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Predictive and diagnostic value of serum sVEGFR-1 level in women with preeclampsia: A prospective controlled study

Preeklampsili kadınlarda sVEGFR-1 serum düzeyinin prediktif ve tanısal değeri: Prospektif kontrollü bir çalışma

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Abstract

Objective: Pre-eclampsia (PE), a pregnancy-specific syndrome consisting of hypertension and proteinuria occurring *de novo* after the 20th week of gestation, remains the leading cause of maternal and fetal morbidity and mortality worldwide. Endothelial dysfunction is proposed to be a central feature of the pathophysiology of preeclampsia. However, the mechanism by which this endothelial dysfunction occurs remains uncertain. We investigated the predictive and diagnostic value of serum soluble vascular endothelial growth factor receptor-1 (VEGFR-1) with by comparison of its prepartum and postpartum serum levels in the management of women with PE.

Materials and Methods: This prospective case-controlled study was composed of pre-eclamptic (n=44) and normal, healthy pregnant (n=44) women. Blood samples were collected before any intervention at the first antenatal examination of the women in the control group and at the admission of the women to the hospital in the PE group, additionally, from all women in the study groups within six hours of the postpartum period, and used for the serum VEGFR-1 analyses.

Results: Within both groups, prepartum serum levels of sVEGFR-1 were higher than postpartum levels ($p<0.05$). In PE, pre-partum and postpartum serum levels of sVEGFR-1 were higher than levels in the control group ($p<0.05$). Serum sVEGFR-1 levels of preeclamptic women were positively correlated with the degree of proteinuria ($p<0.05$, $r=0.25$), systolic ($p<0.05$, $r=0.25$), and diastolic blood pressure ($p<0.05$, $r=0.31$).

Conclusion: These findings seem to point to an involvement of sVEGFR-1 in the pathophysiology of PE. Serum sVEGFR-1 has the potential to be used as a valuable biomarker in the prediction, diagnosis, and risk management of women with subtypes of PE including mild and severe PE, HELLP syndrome, and eclampsia. There is a need to study serum sVEGFR-1 as a biomarker in pregnant women with different subtypes of PE.

Keywords: Preeclampsia, eclampsia, HELLP syndrome, hypertension, pregnancy, sVEGFR-1, soluble vascular endothelial growth factor receptor

Öz

Amaç: Gebeliğin 20. haftasından sonra meydana gelen hipertansiyon ve proteinüriden oluşan gebeliğe özgü bir sendrom olan preeklampsi (PE), dünya çapında maternal ve fetal morbidite ve mortalitenin önde gelen nedeni olmaya devam etmektedir. Preeklamsi patofizyolojisinde endotel disfonksiyonunun temel bir neden olduğu bilinmektedir. Bununla birlikte, bu endotel disfonksiyonunun meydana geldiği mekanizma belirsizliğini korumaktadır. PE'li kadınların tedavisinde prepartum ve postpartum serum seviyelerinin karşılaştırılmasıyla serum çözünür, vasküler endotelyal büyüme faktörü reseptörü-1'in (VEGFR-1) öngörücü ve tanısal değerini araştırdık.

Gereç ve Yöntemler: Bu prospektif olgu kontrollü çalışma preeklamptik (n=44) ve normal sağlıklı hamile (n=44) kadınlardan oluşmaktaydı. Kan örnekleri, kontrol grubundaki kadınların ilk doğum öncesi incelemesinde ve kadınların PE grubundaki hastaneye kabul edilmesinde, ayrıca doğum gruplarındaki tüm kadınlardan, altı saat sonra serum VEGFR-1 analizleri için serum toplandı.

PRECIS: Serum sVEGFR-1 has a potential be used as a valuable biomarker in the prediction, diagnosis, and risk management of women with subtypes of preeclampsia.

