Chron Precis Med Res 2023; 4(1): 45-49
DOI: 10.5281/zenodo.7715692

ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Does Maternal Vitamin D Deficiency Affect Perinatal Outcomes?

Maternal Vitamin D Eksikliği Perinatal Sonuçları Etkiler Mi?

Münire Funda Cevher Akdulum[1], Kutay Ömer Biberoğlu[2]

[1]Department of Obstetrics and Gynecology, Gazi University, Faculty of Medicine, Ankara, Turkey
[2]Biberoğlu Clinic Women Health Center, Ankara, Turkey

ABSTRACT

Aim: Vitamin D affects placental joining, immune functions, inflammatory response and glucose homeostasis. Vitamin D deficiency can harm both the mother and the fetus' health by boosting the generation of inflammatory cytokines and activating the activation of T- regulatory cells. We aimed to evaluate the perinatal outcomes of vitamin D deficiency.

Material and Method: We evaluated 290 pregnant women who were seen at the Gazi University Medical Faculty Obstetrics and Gynecology Department. The perinatal effects of maternal vitamin D deficiency are studied to learn whether it increases complications during pregnancy such as gestational diabetes mellitus (GDM), preeclampsia, small-for-gestational age (SGA).

Results: Vitamin D insufficiency and vitamin D deficiency in the pregnant women were established as 91% and 66%, respectively. GDM, preeclampsia, type of delivery, preterm delivery, SGA, median baby birth weight, and median baby birth height also did not differ significantly among the groups (p>0.05).

Conclusions: Maternal complications that may result from vitamin D deficiency are currently being examined. In our study, we could not demonstrate a correlation between vitamin D and GDM, SGA or preeclampsia.

Keywords: Pregnancy, vitamin D insufficiency

ÖZ

Amaç: D vitamini plasental tutunmayı, immün fonksiyonları, inflamatuar yanıtı ve glukoz homeostazını etkiler. D vitamini eksikliği, inflamatuar sitokinlerin üretimini artırarak ve T-regulatuar hücrelerin aktivitesini uyararak hem annenin hem de fetüsün sağlığını etkileyebilir. D vitamini eksikliğinin perinatal sonuçlarını değerlendirmeyi amaçladık.

Gereç ve Yöntem: Gazi Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Anabilim Dalı'nda görülen 290 gebe değerlendirildi. Maternal D vitamini eksikliğinin perinatal etkileri, gebelik sırasındaki komplikasyonları (Gestasyonel diabetes mellitus (GDM), preeklampsi, gestasyonel yaşa göre küçük bebek (SGA)) artırıp artırmadığını öğrenmek için araştırma yapıldı.

Bulgular: Gebelerde D vitamini yetersizliği ve D vitamini eksikliği sırasıyla %91 ve %66 olarak saptandı. GDM, preeklampsi, doğum şekli, erken doğum, SGA, medyan bebek doğum ağırlığı ve medyan bebek doğum boyu da gruplar arasında anlamlı farklılık göstermedi (p>0,05).

Sonuç: D vitamini eksikliğinden kaynaklanabilecek maternal komplikasyonlar halen araştırılmaktadır. Çalışmamızda D vitamini ile GDM, SGA veya preeklampsi arasında bir ilişki görülmedi.

Anahtar Kelimeler: Gebelik, D vitamini, vitamin D eksikliği

Corresponding Author: Münire Funda Cevher Akdulum
Address: Department of Obstetrics and Gynecology, Gazi University School of Medicine, 06500, Besevler, Ankara, Turkey.
E-mail: fundacevher@gmail.com

Başvuru Tarihi/Received: 20.01.2023
Kabul Tarihi/Accepted: 11.02.2023

INTRODUCTION

Vitamin D deficiency during pregnancy is a worldwide epidemic (1). According to studies, the prevalence ranged from 18% to 84% depending on the country that subjects were from and the type of clothing they wore (2-5).

Calcium homeostasis in the mother and fetus is impacted by vitamin D levels during pregnancy. A mother provides a fetus with the vitamin D it needs through the placenta (6).Vitamin D deficiency can harm both the mother and the fetus' health by boosting the generation of inflammatory cytokines and activating the activation of T- regulatory cells (7). Additionally, vitamin D influences the placental joining, immune system, inflammatory response, and glucose homeostasis (8-10). Low vitamin D levels have been linked in several studies to a number of pregnancy-related problems, such as preeclampsia (11–13), gestational diabetes mellitus (14), delivery of small-for-gestational-age (SGA) newborns (15, 16), an increase in the cesarean delivery rate (17), and preterm delivery (12, 18).

