

Changes Of Serum PIGF, PECAM-1 and PAF In Patients with Gestational Hypertension and Their Relationship with Pregnancy Outcomes

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Abstract

Objective: To explore the changes of serum Placental Growth Factor (PIGF), platelet endothelial cell adhesion molecule 1 (PECAM-1) and Platelet Activating Factor (PAF) in patients with gestational hypertension and their relationship with pregnancy outcomes. **Methods:** According to types of diseases, they were divided into simple gestational hypertension group (n=31) and preeclampsia group (n=42). And 73 normal pregnant women during the same period were enrolled as normal group. The general obstetric data of all women were collected. The levels of serum PIGF, PECAM-1 and PAF were detected by enzyme-linked immunosorbent assay. The predictive value of serum PIGF, PECAM-1 and PAF for adverse pregnancy outcomes was analyzed by Receiver Operating Characteristic (ROC) curves.

Results: The levels of serum PIGF and PECAM-1 in simple gestational hypertension group and preeclampsia group were significantly lower than those in normal group, while PAF level was significantly higher than that in normal group ($P<0.05$). The incidence of neonatal asphyxia, neonatal growth restriction and neonatal distress in simple gestational hypertension group was lower than that in preeclampsia group. ROC results showed that the Area Under The ROC Curve (AUC) values of serum PIGF, PECAM-1, PAF and combined detection for predicting adverse pregnancy outcomes were 0.746, 0.723, 0.739 and 0.881, respectively ($P<0.05$). **Conclusion:** The changes of serum PIGF, PECAM-1 and PAF are closely related to adverse pregnancy outcomes in patients with gestational hypertension. Clinically, early prevention and intervention should be conducted to reduce the risk of diseases.

1. Introduction

Pregnancy-induced hypertension is a common and high morbidity of pregnant women during pregnancy, and it is also one of the main causes of maternal and neonatal mortality. It is mostly related to genetic factors, diabetes and insufficient nutritional intake, and often leads to limb edema, elevated blood pressure, body weakness, nausea and vomiting in pregnant women. In severe cases, systemic organ damage and pre-eclampsia may occur in pregnant women [1,2]. Therefore, how to prevent the occurrence of hypertension during pregnancy through early intervention has great clinical significance, which can reduce the incidence of adverse pregnancy outcomes. Previous studies have shown [3] that uterine arterial blood supply is very important for fetal growth and development. With the progress of pregnancy, serum Placenta Growth Factor (PIGF) gradually increases in trophoblast cells, which can effectively predict the occurrence and development of gestational hypertension and has certain value in the diagnosis of pregnancy outcome. The important cause of hypertension during pregnancy is superficial placental implantation caused by vascular

endothelial injury [4], and there is Platelet Endothelial Cell Adhesion Molecule-1 (PECAM-1) in placental implanted blood vessels. It is speculated that PECAM-1 may be involved in the progression of hypertension during pregnancy. Studies have confirmed that the expression level of platelet activating factor (PAF) is different in different degrees of gestational hypertension, which may affect the pregnancy outcome of pregnant women with gestational hypertension [5]. Therefore, this study mainly retrospectively analyzed the changes of serum PIGF, PECAM-1, PAF and their relationship with pregnancy outcomes in pregnancy-hypertensive parturients who had completed delivery in our hospital, in order to predict the occurrence of pregnancy-hypertensive parturients early and improve pregnancy outcomes.

2. Data and Methods

2.1. General data

A total of 73 pregnant women with gestational hypertension who delivered in our hospital from June 2020 to June 2021 were retrospectively selected as gestational hypertension group. According to the type of disease, they were divided into simple gestational hypertension group (n=31) and preeclampsia group (n=42). Seventy-three normal pregnant women in the same period were selected as the normal group. Inclusion criteria: ① meeting the diagnostic criteria of hypertensive disorders in pregnancy (2015); All were singleton pregnancies [6]. ② Complete clinical data. Exclusion criteria: ① pregnant women with hypertension before pregnancy; ② pregnant women with heart and cerebrovascular injury; ③ Complicated with hematological diseases; ④ patients with liver and kidney dysfunction; ⑤ Complicated with malignant tumor. This study was reviewed and approved by the Ethics Committee.