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Bulgular: Her iki grupta da sVEGFR-1 prepartum serum seviyeleri postpartum seviyelerden daha yüksekti (p<0,05). PE'de, sVEGFR-1'in prepartum ve postpartum serum seviyeleri, kontrol grubundaki seviyelerden daha yüksekti (p<0,05). Preeklamptik kadınların serum sVEGFR-1 seviyeleri, proteinüri derecesi (p<0,05, r=0,25), sistolik (p<0,05, r=0,25) ve diyastolik kan basınçları (p<0,05, r=0,31) ile pozitif korelasyon göstermiştir.

Sonuç: Bu bulgular sVEGFR-1'in PE'nin patofizyolojisine etkili olduğu görülmektedir. Serum sVEGFR-1, hafif ve şiddetli PE, HELLP sendromu ve eklampsi dahil PE alt tipleri olan kadınların tahmini, tanı ve risk yönetiminde değerli bir biyobelirteç olarak kullanılabilir. PE'nin farklı alt tiplerine sahip hamile kadınlarda biyobelirteç olarak serum SVEGFR-1'i incelemeye ihtiyaç vardır.

Anahtar Kelimeler: Preeklampsi, eklampsi, HELLP sendromu, hipertansiyon, gebelik, SVEGFR-1, çözünür vasküler endotelyal büyüme faktörü reseptörü

Introduction

Pre-eclampsia (PE) is a multisystem disorder that begins after the 20th week of pregnancy, progresses by hypertension and proteinuria, and has fatal complications. The fetus is at risk because of the possibility of adverse outcomes such as intrauterine growth retardation, preterm labor, placenta abruption, and intrauterine fetal hypoxia due to hypertension and uteroplacental vascular insufficiency during pregnancy. The incidence of PE is approximately 3-8% in pregnant women[1-3]. PE usually occurs during the first pregnancy. Multiple pregnancies, history of PE, chronic hypertension, pre-pregnancy diabetes mellitus, vascular and connective tissue diseases, nephropathy, antiphospholipid antibody syndrome, obesity, dyslipidemia, high testosterone and homocysteine levels, pregnancies aged 35 and over are other risk factors[4]. In normal pregnancies, the spiral arteries are enlarging, and their walls are reshaping. These changes extend to the inner 1/3 of the myometrium, providing low resistance flow to the intervillous space and are related to the invasion of fetal trophoblasts. While the trophoblast invasion is complete before the 22nd week of normal pregnancies, in PE cases, is not complete during these weeks. The pathogenesis of PE has three components: poor placentation, placental ischemia, and endothelial cell dysfunction that causes placental vascular complications[2]. Many factors have been considered in the development of PE. Many factors, such as disruption of prostaglandin I2-thromboxane balance and nitric oxide metabolism, production of vasoconstrictor agents, increased oxidative stress, toxic compounds produced by the placenta, disruption of placental cytokine production cause endothelial dysfunction in PE. The effects of placental agents on maternal vascular structures (e.g., platelets, endothelial cells, and neutrophils), maternal risk factors (renal, metabolic, and vascular diseases), genetic factors, and immune disorders predispose for developing PE during pregnancy[5]. Secondary to the vasospasm caused by the increased sensitivity of the vessels to vasopressor agents, blood flow to all organs decreased. Perfusion impairs by the activation of the coagulation. Additionally, plasma volume decreases with fluid loss from the intravascular space[6]. The human placenta needs extensive angiogenesis to supply oxygen and nutrients to the fetus and to form its vascular network. Many angiogenic growth factors such as vascular endothelial growth factor (VEGF), placental growth factor (PIGF), and soluble VEGF receptor (sVEGFR)-1 are produced in the placenta. The biological effects of the VEGF family are regulated by the type III subgroup of receptor tyrosine kinases (RTKs), including VEGFR-1 (Flt-1), VEGFR-2 (KDR/Flk-1), and VEGFR-3 (Flt-4) that bind to VEGF family members[7].

The development of PE includes mainly three factors: Abnormal placental vasculature, endothelial dysfunction, and placental ischemia. VEGF and PIGF, having angiogenic effects, are suggested important promoters in the human placenta. Moreover, decreased concentrations of circulating free VEGF and PIGF have been reported in PE. Additionally, it has been shown that the soluble form of VEGF receptor-1 is increased in the placenta and serum in pregnant women with PE[8].

