbilical artery (UA), and fetal middle cerebral artery (MCA).

Peripheral blood PLGF detection

On the day of delivery, fasting peripheral blood was collected from the patient's antecubital vein. After anticoagulation treatment, the sample was centrifuged at 3000 rpm for 10 minutes, to collect supernatant. Serum PLGF level was measured employing a fluorescence immunoassay with a fluorescence-labeled monoclonal antibody for PLGF (Shijiazhuang Huanzhong Biotechnology Co., Ltd., China). The detection range was 12–3000 pg/mL. The normal range for PLGF at 24–29 weeks of gestation was 131.4 pg/mL, and at 29–32 weeks of gestation, the normal range was 129.5 pg/mL.

Statistics

SPSS 23.0 was employed. Categorical data were denoted as frequencies or percentages, compared employing the $\chi 2$ test. For continuous data, those in normal distribution were presented as $\bar{x}\pm s$, compared employing t-test. Data not in normal distribution were presented as median (percentiles) [M (P25, P75)], compared employing the Wilcoxon or Mann-Whitney U test. ROC curves assessed the PV of ultrasound BFPs and serum PLGF for SP, and AUC was calculated. The optimal diagnostic cutoff value was also determined. $P<0.05$ means statistically significant.

Ethical considerations

This study had been approved by the Ethics Committee of Xi'an International Medical Center Hospital (approval number 2025-009).

Results

General data for postpartum women

A comparison of the general characteristics between the NC and SP groups revealed no significant differences in maternal age and gestational age ($P>0.05$). However, the SP group exhibited significantly higher systolic and diastolic blood pressure compared to the NC group. Additionally, the fetal amniotic fluid index, biparietal diameter, head circumference, abdominal circumference, femur length, and estimated fetal weight were all significantly lower in the SP group ($P<0.05$) (Table 1).

Ultrasound BFPs in postpartum women

A comparison of the ultrasound BFPs between groups revealed that S/D, RI, and PI values in the UtA and UA were drastically higher in SP group versus NC group, while the S/D, RI, and PI values in the MCA were markedly lower in SP group than in NC group ($P<0.05$) (Figure 1).

Note: A–C show S/D, RI, and PI parameters of the UtA, respectively; D–F show S/D, RI, and PI parameters of the UA, respectively; G–I show S/D, RI, and PI parameters of the MCA, respectively. *$P<0.05$ vs. NC group.

PLGF levels in maternal peripheral blood

A comparison of peripheral blood PLGF levels between groups showed that the PLGF levels were (238.4 ± 36.1) pg/mL in NC group and (10.9 ± 4.0) pg/mL in SP group. The PLGF levels in SP group were significantly less than the NC group ($P<0.05$) (Figure 2).

Diagnostic value of ultrasound BFPs and peripheral blood PLGF levels in SP

The PV of ultrasound BFPs (S/D, RI, and PI in UtA, UA, and MCA) and peripheral blood PLGF for SP was analyzed, and ROC curves were plotted. The optimal diagnostic cutoff values for UtA S/D, UtA RI, UtA PI, UA S/D, UA RI, UA PI, MCA S/D, MCA RI, MCA PI, and PLGF were determined to be 2.21, 0.66, 0.95, 2.79, 0.70, 1.04, 3.39, 0.71, 1.32, and 63.15 pg/mL, respectively. The corresponding AUC were 0.743, 0.738, 0.771, 0.806, 0.754, 0.811, 0.773, 0.650, 0.734, and 0.792 (Figure 3 and Table 2).

Note: A shows ROC curves for S/D, RI, and PI parameters of the UtA; B shows ROC curves for S/D, RI, and PI parameters of the UA; C shows ROC curves for S/D, RI, and PI parameters of the MCA; D shows ROC curve for peripheral blood PLGF levels.

