Plasma selenium levels in pregnant women with preeclampsia

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Abstract

Objective: In this study we aimed to compare selenium (Se) levels in preeclamptic women to healthy pregnant women.

Methods: The study included 84 pregnant women: 39 women with preeclampsia (Group 1), and 45 maternal age, gestational age, and body mass index (BMI) matched healthy pregnant women (Group 2). The maternal levels of plasma Se were analyzed in flame photometer of atomic absorption spectrophotometer.

Results: Plasma Se levels in preeclamptic group were significantly lower than those in the healthy control group (p<0.05). There was no significant correlation between Se levels and BMI, gestational week at sampling, birth weight, triglycerides, cholesterol, the homeostasis model assessment of insulin resistance, and systolic and diastolic blood pressures in preeclamptic and healthy pregnant women (p>0.05).

Conclusion: Our results show that there are decreased levels of Se in plasma of preeclamptic subjects and this may indicate that Se could play a role in the pathogenesis of preeclampsia. However, further experiments are needed to clarify this role.

Keywords: Preeclampsia, selenium.

Özet: Preeklampsili gebelerde plazma selenyum düzeyleri

Amaç: Bu çalışmada, sağlıklı gebe kadınlarla preeklampsili kadınlardaki selenyum (Se) düzeylerini karşılaştırmayı amaçladık.

Yöntem: Preeklampsili 39 kadın (Grup 1) ve maternal yaş, gestasyonel yaş ve vücut kitle indeksi (VKİ) benzer olan 45 sağlıklı gebe (Grup 2) olmak üzere çalışmaya toplam 84 gebe dahil edildi. Maternal plazma Se düzeylerinin ölçümü atomik absorbsiyon spektrofotometri cihazı kullanılarak yapıldı.

Bulgular: Preeklamptik gruptaki plazma Se düzeyleri, sağlıklı kontrol grubundakilere kıyasla anlamlı derecede daha düşüktü (p<0.05). Preeklamptik ve sağlıklı gebe kadınlarda Se düzeyleri ile VKİ, örnek alma tarihindeki gebelik haftası, doğum ağırlığı, trigliseritler, kolesterol, insülin direnci, sistolik ve diyastolik kan basınçları arasında anlamlı bir ilişki saptanmadı (p>0.05).

Sonuç: Elde ettiğimiz sonuçlar, preeklamptik olguların plazmasında Se düzeylerinin azaldığını göstermektedir ve bu durum, Se'nin preeklampsi patogenezinde bir rol oynayabileceğinin bir göstergesi olabilir. Ancak bu rolü netleştirmek için daha fazla araştırmaya ihtiyaç vardır.

Anahtar sözcükler: Preeklampsi, selenyum.

Introduction

Preeclampsia is a human pregnancy specific multisystem disorder in which hypertension arises after 20 weeks of gestation and is accompanied by either proteinuria or thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or cerebral or visual symptoms.[1,2] It is the most common medical complication of pregnancy, occurring in 5–7% of all pregnancies, and is

a leading cause of both maternal-fetal morbidity and mortality.[1,3] Although the mechanisms involved in the etiology of this disorder have not been clearly identified, it is thought to include two components of the placenta: (i) insufficient trophoblast invasion and (ii) insufficient spiral artery with endothelial dysfunction.[3–5]

Previous studies have demonstrated that diminished placental perfusion and vascular endothelial dysfunction

result in placental ischemia, oxidative stress, apoptosis, and necrosis. These cellular changes further result in increased trophoblast shedding into the maternal circulation, which leads to the clinical manifestations of preeclampsia.[6–10]

Selenium (Se) is an essential trace element that has importance for human health and plays a vital role by incorporating selenoproteins into thyroid hormone metabolism, antioxidant defense systems, and immune function.[11] It is incorporated as selenocysteine (SeCys) at the active site of antioxidant enzymes. In the human body, more than 25 selenoproteins have been identified that play significant roles in the cellular redox system.[12] Glutathione peroxidases (GPx), thioredoxin reductases (Thx-R), and iodothyronine deiodinases are the main Se containing enzymes involved in redox reactions.[13] Human placentas produce important antioxidant proteins, which support placentation and reduce inflammation and certain forms of oxidative stress, such as superoxide dismutase (SOD), GPx, Thx, and Thx-R.[10]