In recent studies, the disorder of circulating angiogenic and antiangiogenic factors has clarified as a significant biomolecule in the pathophysiology of PE, but there are no reliable biomarkers are available to predict and diagnose PE[9]. This condition needs the investigation of RTKs. Maynard et al.[10] have shown that sVEGFR-1 levels increase in the preeclamptic subjects. They reported that if sVEGFR-1 was removed from the preeclamptic placenta or VEGF was administered to block sVEGFR-1, the antiangiogenic situation returned to normal. Those SVEGFR-1-related data make further studies possible in clinical settings with women with or without hypertensive disorders of pregnancy. We thought that serum sVEGFR-1 may change differently in pregnant and puerperal women with or without PE. Although there are extensive research activities, it remains unclear when during the third trimester that delivery should be accomplished for maximal maternal safety and minimal fetal risk; and there is a need for clinical studies examining the potential use of possible biomarkers of PE. In this research project, we assessed the predictive and diagnostic value of serum sVEGFR-1 with the comparison of its prepartum and postpartum serum levels in the management of women with PE.

Materials and Methods

This prospective controlled study included consecutive women with or without PE in the Sivas Cumhuriyet University Department of Obstetrics and Gynecology. All participants signed a written informed consent form on enrollment. Forty-nine women diagnosed with PE, and 49 healthy pregnant women, 98 patients, were included in this study. The study protocol was performed according with the principles of the Declaration of Helsinki and was approved by the Human Ethics Committee of Sivas Cumhuriyet University (protocol ID: 05.04.2005-4/5).

The control group consisting of healthy pregnant women included pregnant women with a singleton pregnancy without health problems including hypertensive disorders of pregnancy, diabetes mellitus, and liver, kidney, or endocrine disease, pregnancy with intrauterine growth retardation (IUGR) below the 10th percentile, and multiple pregnancies, pregnant women were excluded from the control group. The PE group included women with subtypes of PE, including mild and severe PE, eclampsia, and HELLP syndrome. PE criteria in pregnant women after 20 weeks of gestation who made up the PE study group were based on blood pressure of at least 140/90 mm Hg persisting for 6 h or more and proteinuria (urine protein of 300 mg/L or more or 1+ with a urine test stick) in two random urine samples[11]. If one or more of the following criteria were present, the women were diagnosed with severe PE, if (1) systolic blood pressure of 160 mmHg or higher or diastolic blood pressure of 110 mmHg or higher twice, at least 6-hour interval; (2) proteinuria in 24-hour urine 5 g or more, or 3+ or more in two random urine samples taken at least 4-hour interval; (3) oliguria (less than 400 mL in 24 h), elevation in serum creatinine; (4) cerebral dysfunction or visual impairment; (5) pulmonary edema or cyanosis; (6) epigastric or right upper quadrant pain, nausea, vomiting; (7) impaired liver function tests; (8) thrombocytopenia (<100x10^3/mm^3); and (9) IUGR. Other patients with PE were diagnosed as mild PE. Additionally, if patients had convulsions, they were diagnosed with eclampsia. In the presence of hemolysis, high liver enzymes, and decreased platelet criteria, the women were accepted to have HELLP syndrome[11]. Preeclamptic pregnant women with a history of chronic hypertension, diabetes mellitus, renal disease, and endocrine diseases were excluded from the PE group.

Clinical parameters including the age, gravidity, body mass index (BMI), weight gain during pregnancy, smoking, gestational week, systolic and diastolic blood pressures, amount of protein in the urine, hemoglobin, platelet count, blood urea nitrogen (BUN), creatinine, alanine transaminase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH), estimated fetal weight, and amniotic fluid index obtained by obstetric ultrasonography, mode of delivery, APGAR scores at 1 and 5 min, newborn weight, postpartum maternal complications, prepartum, and postpartum serum sVEGFR-1 levels, the presence of IUGR and placental abruption were recorded.