Table 1: Contrast of general information

Data	NC group	SP group	*T*	*P*
Sample size	100	105		
Age (years old)	30.3±4.4	29.7±5.0	0.561	0.639
Gestational age (week)	32.5±1.6	33.1±3.4	0.329	0.740
Systolic blood pressure (mmHg)	120.6±10.8	161.8±12.5	11.447	0.000
Diastolic blood pressure (mmHg)	90.5±7.1	103.2±10.9	9.298	0.000
Amniotic fluid index	118.8±13.3	95.2±16.1	-9.749	0.000
Double top diameter (mm)	87.2±8.8	80.5±8.0	-4.126	0.002
Head circumference (mm)	310.4±21.5	297.7±24.6	-3.670	0.003
Abdominal circumference (mm)	289.9±30.4	270.3±33.1	-2.031	0.010
Femoral length (mm)	65.2±6.6	60.1±7.9	-4.542	0.002
Estimated weight (g)	2495.7±431.1	2073.6±542.9	-1.894	0.026

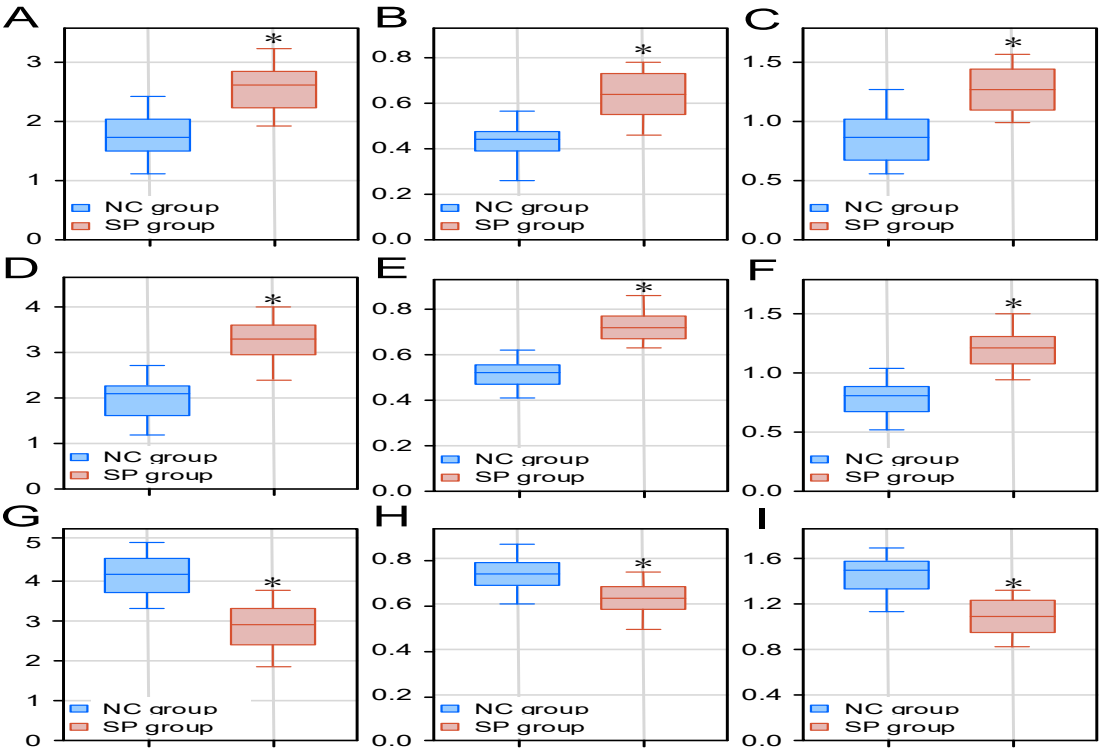

Figure 1: Contrast of ultrasound BFPs between groups.