Several studies have found depleted Se levels in preeclamptic women and shown a correlation with the activity of plasma GPx levels.[14,15] Rayman et al. notably showed that preeclamptic mothers have a lower Se status prior to diagnosis of the syndrome.[15] Similarly, many additional studies have reported Se deficiency in the development of preeclampsia.[15–24] By contrast, other studies have found either similar or higher plasma Se levels in preeclamptic pregnant women.[25–30]

As seen from the studies mentioned, there is considerable inconsistency in the literature regarding the relation between plasma Se levels and preeclampsia. In this study, we aimed to accomplish the following: (1) evaluate plasma Se concentrations in preeclamptic, normotensive pregnant women and (2) investigate the association between maternal plasma Se concentrations and body mass index (BMI), triglycerides (TG), cholesterol, insulin resistance (IR), and a variety of other parameters.

Methods

A total of 84 pregnant women who were recruited from the antenatal clinics of the Department of Gynecology and Obstetrics of the Faculty of Medicine, Kahramanmaraş Sütçüimam University (Kahramanmaraş, Turkey) were included in the study. Research ethics approval was obtained from the Ethics Committee of Kahramanmaraş

Sütçüimam University before the initiation of the study and signed informed consent was obtained from all patients and volunteers. The study population consisted of 2 groups; the Group 1 included 39 women with preeclampsia and the Group 2 consisted of 45 normotensive healthy pregnant women.

The diagnosis of preeclampsia was made according to the guidelines of the American College of Obstetricians and Gynecologists[2] and to the criteria of the International Society for the Study of Hypertension in Pregnancy (ISSHP).[31] Preeclampsia was diagnosed in the presence of hypertension (blood pressure of 140/90 mmHg or higher, on at least two occasions, at least 6 h apart, after the 20th week of gestation) and proteinuria (>300 mg in a 24-h urine collection or ≥1+ by dipstick and more) or other maternal organ dysfunction (thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or cerebral or visual symptoms) or uteroplacental dysfunction (fetal growth restriction). Preeclamptic women and normal controls were carefully matched for maternal age, gestational age, and body mass index (BMI). Gestational age was calculated based on menstrual history or, in the case of irregular cycles, from ultrasound data obtained during the first or second trimester of pregnancy. The BMI was calculated as weight (kg) / height squared (m²). All participants were non-smokers, had not received any medication before becoming pregnant, and had no clinical evidence of cardiovascular, metabolic, or inflammatory diseases. Exclusion criteria were multiple gestation, confirmed diabetes mellitus, chronic hypertension, connective tissue disease, inflammatory or infective disorders and heart disease, as well as treatment with aspirin, warfarin, lipid-lowering drugs, nonsteroidal anti-inflammatory drugs, or antibiotics. Other exclusion criteria were ruptured fetal membranes, active labor, and polyhydramnios. The normotensive pregnant women selected as controls had no signs of gestational complications or fetal distress.

Blood sampling

A blood sample was taken from each participant before administration of any medication and before any medical or surgical intervention. None of them were in active labor before or at the time of blood collection. The blood samples, which were obtained from the antecubital area, were collected between the hours of 08:00

and 09:00 following 10–12 h of fasting. Fasting venous blood specimens were drawn from the antecubital vein and collected in no additive vacutainer (Becton-Dickinson, Franklin Lakes, NJ, USA) blood-collecting tubes according to standard hospital guidelines for venipuncture and sample collection. The serum separator tube specimens were allowed to clot and then centrifuged for 10 minutes at 3000 g to separate the serum. Serum glucose, TG, cholesterol and insulin levels were measured the same day using a Dade Behring RXL calibrated autoanalyzer (Dade Behring Inc., Newark, DE, USA) and Immulite 2000 instrument (Siemens, Flanders, NJ, USA). Plasma samples were separated and stored at -70°C until the analysis of Se levels.