Before any intervention at the first antenatal examination of the women in the control group and at the admission of the women to the hospital in the PE group, additionally, from all women in the study groups with in six hours of postpartum period, blood samples were collected, and stored at -80 °C until analyses of the sVEGF-1. Collected serum samples were run on the ELISA (Triturus, Grifols Inc., California, USA) device with the sVEGFR-1 kit (BioSource International Inc., California, USA) and the results were recorded. The kit performance characteristics were sensitivity, 0.1 ng/mL, and coefficient of variation (CV%), <10.

Statistical Analysis

The conformity of the data with a normal distribution was evaluated with the Kolmogorov-Smirnov test and the variance homogeneity with the Levine test. Mann-Whitney U test was used to compare non-normally distributed variables. The medians of prepartum and postpartum serum sVEGFR-1 values in each group were compared with the Wilcoxon test. Normally distributed variables were compared with the t-test. The chi-square test was used in the comparison of the categorical variables. The relationship between clinical variables was evaluated with the Spearman and Pearson test according to the suitability of the data. A $p<0.05$ was considered statistically significant. In the power analysis with an effect size of 0.6, when the power was used as 85% and the alpha was accepted as 0.05, it was found that 41 control and 41 preeclamptic patients were required for the main variable of sVEGFR. With the addition of 20% drop-out, the study group had 49 participants.

Results

The study was completed with 44 women diagnosed with PE, and 44 healthy pregnant women, 88 patients. Eight pregnant women with PE did not participate in the study. In five pregnant women in each group, because of the work load, the study data were not collected completely and these participants were excluded from the study (Figure 1).

There were no significant differences between the pregnant women with PE and controls in terms of age, normal spontaneous vaginal delivery, and cesarean section ($p>0.05$).

In pregnant women diagnosed with PE, BMI, the arterial blood pressure (systolic and diastolic), and protein positivity in spot urine testing, the number of births with IUGR and placental abruption, was significantly higher than in healthy pregnant women ($p<0.05$).

The gestational age at delivery, birth weights were significantly lower in pregnant women diagnosed with PE compared with the control group ($p<0.05$) (Table 1).

In the preeclamptic patient group, 16 (36.4%) had mild PE, 12 (27.2%) severe PE, 3 (6.8%) eclampsia, 10 (22.8%) HELLP syndrome, 3 (6.8%) eclampsia and HELLP syndrome.

The medians of prepartum serum sVEGFR-1 values measured in the control and PE groups were higher than the postpartum serum sVEGFR-1 values ($p<0.05$). The median of prepartum serum sVEGFR-1 values of pre-eclamptic patients was

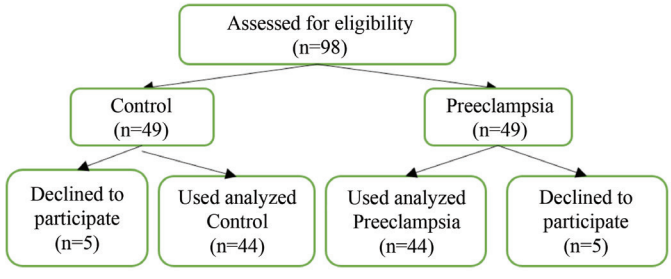

Figure 1. Flowchart of the study

significantly higher than the median of prepartum serum sVEGFR-1 values of the control group (p<0.05). The median of postpartum serum sVEGFR-1 values of pre-eclamptic patients was significantly higher than the median of postpartum serum sVEGFR-1 values of the control group (p<0.05) (Figure 2).

Platelet counts were lower and ALT, AST, and LDH levels were significantly higher in the PE group (p<0.05). There was no significant difference between the groups in terms of hemoglobin, BUN, and creatinine levels (p>0.05). In the preeclamptic patient group, 7 of the newborns had a birth weight below the 10th percentile, and 4 patients had placental abruption. There were no pregnant women with IUGR and placenta abruption in the control group. No correlation was found between IUGR and placental abruption and serum sVEGFR-1 level (p>0.05, r=0.08, and p>0.05, r=-0.08). There was a positive correlation between serum sVEGFR-1 levels and the degree of proteinuria (p<0.05, r=0.25), systolic (p<0.05, r=0.25) and diastolic blood pressure (p<0.05, r=0.31) in preeclamptic patients (Table 2).