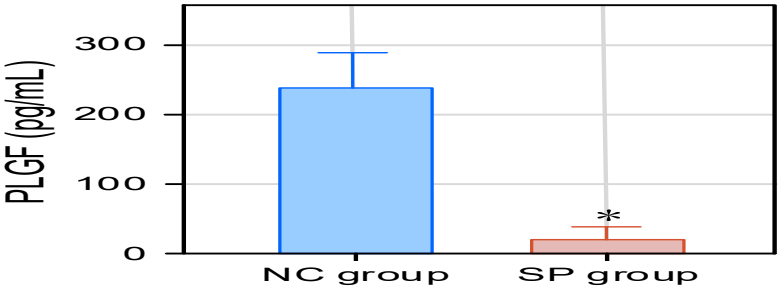

Figure 2: Contrast of peripheral blood PLGF levels between groups.
Note: *P<0.05 vs. NC group.

Table 2: Clinical value of ultrasound BFPs and peripheral blood PLGF levels in predicting SP

Item	Cutoff value	Sensitivity	Sensitivity	AUC	95% *CI*
UtA S/D	2.21	77.14%	71.00%	0.743	0.672~0.813
UtA RI	0.66	68.57%	82.00%	0.738	0.578~0.791
UtA PI	0.95	87.62%	63.00%	0.771	0.610~0.809
UA S/D	2.79	71.43%	84.00%	0.806	0.590~0.763
UA RI	0.70	69.52%	73.00%	0.754	0.556~0.774
UA PI	1.04	74.29%	73.00%	0.811	0.657~0.836
MCA S/D	3.39	86.67%	66.00%	0.773	0.702~0.829
MCA RI	0.71	83.81%	70.00%	0.650	0.691~0.808
MCA PI	1.32	80.95%	61.00%	0.734	0.572~0.816
PLGF	63.15	67.62%	83.00%	0.792	0.574~0.754

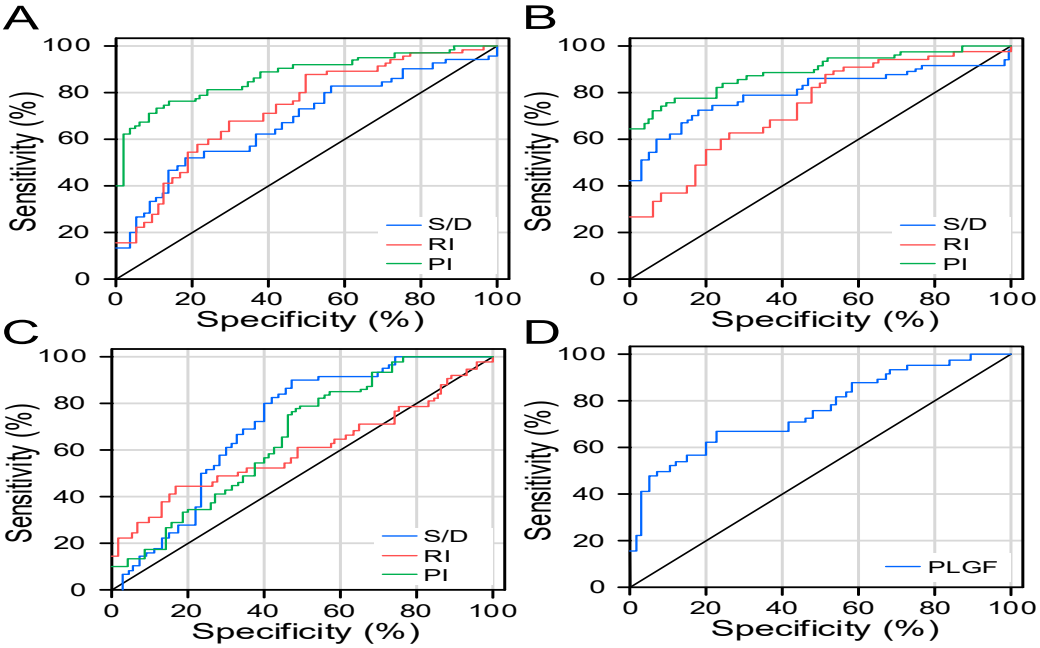

Figure 3: ROC curves for predicting SP employing ultrasound BFPs and peripheral blood PLGF levels.