2.2. Methods

① The clinical data of the two groups were collected by electronic medical record system, including age, gestational age, history of diabetes and history of hypertension. ② One day before delivery, 5 ml of fasting venous blood was collected and stored in non-anticoagulant tubes after admission. After coagulation, the blood was centrifuged (Hettich Mikro220/220R centrifuge, Germany) and serum was separated (3000 R, 10 min). The supernatant was collected and stored in -20°C refrigerator for ≤ 2 h from collection to test. Serum levels of PIGF, PECAM-1 and PAF were detected by Enzyme-Linked Immunosorbent Assay (ELISA). The instrument is a miniature VIPAS automatic fluorescence microplate reader. Serum PIGF reagent and kit were purchased from Jiangxi Aboyin Biotechnology Co., LTD. Pecam-1 reagent and kit were purchased from Wuhan Finn Biotechnology Co., LTD. PAF reagent and kit were purchased from Shanghai Guangrui Biotechnology Co., LTD. All testing procedures are carried out in strict accordance with the instrument and reagent instructions. ③ Adverse pregnancy outcomes, including neonatal asphyxia, neonatal growth restriction and neonatal distress, were recorded.

2.3. Statistical analysis

SPSS 22.0 statistical software was used for data analysis, and ($\pm s$) was used to represent measurement data meeting normal distribution and homogeneity of variance. The differences between groups were compared by two-sample independent t-test, and the rate of count data was expressed by χ^2 test. One-way analysis of variance was used to compare the differences among the three groups. Receiver Operating Characteristic curve (ROC) was used to analyze the diagnostic value of serum PIGF, PECAM-1 and PAF on pregnancy outcome. $P < 0.05$ indicated statistically significant difference.

3. Results

3.1. Comparison of general data among the groups

There were no significant differences in age, gestational times and bad living habits between the two groups ($P > 0.05$). The proportion of history of hypertension and diabetes in the gestational hypertension group was significantly higher than that in the normal group ($P < 0.05$). See table 1. (Table 1).

Table 1: Comparison of general data in each group

| Group | N | Age | The number of pregnancy | | History of high blood pressure | | History of diabetes | | Bad lifestyle | |
|---------------------------------------|----|------------|-------------------------|-----------|--------------------------------|-----------|---------------------|-----------|---------------|-----------|
| | | | 1~2 | >2 | With | Without | With | Without | With | Without |
| Simple gestational hypertension group | 31 | 25.26±2.61 | 19(61.29) | 12(38.71) | 26(83.87) | 5(16.13) | 25(83.87) | 6(19.35) | 16(83.87) | 15(48.39) |
| Preeclampsia group | 42 | 25.37±2.15 | 22(52.38) | 20(47.52) | 30(71.43) | 12(28.57) | 32(76.19) | 10(23.81) | 23(54.76) | 19(45.24) |
| The normal group | 73 | 25.59±2.18 | 34(47.22) | 38(52.78) | 42(58.33) | 30(41.67) | 35(48.61) | 37(51.39) | 35(48.61) | 37(51.39) |
| F/ χ^2 | | 0.273 | 1.728 | | 6.85 | | 13.728 | | 0.407 | |
| P | | 0.761 | 0.422 | | 0.035 | | 0.001 | | 0.816 | |

3.2 Comparison of serum PIGF, PECAM-1 and PAF among groups

The serum PIGF and PECAM-1 levels of pregnant women in gestational hypertension group and preeclampsia group were significantly lower than those in normal group, and the serum PAF level was significantly higher than that in normal group ($P < 0.05$). Are shown in (Table 2).