Discussion

While regarding the age and rate of cesarean section, the control and preeclamptic groups, in terms of other baseline clinical characteristics of the study groups, there were meaningful changes supporting the adverse perinatal effects of PE. PE increased the prepartum and postpartum serum sVEGFR-1 levels. We found a meaningful association between PE with systolic blood pressure and proteinuria. PE caused some adverse results in hepatic function tests.

At currently, there is no adequate and practical screening method for PE. In the placenta, sVEGFR-1 is found in excess in the trophoblast layer. Studies have shown that sVEGFR-1 is increased in the placenta, serum, and amniotic fluid in PE[12]. It has been reported that sVEGFR-1 increases after the 12th week in patients who will develop PE, and serum levels decrease 24 h after delivery. However, VEGF level was evaluated as normal during these weeks. This indicates that sVEGFR-1 plays a more essential role in the pathogenesis of PE[13]. The increase in VEGF production in the following weeks is thought to be due to placental hypoxia resulting from insufficient invasion of spiral arteries by trophoblasts. The increase in sVEGFR-1 in PE

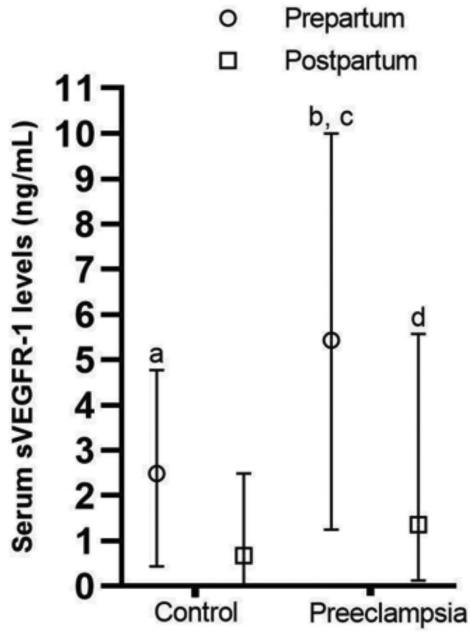

Figure 2. Prepartum and postpartum serum sVEGFR-1 levels of control and preeclampsia groups. Data are shown as median (minimum-maximum). a, p<0.05 vs postpartum serum sVEGFR-1 level of the control group. b, p<0.05 vs postpartum serum sVEGFR-1 level of preeclampsia group. c, p<0.05 vs prepartum serum sVEGFR-1 level of the control group. d, p<0.05 vs postpartum serum sVEGFR-1 level of the control group

sVEGFR-1: Soluble vascular endothelial growth factor receptor -1

Table 1. Selected clinical data of control and preeclampsia groups

	Control (n=44)	Preeclampsia (n=44)	p-value
Age (y)	27.1±5.8	29.1±6	NS
BMI (kg/m^2)	28.1±3.2	31±4.3	p<0.05
Gestational age at delivery (w), min-max (median)	29-42 (38)	26-40 (36)	p<0.05
Blood pressure (mmHg) Systolic, min-max (median) Diastolic, min-max (median)	 120 (90-135) 72.5 (60-85)	 140-200 (160) 90-140 (110)	p<0.05
Proteinuria (mg/dL), min-max (median)	0	30-500 (500)	p<0.05
Birth weight (g)	3025.9±669.8	2318±855.1	p<0.05
IUGR	0	7 (16%)	p<0.05
Placental abruption	0	4 (9.1%)	p<0.05
NSVD	18 (40.9%)	11 (25%)	NS
C/S	26 (59.1)	33 (75%)	NS

BMI: Body mass index, IUGR: Intrauterine growth restriction, NSVD: Normal spontaneous vaginal delivery, C/S: Cesarean section, NS: Non-significant

is also likely due to hypoxia or parallel to the increase in VEGF. It has been reported that VEGF stimulates the production of sVEGFR-1 in cultured endothelial cells[14].