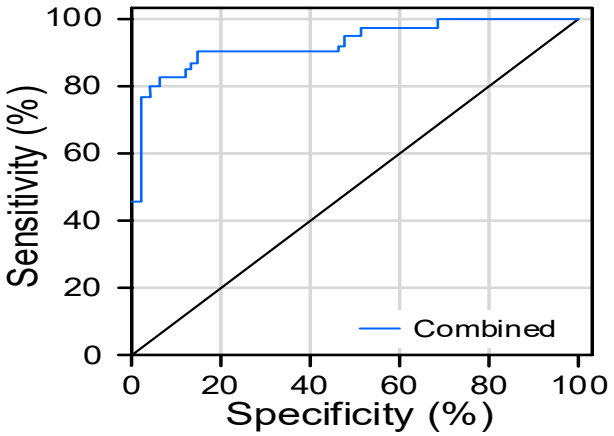

Figure 4: ROC curves for predicting SP employing combined ultrasound BFPs and peripheral blood PLGF levels.

Diagnostic value of ultrasound BFPs combined with peripheral blood PLGF levels in SP

The PV of combined ultrasound BFPs (S/D, RI, and PI in UtA, UA, and MCA) and peripheral blood PLGF for SP was analyzed, and ROC curves were plotted. The sensitivity of the combined prediction was 91.43%, the specificity was 90.00%, and AUC was 0.896, with a 95%CI of 0.707–0.890 (Figure 4).

Discussion

Preeclampsia is a hypertensive disorder of pregnancy, and SP represents a more severe form of this condition. The etiology of SP is complex and may be linked to abnormal activation of immune-inflammatory responses in the pregnant woman, leading to excessive proliferation of trophoblast cells, damage to endothelial cells in capillaries, and clinical manifestations such as edema and hypertension[13]. Preeclampsia is a key factor contributing to adverse pregnancy outcomes. Ardissino *et al*. (2023) demonstrated that hypertensive disorders during pregnancy increase the incidence of preeclampsia or eclampsia, and to some extent, raise the risk of preterm birth and placental abruption[14]. Therefore, early diagnosis of SP is crucial for improving pregnancy outcomes.

Color Doppler ultrasound examination can display the intrauterine growth of the fetus and assess the hemodynamic status of important maternal and fetal organs, thereby evaluating the maternal and fetal conditions[15]. This study found that, in women with SP, the amniotic fluid index, biparietal diameter, head circumference, abdominal circumference, femur length, and estimated fetal weight were significantly smaller compared to those in NC women. This suggests that fetal intrauterine growth is impaired in SP. This may be attributed to inadequate remodeling of small arteries in SP, leading to increased placental vascular resistance and reduced BF perfusion, which results in intrauterine fetal hypoxia and a slowed growth rate[16]. Adequate blood circulation during pregnancy is key to maintaining normal intrauterine fetal development, and hemodynamic parameters such as UtA, UA, and MCA are important indicators of the uteroplacental-fetal blood circulation during pregnancy[17,18] evaluated the effects of magnesium sulfate treatment and prevention for SP employing ultrasound hemodynamic parameters. They found that after medication, the UA RI and MCA RI markedly decreased, but the changes in the PI and S/D parameters of UA and MCA differed slightly [18]. In this study, UtA S/D, UtA RI, UtA PI, UA S/D, UA RI, and UA PI parameters in women with SP were notably inferior to those in NC women, while MCA S/D, MCA RI, and MCA PI parameters were greatly lower in women with SP versus NCs. This result is similar to the findings[19], who examined the changes in UtA, UA, and MCA hemodynamic parameters (S/D, RI, and PI) during pregnancy and observed that the parameters of UtA and PI were dramatically higher in women with SP compared to normal and mild preeclampsia groups, while the MCA parameters were dramatically lower[19].