Table 2: Comparison of serum PIGF, PECAM-1 and PAF among pregnant women in each group ($\pm s$)

| Group | N | PIGF (pg/mL) | PECAM-1 (pg/mL) | PAF (μ g/L) |
|---------------------------------------|----|----------------|-----------------|------------------|
| Simple gestational hypertension group | 31 | 161.25±10.42ab | 110.34±7.23ab | 16.45±2.35ab |
| Preeclampsia group | 42 | 156.62±9.55a | 108.02±6.90a | 19.31±3.15a |
| The normal group | 73 | 211.28±12.50 | 115.09±7.16 | 9.24±1.14 |
| F | | 398.632 | 14.351 | 322.919 |
| P | | <0.001 | 0.003 | <0.001 |

3.3 Comparison of adverse pregnancy outcomes between the simple gestational hypertension group and the preeclampsia group

The incidence of neonatal asphyxia, neonatal growth restriction, and neonatal distress in the simple gestational hypertension group were lower than those in the preeclampsia group ($P < 0.05$), as shown in (Table 3).

Table 3: Comparison of adverse pregnancy outcomes between gestational hypertension alone group and preeclampsia group

| Group | Asphyxia of newborn | Neonatal growth restriction | Neonatal distress |
|--|---------------------|-----------------------------|-------------------|
| Simple gestational hypertension group (n=31) | 4 (12.90) | 6 (19.35) | 5 (16.13) |
| Preeclampsia group (n=42) | 14 (33.33) | 20 (47.62) | 19 (45.24) |
| χ^2 | 4.007 | 6.214 | 6.848 |
| P | 0.045 | 0.013 | 0.009 |

3.4 Predictive value of serum PIGF, PECAM-1 and PAF levels on adverse pregnancy outcomes

The area under the ROC curve (AUC) of serum PIGF, PECAM-1, PAF and their combined detection in predicting adverse pregnancy outcome were 0.746, 0.723, 0.739 and 0.881 ($P < 0.05$), as shown in (Table 4) and Figure 1.

Table 4: ROC characteristics of serum PIGF, PECAM-1 and PAF levels in predicting adverse pregnancy outcomes

| Test result variable | AUC | 95%CI | P |
|----------------------|------|-------------|-------|
| PIGF | 0.75 | 0.590~0.902 | 0.007 |
| PECAM-1 | 0.72 | 0.569~0.878 | 0.014 |

| | | | |
|---------------------|------|-------------|--------|
| PAF | 0.74 | 0.589~0.889 | 0.008 |
| The joint detection | 0.88 | 0.775~0.987 | <0.001 |

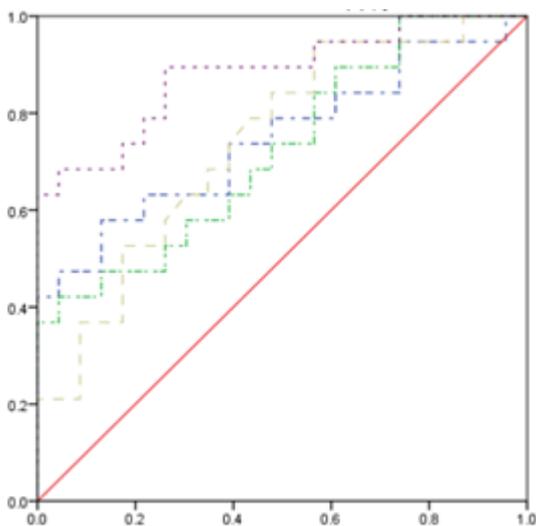


Figure 1: ROC curve of serum PIGF, PECAM-1 and PAF levels in predicting adverse pregnancy outcome

3. Discussion

Gestational hypertension is a unique and common obstetric complication that seriously threatens the life and safety of pregnant women. With the rise of living standards, the incidence of gestational hypertension is gradually increasing [7]. Gestational hypertension has a great impact on the health of pregnant women and fetuses, and is prone to cause adverse pregnancy outcomes such as premature birth, underweight, malformation, distress and growth restriction [8]. Therefore, early prediction of hypertension during pregnancy can effectively control the progression of the disease and improve adverse pregnancy outcomes. This paper studied the changes of serum PIGF, PECAM-1, PAF and their relationship with pregnancy outcomes, in order to provide a reference for clinical selection of appropriate detection indicators.

