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Research Article

Does Vitamin D Status Alter the Severity af Preeclampsia? A Single-Center Case-Control Study

D Vitamini Seviyesi Preeklampsinin Şiddetini Değiştirir mi? Tek Merkezli Vaka Kontrol Çalışması

Duygu Demiroz Aslan[1], Karolin Ohanoglu[2], Mediha Kubra Ceylan[3], Fatma Ferda Verit Atmaca[3]

[1]Inonu University, School of Medicine, Department of Anesthesiology and Reanimation, Malatya, Turkey
[2]Istanbul Basaksehir Cam and Sakura City Hospital, Clinic of Gynecology and Obstetrics İstanbul, Turkey
[3]Istanbul Training and Research Hospital, Clinic of Gynecology and Obstetrics Health, İstanbul, Turkey

Abstract

Aim: We aimed to investigate the association between vitamin D deficiency and severity of preeclampsia.
Material and Methods: We conducted a case-control study aiming to evaluate vitamin D serum levels in patients with preeclampsia(PE), severe preeclampsia, eclampsia and HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelets). Total number of 69 patients between the ages of 18 and 40 either had a spontaneous vaginal delivery or C-section were included in the study.
Results: The demographic data of the patients were similar, and age was higher in severe PE than in the other groups. When body mass index (BMI) was evaluated, the average BMI of the patients in the severe PE group was found to be significantly higher than PE and similar to the other groups. The average vitamin D levels of all groups was 8.75±3.5 and the mean of severe PE was 6.69±3, which was significantly lower than the other groups. The average vitamin D level in PE was 10.99±2.91, and it was higher than all groups and was significantly higher than patients with severe PE and HELLP syndrome.
Conclusion: We think that there is a significant relationship between the severity of hypertensive disorders that begin during pregnancy and the degree of vitamin D deficiency. We think that the control of vitamin D level and its addition to the treatment will positively affect the course of the disease in order to prevent hypertensive disorders and reduce the severity of disease.

Keywords: Pregnancy, pre-eclampsia, hypertension, vitamin D

Öz

Amaç: D vitamini eksikliği ile preeklampsinin şiddeti arasındaki ilişkiyi araştırmayı amaçladık.
Materyal Metot: Preeklampsi(PE), şiddetli preeklampsi, eklampsi ve HELLP sendromu (Hemoliz, Yüksek Karaciğer enzimleri, Düşük Trombosit) hastalarında D vitamini serum düzeylerini değerlendirmeyi amaçlayan bir vaka-kontrol çalışması gerçekleştirdik. 18-40 yaşları arasında spontan vajinal doğum veya sezaryen olan toplam 69 hasta çalışmaya dahil edildi.
Bulgular: Hstaların demografik verileri benzer olup şiddetli PE de yaş diğer gruplardan yüksek olarak bulundu. BMI değerlendirildiğinde şiddetli PE de hafif pe ye göre anlamlı olarak yüksek olup diğer gruplarla benzer bulundu. Tüm grupların d vit değeri ortalama 8,75±3,5 olup şiddetli PEi nin ortalaması 6,69±3 olup diğer gruplara göre anlamlı olarak düşük bulundu. Hafif PE de d vitamini seviyesi ortalama 10,99±2.91 olup tüm gruplardan yüksek olup.şiddetli PE ve HELLP sendromlu hastalara göre anlamlı olarak yüksek bulundu.
Sonuç: Gebelikte yeni başlayan hipertansif bozuklukların şiddeti ile D vitamini eksikliği derecesi arasında anlamlı bir ilişki olduğunu düşünmekteyiz. Bunları önlemek ve şiddetini azaltmak içim d vitamini seviyesinin kontrolü ve tedaviye eklenmesinin hastalık seyrini olumlu etkileyeceğini düşünmekteyiz.

Anahtar Kelimeler: Gebelik, preeklampsi, hipertansiyon, vitamin D

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Corresponding Author: Duygu Demiroz Aslan, Inonu University, School of Medicine, Department of Anesthesiology and Reanimation, Malatya, Turkey, **E-mail**: drduygudemiroz@hotmail.com

INTRODUCTION

Considering the increased consumption vitamin D deficiency is very common during pregnancy and especially during breastfeeding (1) As defined by Endocrine Society level of 25(OH)D below 20ng / ml is vitamin D insufficiency and levels between 21-29ng / ml are Vitamin D deficiency. (2) Vitamin D deficiency is known to have an association with any poor pregnancy consequences including preeclampsia gestational diabetes, preterm birth and low birth weight in newborns (3-5).