The UtA is a key component of the uteroplacental circulation, where nutrient exchange occurs between the mother and fetus. The UA serves as an important vascular conduit between the placenta and fetus, and changes in its hemodynamic parameters can reflect physiological alterations in both the placenta and fetus. The UA is primarily influenced by cardiac contraction and vascular terminal resistance. When the end-diastolic flow in the UA disappears or reverses, it indicates damage to the placental-fetal circulation[20-22]found that the incidence of abnormal UA Doppler waveforms was markedly higher in women with SP, and an increased UA RI was associated with an increased risk of preterm birth. An elevated S/D ratio can also serve as a risk assessment marker for cesarean section and abnormal fetal monitoring[22,23]. showed that both UA RI and UA PI were notably elevated in women with SP, and these parameters can serve as independent risk factors for disease prediction[23]. MCA is the continuation of the fetal internal carotid artery trunk and an arterial vessel that supplies nutrients to the fetus's brain. In women with SP, the MCA S/D, MCA RI, and MCA PI values are reduced, which may be due to placental dysfunction. In response to hypoxic conditions, the fetus adapts its circulatory system by regulating fluid to prioritize blood supply to vital organs. This adaptive mechanism leads to reduced BF resistance in the MCA and an increase in BF.

This finding suggests that fetuses of women with SP may experience intrauterine growth restriction or other potential health issues, necessitating close monitoring and the implementation of appropriate interventions to ensure fetal safety. Subsequently, this study evaluated the PV of various ultrasound BFPs for SP and found that the prediction AUCs for UtA S/D, UtA RI, UtA PI, UA S/D, UA RI, UA PI, MCA S/D, MCA RI, and MCA PI were 0.743, 0.738, 0.771, 0.806, 0.754, 0.811, 0.773, 0.650, and 0.734, respectively. The corresponding sensitivities were 77.14%, 68.57%, 87.62%, 71.43%, 69.52%, 74.29%, 86.67%, 83.81%, and 80.95%, while the specificities were 71.00%, 82.00%, 63.00%, 84.00%, 73.00%, 73.00%, 66.00%, 70.00%, and 61.00%.[24]utilized continuous UtA Doppler ultrasound to predict preeclampsia and found that the sensitivity of UtA RI, PI, and bilateral notch for predicting preeclampsia in weeks 14–20 of pregnancy was 17.60%, 56.25%, and 71.00%, respectively. In weeks 20–28, the sensitivity for these parameters was 16.60%, 36.80%, and 55.50%, respectively[24,25]found that the sensitivity of UtA PI for screening preeclampsia in early pregnancy (11–13+6 weeks) was 68.00%, with a specificity of 52.99% [25]. These findings suggest that the ultrasound BFPs of UtA, UA, and MCA can be utilized for the prediction of SP.[26] included 353 early-pregnancy women in their study and found that the sensitivity, specificity, positive PV, and negative PV of UtA PI for predicting preeclampsia were 10.3%, 95.7%, 17.7%, and 92.3%, respectively. However, when combined with serum placental protein 13, the diagnostic efficacy greatly improved, with sensitivity, specificity, positive PV, and negative PV of 58.6%, 62.9%, 12.4%, and 94.4%, respectively[26]. Therefore, solely relying on ultrasound BFPs for the prediction of SP has certain limitations and is susceptible to operator skill. To enhance the predictive efficacy for SP, it is important to further understand its pathogenesis and identify effective risk biomarkers.