Measurement of serum Se levels

Selenium measurement was performed in a graphite furnace atomic absorption spectrophotometer (Analyst 800; Perkin Elmer, Waltham, MA, USA) using Zeeman background correction. Matrix modifiers were palladium (4 mg in a 20-mL sample) and magnesium sulfate (3 mg in a 20-mL sample). Samples and calibration standards were diluted 1:3 with 0.05% Triton X-100 to improve the sample viscosity and the reproducibility of the results. Selenium levels in all groups were evaluated according to a standard curve as µg/L, and Se calibration standards were prepared from the commercial Se standard (1000 mg/L) by serial dilutions.[32] According to the Se tests of the control and patient groups, a sensitivity of 72% and a specificity of 55.5% were found.

IR was assessed by Homeostasis Model Assessment (HOMA), HOMA-IR = [fasting insulin (U/ml)] × [fasting glucose (mg/dl)] / 405.[33]

Statistical analyses

All data were analyzed using the Statistical Package for the Social Sciences for Windows version 17.0 (SPSS, Chicago, IL, USA). The data were initially tested for normal distribution by Kolmogorov-Smirnov test and found abnormal (p<0.05). The Mann-Whitney U test was used to test the significance of differences in variables among groups. A correlation analysis by the Spearman's rho test was used to test the relationship between levels of Se and variables. Data are presented as mean±SD. Statistical significance was defined as p<0.05.

Results

The clinical characteristics of the groups are reported in **Table 1**. Demographic features (median maternal age, gestational age at sampling, and BMI) in all groups were similar (p>0.05). Gestational age at delivery and birth weight were significantly lower in the preeclamptic group than in the healthy control group (p<0.05). When compared to Group 2, significant increases in both the systolic and diastolic blood pressures were found in Group 1 (p<0.05).

The plasma Se levels and other laboratory findings of the groups are shown in **Table 2**. Plasma Se levels were significantly lower in Group 1 when compared to Group 2 (46.81±15.35 vs. 61.77±14.49, respectively) (p<0.05). Fasting serum TG and cholesterol levels were similar in

Table 1. The clinical characteristics of groups.*

| | Preeclamptic pregnant women | Healthy pregnant women | |
	(Group 1) (n=39) Mean ± SD	(Group 2) (n=45) Mean ± SD	p
Age (year)	29.36±6.45	27.89±7.06	0.257
BMI (kg/m²)	29.57±4.42	28.86±3.88	0.693
Gestational age at sampling (week)	34.90±2.01	34.02±1.67	0.053
Gestational age at delivery (week)	34.74±1.45	39.11±1.56	0.000
Birth weight (g)	2233.64±712.79	3224.67±334.51	0.000
Systolic blood pressure (mmHg)	158.21±11.89	106.22±10.72	**0.000**
Diastolic blood pressure (mmHg)	99.23±8.07	65.78±8.39	**0.000**

*All parameters are given mean±standard deviation. **BMI:** body mass index; **n:** subject number.

Table 2. Laboratory results of groups.*

| | Preeclamptic pregnant women | Healthy pregnant women | |
	(Group 1) (n=39) Mean ± SD	(Group 2) (n=45) Mean ± SD	p
Triglyceride (mg/dL)	294.30±133.83	256.64±82.18	0.389
Cholesterol (mg/dL)	232.62±79.79	265.76±185.49	0.136
HOMA-IR	3.09±2.09	1.61±1.74	0.000
Selenium (µg/L)	46.81±15.35	61.77±14.49	0.000

*All parameters are given mean±standard deviation. **HOMA-IR:** homeostasis model assessment of insulin resistance; **n:** subject number. p>0.05 insignificant, p<0.05 significant.

both groups (p>0.05). The HOMA-IR was significantly higher in Group 1 than in Group 2 (p<0.05).

