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Clinical Analysis of Placental Growth Factor and Soluble FMS-Like Tyrosine Kinase-1 in Serum on the Severity of Preeclampsia

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Abstract: *Objective:* This study aims to analyze the differences in the expression of Placental Growth Factor (PLGF) and soluble Fms-like tyrosine kinase-1 (sFlt-1) in serum and their clinical significance in the severity of preeclampsia. *Methods:* This study selected 58 preeclampsia patients who underwent prenatal check-ups and gave birth in our hospital from September 2021 to September 2023 as the observation group. Based on the severity of their condition, they were divided into a mild group (n = 38) and a severe group (n = 20). Additionally, 795 healthy pregnant women who underwent prenatal check-ups in the hospital during the same period were included as the control group. Pearson correlation analysis was used to examine the correlation between serum sFlt-1 and PLGF expression and the severity of preeclampsia. *Results:* The observation group had higher sFlt-1 and lower PLGF levels compared to the control group. The severe group had higher sFlt-1 levels and lower PLGF levels compared to the mild group. The 24-hour urinary protein level was significantly higher in the observation group than in the control group ($p < 0.05$). Pearson correlation analysis revealed a positive correlation between 24-hour urinary protein quantification and serum sFlt-1 levels and a negative correlation with PLGF expression in preeclampsia patients ($p < 0.05$). *Conclusion:* The expression of sFlt-1 and PLGF in serum is closely related to the severity of preeclampsia, suggesting their potential as biomarkers for assessing the severity of preeclampsia.

Keywords: Placental Growth Factor; Soluble Fms-like tyrosine kinase-1; Preeclampsia

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1. Introduction

Preeclampsia (PE) is a complex syndrome specific to pregnancy, characterized by hypertension and proteinuria. It commonly occurs in pregnant women after 20 weeks of gestation [1]. Previous studies have found that the incidence of PE ranges from 2% to 8% [2]. PE not only threatens the health of the mother but may also lead to fetal growth restriction, intrauterine distress, premature birth, and increased risk of cardiovascular disease. Although the exact cause of this disease is not fully understood, studies have suggested that placental dysplasia, inadequate blood

flow supply, and placental hypoxia play a central role [3]. PLGF is a protein that promotes blood vessel growth, stimulating cell proliferation, differentiation of vascular endothelial cells, and angiogenesis. Conversely, sFlt-1 is a natural inhibitor of VEGF, strongly inhibiting its effects [4]. When PLGF binds to sFlt-1, it inhibits the angiogenic effect of PLGF, affecting the remodeling of spiral arteries in placental blood vessels, reducing placental blood perfusion, and triggering the onset of PE {5}. Therefore, this study aims to analyze the correlation between serum levels of PLGF and sFlt-1 and the severity of PE, aiming to provide more effective monitoring and intervention strategies for clinical practice, thereby improving the prognosis of both mother and child.

2. Materials and methods

2.1. General information

After review and approval by the hospital's medical ethics committee, 58 PE patients who underwent prenatal check-ups and gave birth in the hospital were selected as the observation group. Based on the severity of their condition, they were divided into a mild group (n = 38) and a severe group (n = 20). Additionally, 795 healthy pregnant women who underwent prenatal check-ups in the hospital during the same period were included as the control group. The observation group consisted of women aged 23–35 years, with an average age of (27.41 ± 3.30) years old, a gestational age range of 23–36 weeks, with an average of (31.68 ± 4.15) weeks. There were 42 primiparous and 16 multiparous women, with a body mass index ranging from 23–29 kg/m^2, averaging (24.08 ± 1.13) kg/m^2. The control group consisted of women aged 21–33 years old, averaging (26.83 ± 3.45) years old, with a gestational age range of 22–37 weeks, averaging (32.69 ± 4.57) weeks. There were 597 primiparous and 198 multiparous women, with a body mass index ranging from 22–29 kg/m^2, averaging (24.21 ± 1.43) kg/m^2. There were no statistically significant differences in baseline characteristics between the two groups (p > 0.05), indicating comparability.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Meet the diagnostic criteria for PE [6], including new-onset hypertension (blood pressure ≥ 140/90 mmHg) after 20 weeks of gestation with or without proteinuria (≥ 0.3 grams/24 hours); (2) Singleton pregnancy; (3) All participants must sign an informed consent form after fully understanding the study content.

Exclusion criteria: (1) Have chronic hypertension, diabetes, kidney disease, heart disease, or other chronic systemic diseases; (2) Experience severe complications during pregnancy, such as placenta previa, placental abruption, etc.; (3) Are receiving medication that may affect blood pressure or proteinuria levels.

2.3. Methods

(1) Detection of serum PLGF and sFIt-1: Draw 3 mL of fasting elbow venous blood from the pregnant woman. After the blood clots, centrifuge it at a rate of 3000 r/min for 10 minutes to separate the serum and store it frozen at -80 ℃. Use an electrochemical luminescence analyzer (Ningbo Aocheng Biotechnology Co., Ltd., model: Shine i1910) for measurement.

(2) 24-hour urine protein level detection: Collect urine from the pregnant woman from 8 a.m. on the day after admission to 8 a.m. on the following day. Use the orthophenanthroline molybdenum colorimetric method to determine the protein content in the 24-hour urine sample.

2.4. Observation indicators

According to the relevant diagnostic criteria for PE in "Obstetrics and Gynecology," 38 patients with 24-hour urine protein quantification < 300 mg were included in the mild group, and 20 patients with 24-hour urine protein ≥ 300 mg were included in the severe group.