Research on vitamin D is currently being conducted worldwide and in Turkey. In the current study, the perinatal effects of maternal vitamin D deficiency are examined to determine whether it led to more pregnancy complications (GDM, preeclampsia, SGA).

MATERIALS AND METHODS

Case Selection

In this cohort study, 290 pregnant women in the third trimester who had visited the Obstetrics and Gynecology Department of Gazi University Medical Faculty were included. The Ethics Committee of the Gazi University Faculty of Medicine approved this single-center study.

Written consent was obtained from all patients. Patients' medical history was recorded. The study excluded pregnant women with liver diseases, kidney diseases, inflammatory bowel disease, diseases that may cause enteropathy, and diabetes mellitus.

Pregnant women were divided into four groups based on the categories of sufficient, insufficient, deficient, and severely deficient vitamin D levels, which were defined as levels above 30 ng/ml, between 29.9 ng/ml and 20 ng/ml, between 19.9 ng/ml and 10 ng/ml, and below 9.9 ng/ml, respectively.

The pregnant women's follow-up files were examined to see if they had GDM or preeclampsia. Between the 24th and 28th pregnancy weeks, patients underwent a 50 gram oral glucose tolerance test. The 100 gr oral glucose tolerance test was administered to cases whose first-hour (1 h) glucose levels were greater than 140 mg/dl. During the 3-hour OGTT carried out using 100 gr glucose; fasting, and 1 h, 2 h, and 3 h glucose levels were measured. The following normal values were noted: fasting 95 mg/dl, 1 h 180 mg/dl, 2 h 155 mg/dl, and 3 h 140 mg/dl. GDM was identified in cases with at least two high glucose test results (18).

Preeclampsia was diagnosed when the blood pressure reached 140/90 mmHg or higher after the 20th week of pregnancy, and it was associated with one or more of the following symptoms and laboratory findings: Proteinuria (300 mg protein in 24-hour urine or urine protein to creatinine ratio ≥0.3 or +1 protein determination by dipstick in spot urine specimen); or thrombocytopenia (platelet <100.000/microL); renal failure (creatinine >1.1 mg/dl or two-fold increase when compared to baseline); liver involvement (two-fold increase in serum transaminase levels); cerebral symptoms (headache, visual symptoms, convulsions); pulmonary edema symptoms [18].

The delivery types were documented, and the delivery times were classified as preterm or term. The newborns' height, weight, and gender were all recorded. SGA was diagnosed based on the Turkish Neonatology Association's 2011 growth curves.

Analysis

The pregnant women's calcium and phosphorus levels were analyzed by using the spectrometric method (Beckman Coulter AU auto analyzer). The electrochemiluminescence method was used to determine the levels of parathyroid hormone (Roche cobas E601 auto analyzer). Maternal vitamin D levels were measured using the LC-MSMS method (ULTIMATE 3000 device). Vitamin D levels of all samples were measured using the LC-MSMS method (ULTIMATE 3000 device).

Statistical Methods

Statistical analysis of the data was performed by using SPSS Statistics Program 22. The Kolmogorov–Smirnov test was used to determine if continuous and discrete numerical variables showed normal distribution and Levene's test was used to determine the homogeneity of variances. Descriptive statistics for continuous and discrete variables were expressed as a mean±standard deviation or median (minimum-maximum) while categorical variables were expressed in number of cases and percentage (%).

One-way variance analysis (one-way ANOVA) was used to determine the significance of differences between the groups. To determine the significance of differences between the median values, the

Mann–Whitney-U test was used in evaluating the significance between two independent groups and the Kruskal–Wallis test was used in evaluating the significance in more than two groups. The categorical variables were evaluated using Pearson's chi-square test, Fisher's exact test or a probability ratio test. P value <0.05 was accepted to be significant.

RESULTS

The following number of pregnant women were included in the study groups: 25 pregnant women with sufficient vitamin D levels, 73 with insufficient vitamin D levels, 113 with deficient vitamin D levels and 79 with severely deficient vitamin D levels. The prevalence of vitamin D deficiency and insufficiency in pregnant women was 91% and 66%, respectively.