Mateus et al.[15] found that VEGF-1 treatment in an animal study of PE reduces arterial blood pressure and prevents the onset of hypertension in late pregnancy. Their data demonstrated that VEGF administration reverses the effects of sVEGFR-1, playing an important role in PE.

Geva et al.[16] reported that pregnant women who have a baby with IUGR, had increased serum levels of VEGFR-1, VEGF-A, and sVEGFR-1, but there was no difference in the levels of free PIGF (fPIGF), VEGFR-2, neuropilin-1 (NRP-1). Bahlmann and Al Naimi[17] investigated the sFlt-1/PGF ratio and uterine artery Doppler indices for the diagnosis of PE. It studies reported that sFlt-1 levels were higher in early-onset pregnant of PE by other studies[18].

Muy-Rivera et al.[6] investigated the relationship between maternal plasma sVEGFR-1, VEGF, and PIGF levels in 206 Zimbabwean women consisting of 131 preeclamptic and 175 normal pregnancies. They found that plasma VEGF level decreased and sVEGFR-1 level increased in preeclamptic pregnant women. They did not define any relationship between PE and plasma PIGF level. The high sVEGFR-1 levels in preeclamptic pregnant women in this study are consistent with the results of our study. Maynard et al.[10] showed that low PIGF and high sVEGFR-1 levels accompanying VEGF impair endothelial functions in PE. Additionally, studies are showing that an increase in the sVEGFR-1/PIGF ratio in early gestational weeks is an important finding indicating the risk of developing PE[19].

Chaiworapongsa et al.[20] investigated that plasma levels of sVEGFR-1 are correlated with the severity of PE, the degree of proteinuria and increases in resistance of uterine artery and umbilical arteries. They have also found a negative correlation between the maternal plasma levels of sVEGFR-1 and platelet count, neonatal birth weight, as well and gestational age at delivery. Similar findings were reported for maternal plasma PlGF[20].

In a longitudinal case-controlled study, plasma sVEGFR-1 levels were measured in 44 preeclamptic and healthy pregnant women after 7-16, 16-24, 24-28, 28-32, 32-36, and 37 weeks of gestation. Mean sVEGFR-1 levels at the gestational week were higher than those in the control group. Similarly, it was reported that sVEGFR-1 levels were higher 2-5 and 6-10 weeks ago in the PE group, and sVEGFR-1 levels increased earlier in early-onset PE[21]. In our study, the median serum sVEGFR-1 level was higher in PE, and there was a positive correlation between the severity of the disease and the sVEGFR-1 level. However, no relationship was found between sVEGFR-1 level and gestational week.

sVEGFR-1 was thought to be important in assessing the severity of PE, similar to proteinuria. Also, this situation was supported by the correlations of maternal PIGF, sVEGFR-1, placental weight, and fetal weight weight[22].

Levine et al.[23] measured serum sVEGFR-1, fPIGF, and VEGF levels in 655 serum samples during pregnancy in

Table 2. The correlation between serum level of sVEGFR-1 and demographic and clinical variables

	Control		Preeclampsia	
Age (y)	r=0.19	NS	r=0.01	NS
BMI (kg/m^2)	r=-0.04	NS	r=0.01	NS
Gravida	r=-0.06	NS	r=-0.01	NS
Blood pressure (mmHg) Systolic Diastolic	 r=-0.13 r=-0.12	NS	 r=0.25 r=0.31	p<0.05
Proteinuria (mg/dL)	r=-0.15	NS	r=0.25	p<0.05
Platelet counts (10^3/mm^3)	r=-0.01	NS	r=-0.03	NS
Birth weight (g)	r=0.20	NS	r=-0.10	NS
Smoking	r=0.18	NS	r=-0.22	NS
Weight gain during pregnancy (kg)	r=0.19	NS	r=0.15	NS
AFI	r=0.17	NS	r=0.08	NS
APGAR score at 1 min	r=0.18	NS	r=0.09	NS
APGAR score at 5 min	r=0.21	NS	r=0.10	NS
Gestational age at delivery (weeks)	r=0.12	NS	r=0.01	NS
Abruptio placenta	r=-0.17	NS	r=-0.08	NS
IUGR	r=-0.19	NS	r=0.08	NS