The exact pathogenesis of preeclampsia is currently believed to result from interaction of multiple factors, including maternal, placental, and fetal influences[27]. PLGF is a key angiogenic factor secreted by trophoblast cells in the placenta. It is primarily expressed in the placenta and plays a critical role as a paracrine factor in placental angiogenesis. Upon binding to its corresponding receptor, PLGF activates the receptor through phosphorylation, thereby mediating signal transduction via the tyrosine kinase pathway. This activation induces biological effects such as the proliferation, differentiation, and invasion of trophoblast and endothelial cells, as well as increasing vascular permeability[28,29]. During normal pregnancy, PLGF levels gradually increase as the gestational weeks progress, and it is crucial for maintaining normal placental function and fetal growth.[30] simulated the preeclampsia-like trophoblast environment under hypoxic conditions and found a drastic decrease in PLGF levels, along with trophoblast invasion[30,31]. also found that PLGF levels were considerably lower in the venous blood of patients with late-onset preeclampsia[31]. This is consistent with the findings of our study, where serum PLGF levels in women with SP were significantly lower compared to NCs. This may be attributed to endothelial damage in SP, which leads to systemic small arterial vasoconstriction, capillary constriction in the placental villi, reduced placental function, and a subsequent decrease in PLGF levels. The reduction in PLGF during pregnancy may impair the function of endothelial cells and trophoblasts, thereby triggering SP and contributing to adverse pregnancy outcomes[32,33]. The results confirmed a positive correlation between urinary PLGF levels and serum PLGF levels, with an AUC of 0.866 for urinary PLGF in predicting preeclampsia[33]. This finding is consistent with the present study, where the AUC for serum PLGF in predicting SP was 0.792, with a sensitivity of 67.62% and a specificity of 83.00%. This suggests that peripheral blood PLGF can be utilized for predicting SP. However, peripheral blood PLGF levels gradually increase with gestational age, reaching a peak between 28 and 30 weeks of pregnancy. Therefore, combining PLGF with other indicators is necessary for a more comprehensive evaluation.

In this study, the combination of ultrasound BFPs and peripheral blood PLGF for predicting SP resulted in an AUC of 0.896, with a sensitivity of 91.43% and specificity of 90.00%. This indicates that monitoring changes in ultrasound BFPs and

maternal peripheral blood PLGF levels can enhance the prediction of disease risk and provide clues for early intervention.

Limitations and strengths

This study provides valuable data support for improving the diagnostic efficiency of SP by evaluating the blood flow parameters of 3D power Doppler ultrasound and the PLGF level of maternal peripheral blood. Its advantage lies in the combination of various ultrasonic parameters and PLGF, which not only improves the diagnostic sensitivity and specificity, but also shows good predictive performance, providing a scientific basis for early identification of high-risk patients. However, this study also has some limitations. Firstly, although the sample size is relatively sufficient, the research object may be limited by the characteristics of a specific region or population, which limits the universal applicability of the results. Secondly, although the combination of ultrasound technology and PLGF measurement improves the diagnostic accuracy, the cost-benefit ratio of these methods in actual clinical application has not been clearly discussed, which may affect their wide application. In addition, due to the complexity and individual differences of severe preeclampsia, it is difficult for a single biomarker or imaging index to completely cover all cases, so future research needs to further explore more potential biomarkers or technical means to improve the diagnosis system. From the point of view of policy and practice, the results of this study are of great significance for improving pregnant women's health management and fetal prognosis. On the one hand, it emphasizes the importance of early screening and intervention. It is suggested that 3D power Doppler ultrasound examination and PLGF level determination should be included in the routine prenatal examination, so as to identify the risk factors of SP earlier and take preventive measures in time. On the other hand, for health policy makers, we should consider increasing investment and support in research and development of related detection technologies, promoting their popularization and application, and optimizing resource allocation to ensure efficient and economical service provision. In addition, it is necessary to strengthen the professional training of medical personnel, improve their understanding and operation ability of new technologies, so as to better serve the majority of pregnant women, and finally achieve the long-term goal of reducing the incidence of SP and improving maternal and child health

Conclusion

In conclusion, significant changes in the uteroplacental-fetal arterial BFPs and a marked decrease in peripheral blood PLGF levels were observed in women with SP. Monitoring ultrasound BFPs and peripheral blood PLGF levels plays a crucial role in improving the PV for the onset of SP, as well as in facilitating early intervention to enhance maternal and fetal outcomes.

Availability of data and materials

All data generated reanalyzed during this study are included in this published article (and its supplementary information files).

Competing interests

The authors have no competing interests to declare that are relevant to the content of this article.

Funding

No funding was received for this study

Acknowledgements

We would like to thank the 105 patients with severe preeclampsia and 100 normal controls who participated in this study.

Author contributions

Xiangni Li performed the data analysis; Wei Chen performed the formal analysis; Xiangni Liperformed the validation; Wei Chen wrote the manuscript.

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