There were no statistically significant differences in mean age, educational level, mean pregnancy week, median parity, multiparity ratio, mean BMI before pregnancy, BMI classification before pregnancy, smoking habit, and physical activity among these four groups (p>0.05). GDM, preeclampsia, type of delivery, preterm delivery, SGA, median baby birth weight, and median baby birth height were not significantly different between groups (p>0.05) (**Table 1**).

Furthermore, pregnant women with pathological conditions (GDM, SGA, or preeclampsia) (n=45) were compared to healthy pregnant women (n=245). The levels of vitamin D in these two groups did not differ significantly (p=0.927).

The area below the ROC curve for vitamin D levels was found to be statistically insignificant in separating pathological (pregnancies with GDM, SGA, and preeclampsia) and normal pregnancies (AUC=0.504, 95% CI=0.410-0.599, P=0.927).

DISCUSSION

Vitamin D deficiency and insufficiency were found to be 91% and 66%, respectively, in this study. Although Turkey does not have a lack of sunlight, there is a high rate of vitamin D insufficiency and deficiency. GDM and vitamin D deficiency were found to have no significant relationship (p=0.230).

The second trimester 25(OH)D levels and GDM were not related in a study by Farrant et al. which involved 559 pregnant Indian women (20). Vitamin D deficiency and GDM were not found to be significantly related. Another study by Clifton-Bligh et al. measured maternal serum 25(OH)D levels as part of a GDM screening and discovered a significant negative correlation between fasting glucose and vitamin D levels, but no significant correlation between vitamin D levels and GDM (21). Makgoba et al. evaluated 158 control subjects and 90 patients with GDM, and they found no significant correlation between first trimester 25(OH)D levels and GDM (22). However, there was a negative correlation between the 25(OH)D levels and second hour fasting glucose levels. No significant correlation was found between the third trimester 25(OH) D levels and GDM in a study by Park et al. (23). In this study, the relationship between the first trimester vitamin D level and insulin resistance and beta-cell function was also examined. In another study evaluating 723 women, there was no difference in pregnancy 25(OH) D concentration between GDM and non-GDM mothers (82 vs 82 nmol/L, P=0.99 results of this study support those of ours (24). According to a recent study, individuals with vitamin D deficiency had a 26% higher risk of developing gestational diabetes than those with normal serum vitamin D concentrations (25). Wang et al meta-analysis revealed that pregnant women with GDM had significantly lower vitamin D levels than pregnant women without the condition. GDM risk has been linked to vitamin D deficiency (OR = 1.15, %95 GA: 1.07-1.23) (26).

Table 1: Relationship Between Vitamin D levels and pregnancy complications

	Sufficient	Insufficient	Deficient	Severely Deficient	p-value
Number of cases	25	73	113	79	
GDM	5 (%20.0)	5 (%6.8)	10 (%8.8)	6 (%7.6)	0.230*
Preeclampsia	1 (%4.0)	1 (%1.4)	4 (%3.5)	3 (%3.8)	0.761‡
Delivery types					0.308*
NSVD	6 (%24.0)	13 (%17.8)	16 (%14.2)	8 (%10.1)	
C/S	19 (%76.0)	60 (%82.2)	97 (%85.8)	71 (%89.9)	
Preterm	1 (%4.0)	5 (%6.8)	6 (%5.3)	3 (%3.8)	0.850‡
SGA	-	3 (%4.1)	7 (%6.2)	3 (%3.8)	0.376‡
Birth weight					0.072¶
Median	3400	3250	3170	3330	
Minimum-Maximum	2710-4380	790-4590	1580-5240	2050-4170	
Birth height					0.126¶
Median	50	49	49	50	
Minimum-Maximum	45-52	34-53	41-55	45-54	

* Pearson's chi-square test, ‡ Probability Ratio test, ¶ Kruskal Wallis test. GDM: Gestational Diabetes Mellitus, NSVD: Normal Spontan Vaginal Delivery, CS: Cesarean Section, SGA: Small for Gestational Age