Hypertensive disorders of pregnancy including PE and eclampsia cause 14% of maternal deaths (1). PE presents with new-onset hypertension after 20 weeks of pregnancy and often proteinuria in the mother, and a variety of symptoms which can progress to multi-organ dysfunction. The pathogenesis of PE is still debated. It is thought that due to the placental development abnormalities, the maternal inflammatory system gets activated causing the oxidative stress (6). Having an anti-inflammatory effect vitamin D level was investigated in new-onset hypertensive disorders during pregnancy

We aimed to evaluate the relationship between vitamin D deficiency and the severity of pregnancy-related hypertension.

MATERIAL AND METHOD

A total of 69 consecutive patients ages between 18-40 diagnosed with preeclampsia, severe preeclampsia, eclampsia and Hellp syndrome according to the ACOG criteria and followed in the secondary intensive care unit of our obstetrics and gynecology clinic within a 6-month period (January-June 2020) were included in the study. Exclusion criteria were different ethnic origin and skin color, PE diagnosis in previous pregnancies, having chronic hypertension, diabetes melitus, Lupus and other known serious systemic diseases, multiple pregnancy, history of vitamin D replacement intake and not wanting to participate in the study. This study was approved by the research and ethics committee in Istanbul Training and Research Hospital, written informed consent was obtained from all women recruited into the study and conducted in accordance with the declaration of Helsinki.

PE patients were classified as PE and PE with severe features according to ACOG criteria. Group 1 (G1) was PE; Group 2 (G2) PE with severe features. The patients diagnosed with eclampsia were classified as G3, and the patients diagnosed with HELLP as G4.

Age, weight, height, body mass index (BMI) and blood pressure values of the patients were recorded. History of seizure, neurological findings and additional complaints like epigastric pain, abdominal tenderness were questioned and recorded. Liver enzymes (Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Lactate dehydrogenase (LDH), hemoglobin (HB), hematocrit (HCT), platelet count (PLT) , urea, creatinine values and proteinuria levels tested with protein urine dipstick test were evaluated. Negative for urinary proteinuria =<15mg/dl, trace =15-30mg/dL, 1+= 30-100mg/dL, 2+=100-300mg/dL, 3+=300-100 mg/dL and 4+=›1000mg/dL (7).

Venous blood samples were taken from the patients and 25(OH) D3 levels were measured by spectrometry. A 25(OH) level below 20ng/ml was defined as vitamin D insufficiency, between 21-29ng/ml as vitamin D deficiency, and values above 30 ng/ml as normal (2).

Statistical analysis

SPSS version 20 (SPSS inc., MA, USA) package program was used for the statistical evaluation of the data. Continuous variables were given as mean and standard deviation. The Shapiro Wilk test was used to evaluate whether the data were compatible with the normal distribution. One-way ANOVA or Kruskal-Wallis test was used for statistical evaluation between groups. LSD test was used for post-hoc analysis and for all evaluations $P<0.05$ value was considered statistically significant.

RESULTS

The demographic data of the patients were similar and it was observed that the average age in Group 2 was higher than the other groups. BMI values in Group 2 were significantly higher than Group 1 and were found similar to other groups. Gravidity and parity were similar in all groups. Average gestational age was found to be statistically lower in Group 2 than in Groups 1 and 4 (Table 1).

The systolic and diastolic blood pressure measurements were found to be significantly lower in Group 1 compared to the other groups and measurements in Group 3 were found to be higher than the other groups (Table 2). Urinary dipstick values were simiar in Group 1 and 3 and lower than Group 2 and 4. HB and HCT values were lower in Group 2 than Group 3, and they were similar to the other groups. In Group 4 PLT, AST, ALT, LDH values were significantly lower compared to the other groups while these values were similar in the other groups.

Neurological findings were similar in Groups 2 and 3, and significantly more neurological findings were observed in patients in Groups 2 and 3 compared to Groups 1 and 4. In Group 4, the complaint of abdominal pain was significantly higher than in other groups, and it was found to be the least in Groups 1 and 2 (Table 2).

The average vitamin D levels of all groups were found to be 8.75±3.5. The average level of vitamin D of Group 2 was 6.69±3, significantly lower than the other groups while the average level of Group 1 was 10.99±2.91 and found to be significantly higher than Groups 2 and 4 (Table 2).

The average level of vitamin D in Group 4 was 6.8±1.3, similar to Group 2, but significantly lower than the other groups. In addition, a significant correlation was observed between serum vitamin D levels and disease severity ($r=0.598$, $p<0.001$) (Figure 1).

