

## Association of serum level of 25-hydroxy vitamin D with Oral Lichen Planus. A case-control study.

Asociación del nivel sérico de 25-hidroxi vitamina D con el liquen plano oral. Un estudio de casos y controles.

Mostafa Sadeghi.<sup>1</sup>  
 Mahdieh Zarabadipour.<sup>2</sup>  
 Faezeh Azmodeh.<sup>3</sup>  
 Monirsadat Mirzadeh.<sup>4</sup>  
 Ali Sarbazi Golezari.<sup>1</sup>

### Affiliations:

<sup>1</sup>Qazvin University of Medical Sciences, Qazvin, Iran.

<sup>2</sup>Dental Caries Prevention Research Center, Qazvin University of Medical Sciences, Qazvin, Iran.

<sup>3</sup>Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Qazvin University of Medical Sciences, Qazvin, Iran.

<sup>4</sup>Metabolic Disease Research Center, Qazvin University of Medical Sciences, Qazvin, Iran.

**Corresponding author:** Mahdieh Zarabadipour. Dental Caries Prevention Research Center, Qazvin University of Medical Sciences, Bahonar Blvd., Qazvin, Iran. **Phone:** (98-28) 33353064. **E-mail:** mzarabadipour@qums.ac.ir

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**Abstract: Introduction:** Vitamin D deficiency is a global health problem that can be a risk factor for a broad range of diseases such as some autoimmune diseases. Due to the autoimmune base of lichen planus, it seems that a reduction of the serum level of vitamin D is related to lichen planus. In this study, we investigate the relation between serum level of vitamin D and oral lichen planus patients (OLP). **Material and Methods:** In this case-control study, 35 patients with OLP (including 15 men and 20 women) and 70 healthy volunteers (including 35 men and 35 women), aged between 30-60 years old, referred to Qazvin University of Medical Sciences were investigated. None of these volunteers had systemic diseases. Vitamin D levels were measured with ELFA (Enzyme Linked Fluorescent Assay) and the data was analyzed using the chi-squared test and t-test. **Results:** The mean serum level of vitamin D in the control group was 23.7±9ng/ml and in the case group was 18.12±8/7ng/ml. The results show that the serum level of vitamin D in patients with OLP is significantly less than in the control group ( $p<0.05$ ). **Conclusion:** According to the results, the serum level of vitamin D in patients with OLP was significantly lower than that of healthy people.

**Keywords:** Vitamin D; Lichen Planus, Oral; serum; Autoimmune Diseases; Vitamin D Deficiency; Case-Control Studies.

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**Resumen: Introducción:** La deficiencia de vitamina D es un problema de salud global que puede ser un factor de riesgo para una amplia gama de enfermedades, como algunas enfermedades autoinmunes. Debido a la base autoinmune del liquen plano, parece que una reducción del nivel sérico de vitamina D está relacionada con el liquen plano. En este estudio, investigamos la relación entre el nivel sérico de vitamina D y los pacientes con liquen plano oral (LPO). **Material y Métodos:** En este estudio de casos y controles, 35 pacientes con LPO (incluidos 15 hombres y 20 mujeres) y 70 voluntarios sanos (incluidos 35 hombres y 35 mujeres), con edades comprendidas entre 30 y 60 años, remitieron a la Universidad de Medicina de Qazvin. Se investigaron las ciencias. Ninguno de estos voluntarios padecía enfermedades sistémicas. Los niveles de vitamina D se midieron con ELFA (ensayo fluorescente ligado

a enzimas) y los datos se analizaron utilizando la prueba de chi-cuadrado y la prueba t. **Resultados:** El nivel sérico medio de vitamina D en el grupo de control fue de  $23,7 \pm 9$  ng / ml y en el grupo de casos fue de  $18,12 \pm 8/7$  ng / ml. Los resultados muestran que el nivel sérico de vitamina D en pacientes con OLP es significativamente menor que en el grupo de control ( $p < 0.05$ ). **Conclusión:** De acuerdo con los resultados, el nivel sérico de vitamina

D en pacientes con LPO fue significativamente menor que en personas sanas.

**Palabra Clave:** Vitamina D; Liquen Plano Oral; Suero; Enfermedades Autoinmunes; Deficiencia de Vitamina D; Estudios de Casos y Controles .