There are studies on the correlation of preeclampsia with vitamin D deficiency. It is believed that vitamin D deficiency is related to the vascular endothelial dysfunction due to inflammation and therefore may be related to preeclampsia. Some studies, however, disagree with this association. The relation between preeclampsia and vitamin D is still being debated. In our study, we found no evidence of a link between vitamin D deficiency and preeclampsia (p=0.761). The risk of preeclampsia was found to be increased in a study by Wei et al. when there was a vitamin D deficiency; supporting this finding, the placental growth factor was found to decrease significantly (27). In another study, Dorota et al. found no significant correlation between 25(OH)D levels and preeclampsia markers (28). Bodnar et al. revealed that maternal vitamin D deficiency is associated with severe preeclampsia but not with mild preeclampsia (29). Because our study included cases of mild preeclampsia, this finding backs up ours. Diaz et al. observed that as vitamin D levels decreased, so did the risk of preeclampsia. The meta-analysis, however, contains heterogeneity among studies, and randomized controlled trials were excluded (30).

In our study, there was no significant connection between SGA and vitamin D deficiency (p=0.376). Wei et al. found a significant correlation between vitamin D deficiency and SGA in a review and meta-analysis of six studies on the relationship of vitamin D to SGA, but no significant correlation between SGA and vitamin D insufficiency (27). In a study by Aydoğmuş et al., SGA.. rate was found to be 16.7% in the babies born to mothers with a vitamin D deficiency; this value was 4.9% in the babies born to mothers with normal vitamin D levels and this difference was statistically significant (31). The number of babies with SGA in our study was not as high. Clifton-Bligh et al. noticed that mid-trimester 25(OH)D levels were not related to the infant's birth weight, height, or head circumference (20). We also found no link between vitamin D levels and birth weight and height.

Limitations

A small number of patients were included in the study, whose vitamin D levels were examined. This is the biggest limitation of our study. Additionally, because the study's patients were chosen from the local population, our community is not accurately represented.

CONCLUSION

We were investigate elaborately the maternal problems caused by vitamin D deficiency. In our study, we found no link between vitamin D and GDM, SGA, or preeclampsia. There is a need for more research into the relationship between vitamin D levels and fetal weight or height.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Gazi University, Faculty of Medicine Ethics Committee (Date: 04/2013, Decision No: 122).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Mulligan ML, Felton SK, Riek AE, Bernal-Mizrachi C. Implications of vitamin D deficiency in pregnancy and lactation. Am J Obstet Gynecol 2010;202(5):429 e1-9.
2. Dawodu A, Wagner CL, Mother-child vitamin D deficiency: an international perspective. Arch Dis Child 2007;92(9):737-40.
3. van der Meer IM, Karamali NS, Boeke AJP, et al. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. Am J Clin Nutr 2006;84(2):350-3.
4. Bassir M, Laborie S, Lapillonne A, Claris O, Chappuis MC, Salle BL. Vitamin D deficiency in Iranian mothers and their neonates: a pilot study. Acta Paediatr 2001;90(5):577-9.
5. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr 2005;81(5):1060-4.
6. Parlak M, Kalay S, Kalay Z, Kirecci A, Guney O, Koklu E. Severe vitamin D deficiency among pregnant women and their newborns in Turkey. J Maternal-Fetal Neonatal Med 2014(0):1-12.
7. Tabesh M, Salehi-Abargouei A, Tabesh M, Esmaillzadeh A. Maternal vitamin D status and risk of pre-eclampsia: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2013;98(8):3165-73.
8. Brannon PM, Vitamin D and adverse pregnancy outcomes: beyond bone health and growth. Proc Nutr Soc 2012;71(2):205-12.
9. Grundmann M, von Versen-Hoynck F, Vitamin D - roles in women's reproductive health? Reprod Biol Endocrinol 2011;9:146.
10. Shin JS, Choi MY, Longtine MS, Nelson DM. Vitamin D effects on pregnancy and the placenta. Placenta 2010;31(12):1027-34.
11. Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. J Clin Endocrinol Metab 2007;92(9):3517-22.
12. Baker AM, Haeri S, Camargo Jr, CA, Espinola JA, Stuebe AM. A nested case-control study of midgestation vitamin D deficiency and risk of severe preeclampsia. J Clin Endocrinol Metab 2010;95(11):5105-9.
13. Powe CE, Seely EW, Rana S, et al. First trimester vitamin D, vitamin D binding protein, and subsequent preeclampsia. Hypertension 2010;56(4):758-63.
14. Savvidou MD, Akolekar R, Samaha RBB, Masconi AP, Nicolaides KH. Maternal serum 25-hydroxyvitamin D levels at 11(+0) -13(+6) weeks in pregnant women with diabetes mellitus and in those with macrosomic neonates. BJOG 2011;118(8):951-5.
15. Bodnar LM, Catov JM, Zmuda JM, et al. Maternal serum 25-hydroxyvitamin D concentrations are associated with small-for-gestational age births in white women. J Nutr 2010;140(5):999-1006.