There was no significant correlation between Se levels and BMI, gestational week at sampling, birth weight, TG, cholesterol, HOMA-IR, and systolic and diastolic blood pressures in preeclamptic and healthy pregnant women (**Table 3**) (p>0.05).

Discussion

The present study has shown that serum Se levels were significantly lower in patients with preeclampsia than in maternal age, BMI, and gestational age matched control subjects. Relatively few investigators have assessed the extent to which levels of Se in maternal blood are altered in preeclamptic vs. normotensive pregnancies. Our findings of decreased plasma Se levels in women with preeclampsia were consistent with those of Maleki et al., who found reduced Se plasma levels in preeclamptic women in Iran.[22]

Previous studies of maternal Se level status in preeclamptic and normotensive pregnancies have been inconsistent. Several investigations, which were consistent with our results, have found low Se concentrations in women with preeclampsia compared to normotensive pregnant women.[15–24] However, not all prior studies were consistent with our results, and some failed to find any correlation between Se status and hypertensive disorders in pregnant women.[25–30]

Mistry et al.[27] found no differences in selenoproteins in preeclamptic and normotensive pregnant women who were matched by gestational age, parity, and age; however, serum Se concentrations were 15% higher for the preeclamptic cases, as compared to the controls (55.6 vs. 48.5 ng/cm^3). In a recent study, da Silva et al. found similar Se levels in preeclamptic and normotensive pregnant women.[34] Gromadzinska et al.[35] (in a study with 49 pregnant women) reported higher maternal plasma Se concentration, and Mahomed et al.[6] found an elevation in median leukocyte Se concentrations in preeclampsia cases, as compared to the controls.

An imbalance of decreased expression and activity of antioxidants and a concomitant increase in lipid peroxides in human placenta play major roles in the etiology of preeclampsia.[6,36] Selenium eliminates lipid peroxides through its incorporation into GPx. In order to protect the fetus from damage caused by oxygen radi-

Table 3. Correlations of selenium levels with the clinic features of women with preeclampsia and healthy pregnant women.

	Preeclampsia (n=39)		Healthy pregnant women (n=45)	
	Selenium		Selenium	
	r	p	r	p
BMI	0.033	0.841	-0.017	0.913
Gestational age at sampling	0.015	0.927	-0.136	0.374
Birth weight	-0.079	0.633	-0.127	0.406
Triglyceride	-0.185	0.260	-0.193	0.203
Cholesterol	-0.311	0.054	0.020	0.895
Systolic blood pressure	0.162	0.325	-0.036	0.815
Diastolic blood pressure	0.047	0.775	-0.015	0.921
HOMA-IR	0.135	0.412	0.225	0.136

BMI: body mass index, **HOMA-IR:** homeostasis model assessment of insulin resistance, n: subject number, r: Spearman's correlation coefficient.

cals, the human body consumes excessive Se to eliminate oxidative production, which could decrease the Se concentration in preeclamptic women. However, it is still unclear whether the role of oxidative stress in the mechanism of preeclampsia is either the primary event or merely plays a major role in the pathophysiology of the disease. Selenoproteins are major antioxidatives that protect endothelium by down-regulating cytokine-induced adhesion molecule expression and reduce inflammation.[22]

Elevating blood Se concentrations with Se supplementation during pregnancy may be beneficial in pregnant women who have a high risk for preeclampsia due to low Se status.[37] However, previous studies on the role of antioxidants in reducing the rate of preeclampsia are limited, and the results remain controversial. Several studies have shown beneficial effects in only a small number of cases.[28,37] Cochrane's review of the supplementation of antioxidants, such as vitamin C, vitamin E, lycopene, and Se, reported no impact on the prevention of preeclampsia.[38] Another area that requires further investigation is determining the most beneficial times and doses of Se for pregnant women.

Conclusion

In conclusion, we demonstrated that circulating concentrations of Se were significantly decreased in women with established preeclampsia. Further investigations with larger numbers of preeclamptic women

are necessary to determine the role of Se in the etiopathogenesis of preeclampsia and to assess maternal endogenous antioxidant status.

Conflicts of Interest: No conflicts declared.

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