## INTRODUCTION.

Lichen planus is a chronic inflammatory mucocutaneous disease that was described by Wilson in 1869 for the first time.<sup>1</sup> The disease exclusively affects the squamous epithelium layer.<sup>2</sup> Lesions can be found in the oral mucosa, genital mucosa, skin and nails.<sup>3</sup>

Most of the patients are 40 to 60 years old and the ratio of female to male is 3 to 2.3 Global prevalence of OLP is reported to be between 0.5% and 3%.<sup>4</sup> Its pathogenesis is still unknown,<sup>5</sup> but various factors have been suggested such as depression, hepatitis C virus infection, cirrhosis, some materials used in dentistry and some medications.<sup>6,7</sup> These factors may cause the activation of the immune system and subsequently this inflammatory disease can develop.<sup>5,8</sup>

Gholizadeh *et al.*,<sup>9</sup> and Sahebamee *et al.*,<sup>10</sup> reported in their studies that vitamin B12 and zinc serum levels in lichen planus patients were lower than in healthy people. T cell lymphocytes that act against body tissues are the first initiating factor for the disease.<sup>5</sup>

Vitamin D is one of the essential vitamins for the human body. This vitamin is a fat soluble molecule and has many roles in the regulation of body metabolism and the immune system.<sup>11,12</sup> The most recognizable roles of vitamin D are to regulate and maintain calcium levels and to sustain the normal function of bodily immunity.

Vitamin D deficiency (<20ng/ml, U.S. Endocrine Society Guidelines) is a global health problem that can be a risk factor for a broad range of acute and chronic diseases.<sup>13,14</sup> The most significant factors resulting in Vitamin D deficiency are a lack of exposure to solar radiation, nutritional disorders, some systemic diseases (such as renal failure) and the usage of certain medications (like antiepileptic drugs).

Insufficient serum levels of vitamin D can cause various diseases such as osteomalacia, rickettsia, some

autoimmune disorders such as diabetes mellitus (type 1), rheumatoid arthritis, hypothyroidism, gestational disorders<sup>15</sup> and also infectious diseases such as tuberculosis.<sup>13,16-19</sup> Raab *et al.*,<sup>20</sup> and Jackson *et al.*,<sup>17</sup> reported lower levels of vitamin D in patients with insulin-dependent type of diabetes mellitus.

Because of the autoimmune nature of lichen planus and the association of the insufficient serum levels of vitamin D with these diseases, it seems that the reduction of serum levels of vitamin D may be related to the symptoms of lichen planus.<sup>21,22</sup> The aim of this study is to investigate the relation of serum level of vitamin D in oral lichen planus patients, using healthy people as a control group.

## MATERIALS AND METHODS.

This experimental case control study was conducted in the oral medicine department of Qazvin University of Medical Sciences, Iran, from June to October, 2017. The participants were categorized in two groups: 35 patients with diagnosed oral lichen planus and 70 healthy individuals (control group). The inclusion criteria included: age between 30-60 years old, no history of taking vitamin supplements, no history of systemic diseases, not being pregnant and having acceptable plaque indexes, without cervical and root caries. Exclusion criteria were non-cooperative patients.

For all participants (case and control), complete medical and dental history and systematic examinations (extraoral, intraoral, periodontal) were done.

Patients were asked to relax for a few minutes and then 2ml of venous blood were taken by a trained nurse. Then, the blood tubes were stored at 8°C until processing the laboratory measurements. All the samples were taken between 10 to 12 o'clock in the morning and were sent to the laboratory immediately.

At the time of laboratory analysis, samples were taken out of the refrigerator and centrifuged for 4000 rpm for 5 minutes for homogenization.

Vitamin D levels of the samples were measured using the technique of ELFA (Enzyme Linked Fluorescent Assay) and by using a VIDAS instrument (Biomerieux, France). All the samples were coded and the researcher was blind to the sample and result. After collecting and decoding the data, they were analyzed by statistical software, SPSS21.

### Statistical analysis

After explaining the descriptive data and checking the normality of the results, an independent sample t-test was used for the comparison of vitamin D serum levels in the case and control groups. Error type 1 ( $\alpha$ ) is 0.05 and  $p < \alpha$  is significant.

## RESULTS.

Samples were obtained from 105 people (aged between 30-60) referred to the oral medicine department of Qazvin University of Medical Sciences for routine dental examination; 35 people had OLP (as a case group) and 70 people had no diseases (as control group). The characteristics of the two groups are shown in Table 1. There was a significant difference between the serum level of vitamin D in the oral lichen planus patients group and that of the control group ( $p=0.03$ ) (Table 1).

This study showed that 71.4% ( $n=25$ ) of patients and 35.7% ( $n=25$ ) of individuals from the control group had vitamin D deficiency. Also 17.1% ( $n=12$ ) of people in the control group and 8.6% ( $n=3$ ) of patients had sufficient vitamin D.