16. Leffelaar ER, Vrijkotte TG, van Eijsden M, Maternal early pregnancy vitamin D status in relation to fetal and neonatal growth: results of the multi-ethnic Amsterdam Born Children and their Development cohort. Br J Nutr 2010;104(1):108-17.
17. Merewood A, Mehta SD, Chen TC, Bauchner H, Holick MF. Association between vitamin D deficiency and primary cesarean section. J Clin Endocrinol Metab 2009;94(3): 940-5.
18. Dunlop AL, Taylor RN, Tangpricha V, Fortunato S, Menon R, Maternal micronutrient status and preterm versus term birth for black and white US women. Reprod Sci 2012;19(9): 939-48.
19. Cunningham FG, Williams JW, Williams obstetrics, in McGraw-Hill's AccessMedicine. 2010, McGraw-Hill Education LLC,: New York, N.Y. p. xv, 1385 p.
20. Farrant HJ, Krishnaveni GV, Hill JC, et al, Vitamin D insufficiency is common in Indian mothers but is not associated with gestational diabetes or variation in newborn size. Eur J Clin Nutr 2009;63(5): p. 646-52.
21. Clifton-Bligh RJ, McElduff P, McElduff A, Maternal vitamin D deficiency, ethnicity and gestational diabetes. Diabet Med 2008;25(6): 678-84.
22. Makgoba M, Nelson SM, Savvidou M, Messow CM, Nicolaides K, Sattar N. First-trimester circulating 25-hydroxyvitamin D levels and development of gestational diabetes mellitus. Diabetes Care 2011. 34(5):1091-3.
23. Park S, Yoon HK, Ryu HM, et al, Maternal vitamin D deficiency in early pregnancy is not associated with gestational diabetes mellitus development or pregnancy outcomes in Korean pregnant women in a prospective study. J Nutr Sci Vitaminol (Tokyo) 2014. 60(4):269-75.
24. Hauta-Alus HH, Viljakainen HT, Holmlund-Suila EM, et al, Maternal vitamin D status, gestational diabetes and infant birth size. BMC Pregnancy Childbirth 2017. 17(1): p. 420.
25. Milajerdi A, Abbasi F, Mousavi SM, Esmaillzadeh A. Maternal vitamin D status and risk of gestational diabetes mellitus: A systematic review and meta-analysis of prospective cohort studies. Clin Nutr. 2021;40(5):2576-2586.
26. Wang L, Zhang C, Song Y, Zhang Z. Serum vitamin D deficiency and risk of gestational diabetes mellitus: a meta-analysis. Arch Med Sci. 2020;16(4):742-751.
27. Wei SQ, Audibert F, Luo ZC, et al, Maternal plasma 25-hydroxyvitamin D levels, angiogenic factors, and preeclampsia. Am J Obstet Gynecol 2013. 208(5): 390 e1-6.
28. Bomba-Opon DA, Brawura-Biskupski-Samaha R, Kozlowski S, et al, First trimester maternal serum vitamin D and markers of preeclampsia. J Matern Fetal Neonatal Med. 2014 Jul;27(10):1078-9.
29. Bodnar LM, Simhan HN, Catov JM et al, Maternal vitamin D status and the risk of mild and severe preeclampsia. Epidemiology 2014. 25(2): 207-14.
30. Serrano-Díaz NC, Gamboa-Delgado EM, Domínguez-Urrego CL, Vesga-Varela AL, Serrano-Gómez SE, Quintero-Lesmes DC. Vitamin D and risk of preeclampsia: A systematic review and meta-analysis. Biomedica. 2018 May 1;38 Suppl 1:43-53.
31. Aydogmus S, Kelekci S, Aydogmus H, et al, High prevalence of vitamin D deficiency among pregnant women in a Turkish population and impact on perinatal outcomes. J Matern Fetal Neonatal Med. 2015;28(15):1828-32.