2.5. Statistical analysis

The study used SPSS 20.0 statistical software to process the data. Count data were presented as percentages (%) and analyzed using the χ^2 test. For measurement data that followed a normal distribution, they were presented as (±s) and processed using the *t*-test. Intra-group data analysis was performed using the *q*-test, and correlation analysis was performed using the Pearson method. All tests used two-sided probability tests, and the results were considered statistically significant when the *P*-value was less than 0.05.

3. Results

3.1. sFIt-1 and PLGF levels in the control group and observation group

The sFIt-1 level in the observation group was higher than that in the control group, while the PLGF level was lower ($p < 0.05$). See **Table 1**.

Table 1. Comparison of sFIt-1 and PLGF levels between the control group and the observation group (±s, pg/mL)

Group	*n*	sFIt-1	PLGF
Control group	795	2036.77 ± 362.33	488.36 ± 117.19
Observation group	58	5025.56 ± 1038.31	248.41 ± 63.22
t	-	46.468	15.425
p	-	< 0.001	< 0.001

3.2. Levels of sFIt-1 and PLGF in mild and severe groups

The level of sFIt-1 in the severe group was higher than that in the mild group, while PLGF was lower in the severe group compared to the mild group ($p < 0.05$). See **Table 2**.

Table 2. Comparison of sFIt-1 and PLGF levels between mild and severe groups (±s, pg/mL)

Group	*n*	sFIt-1	PLGF
Mild group	38	3245.42 ± 736.74	301.28 ± 56.45
Severe group	20	8438.78 ± 1515.68	148.76 ± 63.60
t	-	46.989	19.688
p	-	< 0.001	< 0.001

3.3. 24-hour urine protein levels in control and observation groups

The 24-hour urine protein level in the observation group was significantly higher than that in the control group ($p < 0.05$). See **Table 3**.

Table 3. Comparison of 24-hour urine protein between control and observation groups (±s, g/24h)

Group	*n*	24h urine protein
Control group	795	0.21 ± 0.05
Observation group	58	2.06 ± 0.59
t	-	84.930
p	-	< 0.001

3.4. Correlation analysis

According to Pearson correlation analysis, there was a positive correlation between 24-hour urine protein quantification and serum sFt-1 level expression in preeclampsia patients (r = 0.672, $p < 0.001$), and a negative correlation with PLGF expression (r = -0.513, $p < 0.001$).

4. Discussion

Research has shown that damage and activation of vascular endothelial cells are key factors in the development of preeclampsia (PE). Abnormal expression of PLGF and its receptors is also closely related to endothelial cell damage [7]. After vascular endothelial cells are damaged, vascular permeability increases, leading to tissue hypoxia and blood concentration. Meanwhile, coagulation factor levels increase, while anticoagulant proteins and fibrinolytic factor levels decrease, resulting in an imbalance between the coagulation system and fibrinolytic system, which can easily lead to thrombosis or bleeding tendency. The prothrombotic state can cause fibrin deposition in the decidua of the uterine spiral arteries, damaging the placental vasculature and causing placental ischemia, hypoxia, and dysfunction. Subsequently, the placenta releases cytotoxic substances, further damaging the function of the mother's vascular endothelial cells, ultimately leading to the occurrence of PE and affecting the pregnancy outcome of the pregnant woman [8].

The results of this study indicate that the sFlt-1 level in the observation group was higher than that in the control group, while the PLGF level was lower. Within the observation group, the severe subgroup exhibited a higher sFlt-1 level and a lower PLGF level compared to the mild subgroup. Additionally, the 24-hour urinary protein level in the observation group was significantly higher than that in the control group ($p < 0.05$). The primary reason for these differences is placental insufficiency and vascular endothelial damage caused by preeclampsia (PE). sFlt-1, a protein produced by the placenta, regulates the biological effects of VEGF and PLGF by binding to and neutralizing them. Elevated levels of sFlt-1 can trigger vascular inflammatory responses and pathological changes, leading to edema, vasoconstriction, and other preeclampsia-related symptoms [9]. PLGF, a placental growth factor, plays a crucial role in regulating vascular permeability and angiogenesis. Its levels are influenced by placental blood flow conditions. Pregnant women with preeclampsia often experience abnormal placental blood flow and vascular issues, reflected in PLGF level changes. When PLGF levels decrease, the proliferation of endothelial trophoblasts increases, and their infiltration capacity decreases, leading to placental hypoxia and ischemia, ultimately triggering preeclampsia [10]. According to Pearson correlation analysis, there is a positive correlation between 24-hour urinary protein levels and serum sFlt-1 levels and a negative correlation with PLGF levels in women with preeclampsia ($p < 0.05$). These findings align with the research results of Zhao Shenglong *et al.* [11], indicating that using sFlt-1 and PLGF to diagnose PE has high sensitivity and specificity. PE

can cause placental insufficiency and systemic vascular endothelial damage. As an anti-angiogenic factor, elevated sFlt-1 levels reflect inhibition of placental angiogenesis and widespread endothelial damage, leading to impaired renal filtration and increased urinary protein excretion. Conversely, decreased PLGF levels signify a further reduction in placental blood flow and functional deterioration, exacerbating renal damage and increasing urinary protein levels.

5. Conclusion

In summary, serum sFlt-1 and PLGF expression are closely related to the severity of preeclampsia, serving as potential biomarkers for assessing PE severity. The increase in sFlt-1 and decrease in PLGF correlate with the progression of PE, aiding in early diagnosis and risk assessment using these biomarkers.

Disclosure statement

The authors declare no conflict of interest.

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