

## Association between serum levels of vitamin D and chronic periodontitis in premenopausal women in Yazd

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### Abstract

**Introduction:** Periodontal disease is a common chronic inflammatory disease, considered as a primary cause of tooth loss due to the destruction of periodontal tissues. Various studies have shown that vitamin D has anti-inflammatory and anti-microbial properties and plays a significant role in musculoskeletal health. There is strong evidence that vitamin D deficiency may increase the likelihood of osteoporosis and osteopenia as well as chronic inflammatory diseases such as periodontitis.

**Materials & Methods:** This case-control study included 30 females with moderate or severe chronic periodontitis (CP) and 30 periodontally healthy females. The mean age of the CP group and the control group was 34 years. Indices of Probing depth (PD), clinical attachment level (CAL) and bleeding index (BI) as well as the serum level of vitamin D (1,25(OH)<sub>2</sub>D) were measured in both groups. The statistical analyses including t-tests, Pearson correlation coefficient and odd ratio.

**Results:** There was a significant indirect relationship between the serum level of vitamin D and the periodontal indices ( $p < 0.05$ ). The odd ratio (OR) measures showed that subjects with vitamin D dose of less than 10 ng/ml were 5.6 times more likely to have periodontitis compared to those with a normal dose of vitamin D ( $p = 0.03$ ). Moreover, subjects with vitamin D dose of 10-29 ng/ml were about 1.46 times at a higher risk to develop periodontitis than those with sufficient dose of vitamin D ( $p > 0.05$ ).

**Conclusion:** It is recommended that serum levels of vitamin D in patients with chronic periodontitis be measured and then if necessary, treatment should begin.

**Keywords:** Chronic Periodontitis, Pre menopause, Vitamin D, Women

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## ارتباط بین سطح سرمی ویتامین D و پریودنتیت مزمن در زنان قبل از یائسگی در شهر یزد

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## چکیده

**مقدمه:** بیماری پریودنتال یک بیماری التهابی مزمن شایع است که به عنوان علت اولیه ی از دست رفتن دندان در اثر تخریب بافت پریودنتال در نظر گرفته می شود. مطالعات مختلف نشان داده اند که ویتامین D دارای ویژگی های ضد التهابی و آنتی میکروبیال می باشد و نقش مهمی در سلامت عضلانی اسکلتی ایفا می کند. شواهد قوی وجود دارد که کمبود ویتامین D احتمال استئوپروز و استئوپنی و بیماریهای التهابی مزمن مانند پریودنتیت را افزایش می دهد.

**مواد و روش ها:** این مطالعه ی مورد-شاهدی شامل ۳۰ زن با پریودنتیت مزمن متوسط یا شدید و ۳۰ زن با سلامت پریودنتال بود. میانگین سنی هر دو گروه CP و گروه کنترل ۳۴ سال بود. شاخص های عمق پروب، سطح از دست رفتن اتصالات، شاخص خونریزی و هم چنین سطح سرمی ویتامین D در هر دو گروه اندازه گیری شد. برای تمام آنالیزهای آماری از T-test، ضریب همبستگی پیرسون و odd ratio استفاده شد.

**یافته ها:** یک رابطه ی غیر مستقیم بین سطح سرمی ویتامین D و شاخص های پریودنتال وجود داشت ( $p < 0.05$ ). نتایج به دست آمده نشان داد شانس ابتلا به پریودنتیت در افرادی که سطح ویتامین D شان زیر 10 ng/ml بود ۵/۶ برابر افراد با ویتامین D نرمال ( $p = 0.03$ ) و افرادی که سطح ویتامین D شان 10-29 ng/ml بود ۱/۴۶ برابر افراد با ویتامین D نرمال بود ( $p > 0.05$ ).

**نتیجه گیری:** پیشنهاد میگردد در بیماران با پریودنتیت مزمن سطح سرمی ویتامین D مورد بررسی قرار گیرد تا در صورت نیاز، دارو درمانی انجام شود.

**واژگان کلیدی:** پریودنتیت مزمن، قبل از یائسگی، ویتامین D، زنان

## Introduction

Periodontitis is a bacterial infection caused by various oral microorganisms<sup>[1]</sup> which results in the formation of soft tissue pockets and its severe forms can lead to bone loss or tooth mobility. Although bacteria are essential for periodontal disease to take place, susceptible host is also just as important. Host inflammatory response is a protective reaction but both hypo-responsiveness and hyper-responsiveness can result in advanced tissue destruction.<sup>[2]</sup> Vitamin D plays an important role in many inflammatory diseases by regulating the expression of inflammation-related mediators.<sup>[3]</sup> Furthermore, vitamin D has some antimicrobial effects. More recently, 1,25(OH)<sub>2</sub>D (the active form of vitamin D) has been shown to increase transcription of anti-bacterial peptides which can defend against foreign invaders such as oral pathogens.<sup>[4]</sup> 1,25(OH)<sub>2</sub>D can inhibit antigen-induced T-cell proliferation and cytokine production. An inverse association between intake of vitamin D and incidence of some autoimmune diseases such as multiple sclerosis

and type 1 diabetes has been documented in some epidemiologic studies.<sup>[5]</sup> It is also well known that the active form of vitamin D is required for calcium homeostasis in the blood. Decreased serum calcium concentrations may lead to calcium resorption from bone and consequent decreased general bone mineralization.<sup>[4]</sup>