NS: Non-significant, sVEGFR-1: Soluble vascular endothelial growth factor receptor -1, AFI: Amnion fluid index, BMI: Body mass index, IUGR: Intrauterine growth restriction

120 preeclamptic and normal pregnant women each. In normotensive pregnant women, sVEGFR-1 levels were stable in the first and second trimesters of pregnancy, and there was a linear increase starting at 33 and 36 weeks and a decrease in fPIGF levels. They reported that sVEGFR-1 started to increase in the early weeks of gestation in preeclamptic pregnant women, and serum-free PIGF and VEGF levels decreased five weeks before the onset of PE[23].

The biological mechanism of the relationship between VEGF, sVEGFR-1, and PIGF is not fully understood. Chung et al.[24] analyzed endocrine gland-derived VEGF (VEGF-ED), VEGF receptors 1 and 2 and NP-1 and NP-2 in placentas from preeclamptic and normal pregnant women by PCR method. They found that only the VEGFR-1 level of these receptors was high in the placenta of preeclamptic pregnant women. VEGF and its receptors are mainly found in syncytiotrophoblasts, villous capillaries, and endothelial cells of the great vessels. These findings suggest that VEGFR-1 regulates trophoblast function and inhibits angiogenesis and vasodilation[24].

Most of the circulating VEGF in pregnancy is found as sVEGFR-1 released from the placenta. Placental production of VEGFR-1 and sVEGFR-1 is increased in PE due to hypoxia[25]. In our study, it was observed that each serum sVEGFR-1 level decreased in the postpartum period. However, the high level of sVEGFR-1 in essential hypertension may be thought to contribute to the serum sVEGFR-1 level of some tissues other than the placenta in preeclamptic pregnant women.

Sugimoto et al.[26] demonstrated that anti-VEGF antibodies and sVEGFR-1 cause proteinuria, a single dose of intravenous administration of anti-VEGF antibodies to normal healthy mice resulted in excessive albumin excretion in the urine because of massive glomerular endothelial cell damage. These findings indicate that circulating VEGF affects glomerular endothelial cell functions, and proteinuria can be an important side effect of anti-VEGF therapy.

Study Limitations

The study design this work had some limitations because of its inclusion of all subtypes of PE. And the study population with a relatively small sample size needs to be considered during drawing a conclusion on the status of serum sVEGFR-1 in patients with several types of clinical presentation of PE. Recently, various pharmacological agents that can prevent the effects of sVEGFR-1 for treating PE have been investigated[27-29]. These agents may have a significant effect on reducing neonatal morbidity and mortality, given that they are considered safe enough to delay delivery for several weeks and alleviate end-organ findings. As a study strength supporting the value of serum sVEGFR-1 in the management of PE, the measurement of serum sVEGFR-1 may have a value in choosing their doses.

Conclusion

In our study, we obtained findings indicating the involvement of sVEGFR-1 in the pathophysiology of PE. Serum sVEGFR-1 has the potential to be used as a valuable biomarker in the prediction, diagnosis, and risk management of women with subtypes of PE including mild and severe PE, HELLP syndrome, and eclampsia. There is a need to study serum sVEGFR-1 as a biomarker in pregnant women with different subtypes of PE.

Ethics

Ethics Committee Approval: The study protocol was performed according with the principles of the Declaration of Helsinki and was approved by the Human Ethics Committee of Sivas Cumhuriyet University (protocol ID: 05.04.2005-4/5).
Informed Consent: All participants signed a written informed consent form on enrollment.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.Ş., A.Ç., Design: S.Ş., A.Ç., Data Collection or Processing: S.Ş., Analysis or Interpretation: S.Ş., N.Y., A.Ç., Literature Search: S.Ş., N.Y., Writing: S.Ş., N.Y., A.Ç.
Conflict of Interest: No conflict of interest was declared by the authors.
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