**Table 1.** Characteristics of lichen planus patients and healthy controls.

		Lichen planus (n=35)		Control (n=70)		p-value
Sex	N (%)	Men	15 (42.9)	35 (5.0)		0.5
		Women	20 (57.1)	35 (5.0)		
Age	mean (SD)		41.8 (9.7)	40.8 (7.9)		0.6
Vit D	mean (SD)		18.1 (8.7)	23.7 (9)		0.003

## DISCUSSION.

Vitamin D deficiency is a global health problem. This problem is more important in countries with higher latitude because of the sun's angle of sunshine.<sup>23,24</sup> Various studies have shown the relation of vitamin D deficiency with various diseases related to the immune system,<sup>17,18</sup> OLP is an autoimmune disease with unknown etiology. It is for this reason that its treatment is occasionally difficult.

In the present study, we compared serum levels of vitamin D in patients with OLP to a healthy control group. Mean serum level of vitamin D in the control group was  $23.713 \pm 9.00$  ng/ml and in the case group, it was  $18.12 \pm 8.74$  ng/ml. These values were significantly different, similar to that reported by Gupta *et al.*,<sup>25</sup> As OLP is an autoimmune disease and also various studies reported the association of autoimmune diseases with

vitamin D insufficiency,<sup>11,24,26</sup> the present study's results are expected.

Destructive processes of tissue in OLP shows that CD8+ lymphocytes recognize an unknown factor in surface keratinocytes as an antigen that trigger a series of reactions against them, leading to apoptosis of the surface keratinocytes.<sup>4</sup>

Active form of vitamin D can decrease the proliferation of CD4+ lymphocytes and the expression of cytokines such as interferon gamma and interleukin 2. Vitamin D suppresses the inflammatory factors and decreases the immune system affinity for taking part in unnecessary reactions. Vitamin D has negative feedback on all the inflammatory mediators.<sup>24</sup>

In spite of the association of several diseases with vitamin D deficiency (such as rheumatoid arthritis, systemic lupus erythematosus, type 1 diabetes, multiple

sclerosis, and thyroiditis) fewer studies have been done on the relationship between OLP and vitamin D insufficiency. In 2014, a study indicated that none of the patients with OLP had a standard level of serum vitamin D.<sup>21</sup> In that study, 84% of patients with OLP had insufficient serum levels of vitamin D (between 10 and 30 ng/ml) that is similar to the present study's results; however, there was no control group.<sup>21</sup>

In the study by Gupta *et al.*,<sup>25</sup> 70% of OLP patients and 34% of the control group members had Vitamin D insufficiency.<sup>25</sup> The results match our study's results as vitamin D deficiency was exhibited in 71% of the OLP group and 35% of the healthy control group.

In a case-report study, Varma *et al.*,<sup>22</sup> treated the OLP patients with vitamin D deficiency, using vitamin D supplement. In these patients, relative recovery was seen after prescribing vitamin D. It was reported that activation of vitamin D receptors on B and T cell lymphocytes may have the main role in the immune system. Prescribing vitamin D supplement for patients with the treatment-resistant form of the OLP could be a novel recommendation.

One of the important strengths of the present study is that sample collection was done during a specific period, when the amount of exposure to sunlight was similar so that this factor was not a variable. Also, the patients had no history of supplements or corticosteroid drug use within the past year.

Considering the limitations of our study, such as time limit and low enrollment of participants, it is recommended that future studies be designed with a larger sample size. Based on the findings of this study that shows a reduction of vitamin D in OLP patients, it is also recommended to include Vitamin D as a treatment in clinical trials.

## CONCLUSION.

Serum level of vitamin D in the patients with OLP was lower than in the control group.

**Conflict of interests:** All authors declare that there is no conflict of interests.

**Ethics approval:** This study was approved by the ethical committee of Qazvin University of Medical Sciences with an ethical number of IR.QUMS.REC.1395.277.

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**Authors' contributions:** ZM designed the study, prepared, edited and reviewed the manuscript. SM and SGA collected the data. MM analyzed the data. AF edited and reviewed the manuscript. All authors read and approved the manuscript.

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## REFERENCES.