Table 1. Characteristic data of the patients

Parameter	Preeclampsia (n=32)	Severe Preeclampsia (n=29)	Eclampsia (n=3)	HELLP (n=5)	P value ANOVA
Age, Years	26.88±5	29.45±6	31±5	26.4±2	0.249
BMI, kg/m^2	29.15±4	32.83±9	28.33±1	29.20±2	0.100*
Gravidity, n	1.9±0.8	2.2±1.2	2.3±1.1	1.6±0.5	0.504
Parity, n	0.8±0.7	1.8±1.1	1±0.5	0.6±0.9	0.657
Pregnancy Duration, Weeks	33.45±2.9	30.98±3.8	32.97±2.1	34.62±0.7	0.016*.#

*=p<0.05 between group 1 vs group 2, # =p<0.05 between group 2 vs group 4

Table 2. Clinical and laboratory data

Parameter	Preeclampsia (n = 32)	Severe Preeclampsia (n = 29)	Eclampsia (n = 3)	HELLP (n = 5)	P value ANOVA
SAB	157.8±9.4	181.3±18.1	190.0±17.3	186.2±22.9	<0.001
DAB	88.8±5.5	108.0±10.0	123.3±24.6	105.0±23.1	<0.001
Protein urine dipstick	2.5±0.5	2.7±0.4	2.3±0.5	3.0±0.1	0.031∞*
HB	10.3±1.0	10.2±1.5	11.9±1.2	11.5±1.6	0.063°
HCT	31.5±3.4	31.1±3.9	36.0±3.8	34.5±4.4	0.065°
PLT	187.4±96.0	192.2±114.5	156.6±40.4	73.4±21.6	0.106∞
AST	51.8±30.9	71.2±78.3	42.0±5.1	482.2±378.9	<0.001
ALT	54.7±33.6	72.7±59.1	55.0±8.6	619.2±598.4	<0.001
LDH	357.2±101.7	402.9±188.7	367.0±1.7	48.3±2.8	<0.001
URE	46.9±12.9	42.6±12.2	48.3±2.8	45.6±9.9	0.559
KREATİN	0.7±0.2	0.8±0.4	0.9±0.2	0.8±0.3	0.864
Neurological findings	0.2±0.5	1.3±0.7	1.3±0.5	0.4±0.5	<0.001
Seizure	0	0	0,3±0.5	0	<0.001
Epigastric pain	0	0	0.6±0.5	0.4±0.5	<0.001
Vitamin D	10.9±2.9	6.6±3.0	8.2±2.2	6.7±1.3	<0.001

*=p<0.05 between group 1 vs group 2, &=between group 2 vs group 3, ∞between group 1 vs group 4, #=p<0.05 between group 2 vs group 4,°= between group 1 vs group 3 .

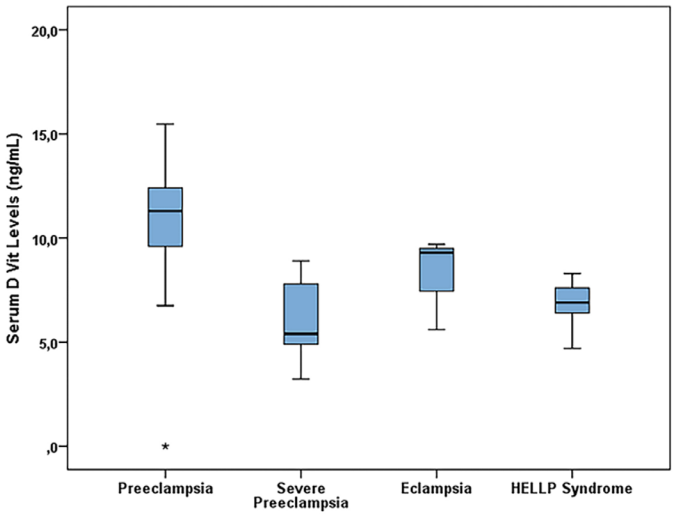

Figure 1. Relationship between vitamin D level and severity of preeclampsia

DISCUSSION

In our study, we concluded that there is a relationship between vitamin D deficiency and the severity of preeclampsia. The average vitamin D level of all groups was 8.75±3.5 which can be classified as deficient. The average of vitamin D values in patients with severe preeclampsia was 6.69±3, which was significantly lower than the other 3 groups.

Many studies have been conducted to determine the maternal risk factors of preeclampsia in pregnant women and to determine the maternal and perinatal effects associated with preeclampsia. Some maternal conditions such as advanced maternal age, obesity, diabetes mellitus, chronic hypertension, antiphospholipid syndrome, chronic kidney disease and systemic lupus erythematosus are known to cause an increased risk of preeclampsia (8,9).