Considering all these properties of vitamin D, some studies were conducted with the purpose of investigating a possible association between vitamin D levels and periodontal disease. Alshouibi et al and Antonglou et al. reported that sufficient total vitamin D intake (>800IU) was associated with lower odds of periodontal disease, and vitamin D intake may protect against periodontal disease progression.<sup>[6,7]</sup> In another case-control study, subjects with a low 1,25(OH)<sub>2</sub>D level were more likely to belong to the periodontal group.<sup>[8]</sup> In contrast, Zhang *et al.* reported that 25(OH)D levels, the major circulating metabolite of vitamin D were higher in patients with generalized aggressive periodontitis.<sup>[1]</sup> Because of some

controversies among studies and lacking similar studies on Iranian populations, the aim of this study was designed to assess possible association between serum levels of vitamin D and chronic periodontitis in premenopausal women of Yazd city.

## Materials & Methods

In this case-control study, thirty women aged 25 to 45 years, in premenopausal span and with confirmed generalized moderate to severe chronic periodontitis were selected as the participants of the study. These subjects were referred to Dental Faculty of Shahid Sadoughi University of Medical Sciences, Yazd, Iran. A complete medical history was taken from each patient to ensure that none of them had any systemic diseases which may have influenced the periodontal status or bone metabolism. Patients did not use vitamin D or calcium supplements, Bisphosphonates and anti-convulsant drugs. They were not pregnant and they did not smoke. Furthermore, none of them reported any history of antibiotic therapy during the last 3 months. Thirty 25 to 45 years old premenopausal females without any periodontal disease were also included as a control group. This study was approved by the ethics committee of Shahid Sadoughi University (17/1/223636).

**Periodontal examination:** Probing depth (PD), clinical attachment level (CAL) and bleeding index (BI) were measured in four surfaces (mesial, distal, buccal and lingual) of all fully erupted teeth except the third molars by using Williams Periodontal probe and patients were divided into two subgroups "A:severe chronic periodontitis, B:moderate chronic periodontitis" (workshop 1999).

**Blood sampling:** Venous blood samples were collected in the morning after taking informed consent from each patient. It should be mentioned that patients need to be fast for 9-12 hours before. Serum 1,25(OH)<sub>2</sub>D was analyzed using an available enzyme-linked immune assay system (DIA source, Belgium). 30-100 ng/ml was considered as the sufficient level of vitamin D and 10-29 ng/ml was considered as insufficiency and <10 ng/ml was assumed as deficiency.

**Data Collection & Statistical Analysis:** Both clinical and laboratory data parameters were reported as mean ± standard deviation. The levels of vitamin D were compared between the chronic periodontitis (CP) and the control groups. Correlation between vitamin D level

and periodontal indices (BI, CAL and PD) were separately analyzed. Odds ratio was calculated for the possible association of severity of periodontitis (subgroup A&B) and vitamin D levels. All statistical analyses were carried out using SPSS17.

## Results

The participants of the study were sixty 25 to 45 years old premenopausal females. The mean age of the CP group and the control group was 34 years. However, as it was expected, there were significant differences between the two groups for all periodontal indices.

Moreover, a significant difference ( $p < 0.001$ ) was observed between the mean of the measured vitamin D for the CP group ( $12.32 \pm 8.36$ ) and the control group ( $19.31 \pm 10.10$ ). (Table. 1) represents the frequency of vitamin D level distribution in two groups.

**Table1. Distribution of participants with different vitamin D levels in CP and control groups**

Vitamin D level	CP	Control
<10 ng/ml (deficiency)	17	7
10-29 ng/ml (insufficiency)	10	16
30-100 ng/ml (sufficiency)	3	7

Chi-square test showed that vitamin D deficiency was more frequent in the CP group compared to the control group and vitamin D sufficiency was more prevalent in control group than CP group ( $p = 0.046$ ). Furthermore, correlation tests indicated that there was a significant negative/inverse relationship between periodontal indices and vitamin D level. (Table 2) illustrates the Pearson's correlation coefficients between the periodontal indices and vitamin D levels.

**Table2. Correlation coefficients between the periodontal indices and vitamin D levels**

Variable	Correlation coefficient	p-value
Vitamin D, BI	-0.375	0.012
Vitamin D, CAL	-0.412	0.005
Vitamin D, PD	-0.321	0.034

In addition, there was a significant negative relationship between the severity of periodontitis (being in A or B subgroups) and vitamin D level ( $p = 0.008$ ).