The results of this study showed that the serum levels of PIGF and PECAM-1 in pregnant women with gestational hypertension were significantly lower than those in normal group, and the levels of PAF were significantly higher than those in normal group, suggesting that early detection of serum levels of PIGF, PECAM-1 and PAF is of great significance for the occurrence of gestational hypertension. Serum PIGF, a member of vascular endothelial growth factor, is closely related to the placenta and can promote placental angiogenesis by stimulating the proliferation of endothelial cells [9,10]. Previous studies have shown [12,13] that low levels of serum PIGF in hypertensive pregnant women during pregnancy will cause disturbances in the normal function of placenta and abnormal maternal blood supply, resulting in reduced nutrient supply to pregnant women, and then induce adverse pregnancy outcomes such as fetal asphyxia and premature delivery. PECAM-1 is a glycoprotein widely distributed in monocytes and granulocytes [13], which is not detected in the trophoblast cells of the placenta of normal pregnant women. However, PECAM-1 is significantly reduced in pregnant women with hypertension during pregnancy, which may be related to the damage of maternal endothelial cells. By neutrophils PECAM 1 mediated through the release of inflammatory factor and other toxic substances that endothelial cell damage, leading to endothelial cell permeability increase, the clinical symptoms such as preeclampsia, along with the illness is aggravating, pregnant women blood vessel function and organization further damage, cause oxidative stress, prone to fetal growth restriction and amniotic fluid to reduce [14, 15], And then lead to adverse pregnancy outcomes. PAF is an inflammatory and platelet aggregation factor, mainly existing in vascular endothelial cells [16-19]. Previous studies [20-24] have shown that PAF levels in pregnant women with gestational hypertension increase with the severity of the disease, which is partially similar to the results of this study. It may be that the increased blood pressure of pregnant women with gestational hypertension leads to the high metabolism of arachidonic acid in vascular endothelial cells, thereby synthesizing excessive PAF and releasing it into the blood.

The PAF level is abnormally increased, and the damaged vascular endothelial cells release excessive PAF to increase vascular permeability, promote the accumulation of neutrophils, and cause the increase of blood pressure. In normal pregnancy, the uterus needs a complete vascular network for material exchange, and PAF plays an important role in the maintenance of embryo development and embryo sac implantation. When the condition of hypertension during pregnancy is more serious, the more PAF will be, leading to fetal birth and development restriction, low weight, and poor pregnancy outcome.

In this study, serum PIGF, PECAM-1 and PAF have predictive value for adverse pregnancy outcomes, suggesting that early detection of serum PIGF, PECAM-1 and PAF levels and timely intervention measures are beneficial to reduce the risk of pregnancy hypertension and adverse pregnancy outcomes. This research shows that, gestational hypertension group of neonatal asphyxia, neonatal growth restriction and the incidence of neonatal distress were higher than in normal group, prompt people with hypertension during pregnancy are more likely to happen adverse pregnancy outcomes, and Duan etc [25] enlightenment research part of the agreement, that control the incidence of hypertension during pregnancy may help to improve the pregnancy outcome.

In conclusion, abnormal changes in serum PIGF, PECAM-1 and PAF are found in pregnant women with gestational hypertension, and the detection of changes in serum PIGF, PECAM-1 and PAF levels can effectively predict the occurrence of adverse pregnancy outcomes. Early clinical prevention and intervention should be done, so as to reduce the risk of disease.

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