Studies emphasize that prognosis of preeclampsia is negatively affected in elderly patients. English et al showed that effective management of preeclampsia is better achieved in younger patients (10). Similarly, in our study, the mean age of patients with severe PE and eclampsia was found to be higher than the other groups. Nulliparity is thought to be the most common predisposing factor

for preeclampsia, but its cause is not entirely clear (11). Similarly, in our study, gravidity was lower in PE and HELLP patients and higher in eclampsia and severe PE. Preeclampsia can be seen in 4.7% of all pregnancies. Of the PE cases, 47% are nonsevere or unspecified preeclampsia, 37% preeclampsia with severe features/ HELLP, 1.4% eclampsia and 15% superimposed preeclampsia (12,13).

In our study, we evaluated HELLP and severe preeclampsia in different groups and excluded superimposed preeclampsia. The incidence of PE was 46.37%, severe PE 42.02%, eclampsia 4.34% and HELLP 7.24%.

Approximately 25% of severe hypertension and / or one or more of nonspecific symptoms occur in PE. These include persistent or severe headache, visual symptoms, upper abdomen, retrosternal or epigastric pain, mental status change, new onset shortness of breath, orthopnea. In our study, as nonspecific symptoms, headache was recorded in 21%, visual complaints in 18.8%, and abdominal pain in 5.7% of the patients.

The prevalence of vitamin D deficiency in the Turkish population was found to be 51.8% (14). Factors affecting vitamin D levels can be listed as ethnicity, skin color, season, dressing style, age, gender and place of residence (15). In our study, we aimed to exclude these factors by excluding pregnants with different ethnic origin and skin color from the study and including those living in the same region under the same seasonal conditions. All of the patients in the study were living in the Istanbul region witk latitude 41 N 0 and longitude 28 E 58 and were hospitalized in the 6-month period between January and June.

Vitamin D deficiency is also common in women of reproductive age and pregnant women. Maternal vitamin D metabolism changes during pregnancy and this leads to widespread vitamin D deficiency among pregnant women (16,17). Vitamin deficiency is a common problem in Turkey. In a study conducted by Alagöl et al in İstanbul with childbearing age women, vitamin D levels found low in 66,6% of pregnant women (18). In our study, the fact that our patient group consisted of all pregnant women with complicated pregnancy outcomes caused a difference in results. Vitamin D deficiency was recorded in all patients in all groups, and the average vitamin D value was calculated as 8.75±3.5ng / dl.

Vitamin D deficiency may cause poor consequences in pregnant women, including PE, gestational diabetes, and low birth weight in the newborn, and preterm delivery (4). Cordero et al concluded in a meta-analysis in which they examined a total of 55 studies and concluded that vitamin D insufficiency and deficiency were associated with a higher risk of developing preeclampsia (19). Similarly, Serrano Diaz emphasized in their meta-analysis that the preeclampsia prevalence increases as the vitamin D level decreases (20). In a study conducted by Gala et al. it was found that vitamin D levels were low in women who developed severe and early-onset preeclampsia, and vitamin D supplementation had a protective effect against recurrent PE (21).

As a result of the studies, it has been determined that the risk of preeclampsia / eclampsia increases in cases where 25 (OH)-D vitamin falls below 10ng/ml (severe deficiency). For example, in a study conducted in the USA with preganant women in the 15th-20th weeks of gestation, the risk of severe preeclampsia was found 5.41 times higher in pregnant women with insufficient 25 (OH)-D level compared to the control group with the normal level vitamin D (22) In our study, vitamin D value was low in all groups with an average of 8.75±3.5, and there was insufficiency.

Similarly, vitamin D level was found to be significantly lower in the severe PE group. As a result, we came to the conclusion that vitamin D level was correlated with disease severity.

In addition to other factors, overweight during pregnancy causes a lower vitamin D level (23). In our study, it was observed that the vitamin D level was low in Group 2, which had the highest BMI average.

Vitamin D has many effects in the body and also has effects on hematopoietic cells, monocytes, lymphocytes and various precursor cells (24). In their study, Shin et al. emphasized that individuals with vitamin D deficiency may have varying degrees and types of anemias depending on gender (25). In our study, the effect on gender could not be evaluated and the average HB value in severe preeclampsia patients was 10.47 and lower compared to other groups. We think that it may be associated with vitamin D deficiency as a result of nutritional deficiency.

CONCLUSION

We think that there is a significant association between the severity of preeclampsia and low vitamin D level during pregnancy. We think that vitamin D monitoring and replacement is important in the follow-up of pregnancy and in the course of pregnancy-related hypertensive disorders.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *This study was approved by the research and ethics committee in Istanbul Training and Research Hospital, written informed consent was obtained from all women recruited into the study and conducted in accordance with the declaration of Helsinki. (Decision No: 2466).*

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