The odd ratio (OR) measures showed that persons with vitamin D level of less than 10 ng/ml were 5.6 times more likely to have periodontitis compared to those with normal levels of vitamin D (30-100 ng/ml). In a same pattern, subjects with vitamin D levels of 10-29 ng/ml were about 1.46 times at a higher risk to develop periodontitis than those with sufficient levels of vitamin D (Table. 3).

**Table 3. The association between vitamin D levels and the presence of periodontal disease**

Vitamin D level	OR	C.I=95%	p-value
<10 ng/ml	5.6	1.13-28.4	0.035
10-30 ng/ml	1.46	0.3-6.9	0.63

## Discussion

The main findings of this study were a negative association between serum 1, 25(OH)<sub>2</sub> D level and chronic periodontitis and also a significant negative relationship between the periodontal indices and vitamin D levels among premenopausal women. Osteoporosis is most prevalent in females over the age of 50, following the suppression of estrogen influence on bone health.<sup>[9]</sup> Some other previous studies reported high prevalence of vitamin D deficiency among postmenopausal women, especially in those with osteoporosis.<sup>[10]</sup> Thus, the participants of this study were selected from 25 to 45-year-old females (premenopausal age).

Low serum levels of vitamin D is associated with poor dietary intake and also inadequate sunshine exposure. Dress styles covering the whole body, may have adverse effects on 25(OH)D levels.<sup>[11]</sup> For example, el-Sonbaty<sup>[12]</sup> reported Vitamin D deficiency in veiled Kuwaiti women while in Dietrich et al's<sup>[5]</sup> study, both males and females were participated. In the current study, only females were as the participants considering that Iranian women wear hijab in public. Therefore, wearing hijab/scarf might possibly affect the amount of vitamin D which is expected to be received through sunlight exposure.

Antonoglou et al in 2013. Studied the relationship between vitamin D serum level and periodontitis in patients with type 1 diabetes. This study included the women without any systemic diseases or pregnancy because periodontal disease is related to these systemic conditions.<sup>[7]</sup> 25(OH)D and 1,25(OH)<sub>2</sub>D are major factors for the assessment of vitamin D level and evaluation of vitamin D metabolism. The major

circulating metabolite is 25(OH)D, and 1,25(OH)<sub>2</sub>D as the active metabolite of this vitamin, which is responsible for the most actions of vitamin D.<sup>[3]</sup> In the present study, a negative relationship was observed between serum level of 1,25(OH)<sub>2</sub>D and periodontal disease. However, Dietrich et al.<sup>[5]</sup> studied the relation between serum levels of 25(OH)D and patients with periodontal disease and they found a negative association. Antonoglou et al in 2013.<sup>[7]</sup> reported that there was a positive relation between serum level of 1,25(OH)<sub>2</sub>D and periodontal health in diabetic subjects. Moreover, they found that the elimination of periodontal infection would increase the serum level of 1,25(OH)<sub>2</sub>D while it had no effect on 25(OH)D serum levels. Antonoglou et al in 2015<sup>[8]</sup> found that although there was a positive relation between 1,25(OH)<sub>2</sub>D level and periodontal health, the 25(OH)D level had no association with periodontal health.

In the present study, the relationship between chronic periodontitis and vitamin D level was studied and it was shown that 1,25(OH)<sub>2</sub>D level was negatively associated with chronic periodontitis. However, Zhang et al.<sup>[1]</sup> measured vitamin D-binding protein (DBP) levels in plasma of patients with generalized aggressive periodontitis and they found no relation between DBP in plasma and periodontal indices.

Antonoglou et al<sup>[8]</sup> reported the odds ratio (OR) of 0.97 and the confidence interval of 0.95-1.00 for the association between serum level of 1, 25(OH)<sub>2</sub>D and the status of periodontal health. In this study, the results of OR measures indicated that the women with vitamin D level below 10 ng/ml are 5.6 times more likely to have periodontitis than those with normal vitamin D levels. In addition, subjects with the vitamin D level between 10-29 ng/ml are about 1.46 times more likely to have periodontitis compared to the subjects with normal levels of vitamin D.

## Conclusion

Results of this study suggest that serum levels of vitamin D in patients with chronic periodontitis should be measured and if needed vitamin D complements should be used as an adjunctive treatment.

## Limitations:

Finding volunteers for taking blood samples was not easy, besides asking them to be fasting in examination session. Chronic periodontitis in premenopausal aged

25-45 was not as common as their older counterparts, so sampling took longer than what we expected. Blood samples should be transmitted up to 2 hours.

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**Conflicts of interest:** There is no conflict of interest.

## Authors' Contributions

The study was designed by Fahimeh Rashidi Maybodi. The study data were collected by Razieh Eshghi and Shahab Shahhosseini. Analysis and interpretation of data, drafting of the manuscript were performed by Razieh Eshghi, Fahimeh Rashidi Maybodi and Shahab Shahhosseini. Critical revision of the manuscript for important intellectual content was performed by Fahimeh Rashidi Maybodi and Arezoo Khabazian. Study supervision was performed by Fahimeh Rashidi Maybodi and Arezoo Khabazian.

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