1. Mollaoglu N. Oral lichen planus: a review. *Br J Oral Maxillofac Surg.* 2000;38(4):370-7.
2. Scully C, Carrozzo M. Oral mucosal disease: Lichen planus. *Br J Oral Maxillofac Surg.* 2008;46(1):15-21.
3. Ismail SB, Kumar SK, Zain RB. Oral lichen planus and lichenoid reactions: etiopathogenesis, diagnosis, management and malignant transformation. *J Oral Sci.* 2007;49(2):89-106.
4. Farhi D, Dupin N. Pathophysiology, etiologic factors, and clinical management of oral lichen planus, part I: facts and controversies. *Clin Dermatol.* 2010;28(1):100-8.
5. Montebugnoli L, Venturi M, Gissi DB, Leonardi E, Farnedi A, Foschini MP. Immunohistochemical expression of p16 (INK4A) protein in oral lichen planus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2011;112(2):222-7.
6. Scully C, Beyli M, Ferreiro MC, Ficarra G, Gill Y, Griffiths M, et al. Update on oral lichen planus: etiopathogenesis and management. *Crit Rev Oral Biol Med.* 1998;9(1):86-122.
7. Lavanya N, Jayanthi P, Rao UK, Ranganathan K. Oral lichen planus: An update on pathogenesis and treatment. *J Oral Maxillofac Pathol.* 2011;15(2):127-32.
8. Fillies T, Werkmeister R, van Diest PJ, Brandt B, Joos U, Buerger H. HIF1-alpha overexpression indicates a good prognosis in early stage squamous cell carcinomas of the oral floor. *BMC Cancer.* 2005;5:84.
9. Gholizadeh N, Mehdipour M, Najafi Sh, Bahramian A, Garjani Sh, Khoeni Poorfar H. Evaluation of the serum zinc level in erosive and non-erosive oral lichen planus. *J Dent (Shiraz).* 2014;15(2):52-6.
10. Sahebamee M, Beitollahi JM, Mansourian A, Shahsavari N, Shabestari SB. Assessment of serum vitamin B12 and folic acid in patients with oral lichen planus: a case control study. *J Dent.* 2010;10:36-9.
11. D'Aurizio F, Villalta D, Metus P, Doretto P, Tozzoli R. Is vitamin D a player or not in the pathophysiology of autoimmune thyroid diseases? *Autoimmun Rev.* 2015;14(5):363-9.
12. Deschasaux M, Souberbielle JC, Partula V, Lécuyer L, Gonzalez R, Srouf B, Guinot C, Malvy D, Latino-Martel P, Druesne-Pecollo N, Galan P, Hercberg S, Kesse-Guyot E, Fassier P, Ezzedine K, Touvier M. What Do People Know and Believe about Vitamin D? *Nutrients.* 2016;8(11):718.
13. Goodman S, Morrongiello B, Meckling K. A randomized, controlled trial evaluating the efficacy of an online intervention targeting vitamin D intake, knowledge and status among young adults. *Int J Behav Nutr Phys Act.* 2016;13(1):116.
14. Oh J, Choi R, Park HD, Lee H, Jeong BH, Park HY, Jeon K, Kwon OJ, Koh WJ, Lee SY. Evaluation of vitamin status in patients with pulmonary tuberculosis. *J Infect.* 2017;74(3):272-280.
15. Hashemipour S, Ziaee A, Javadi A, Movahed F, Elmizadeh K, Javadi EH, Lalooha F. Effect of treatment of vitamin D deficiency and insufficiency during pregnancy on fetal growth indices and maternal weight gain: a randomized clinical trial. *Eur J Obstet Gynecol Reprod Biol.* 2014;172:15-9.
16. Dickerson RN, Van Cleve JR, Swanson JM, Maish GO 3rd, Minard G, Croce MA, Brown RO. Vitamin D deficiency in critically ill patients with traumatic injuries. *Burns Trauma.* 2016;4:28.
17. Jackson JL, Judd SE, Panwar B, Howard VJ, Wadley VG, Jenny NS, Gutiérrez OM. Associations of 25-hydroxyvitamin D with markers of inflammation, insulin resistance and obesity in black and white community-dwelling adults. *J Clin Transl Endocrinol.* 2016;5:21-5.
18. Pérez-Hernández N, Aptilon-Duque G, Nostroza-Hernández MC, Vargas-Alarcón G, Rodríguez-Pérez JM, Blachman-Braun R. Vitamin D and its effects on cardiovascular diseases: a comprehensive review. *Korean J Intern Med.* 2016;31(6):1018-29.
19. Rees JR, Mott LA, Barry EL, Baron JA, Bostick RM, Figueiredo JC, Bresalier RS, Robertson DJ, Peacock JL. Lifestyle and Other Factors Explain One-Half of the Variability in the Serum 25-Hydroxyvitamin D Response to Cholecalciferol Supplementation in Healthy Adults. *J Nutr.* 2016;146(11):2312-24.
20. Raab J, Giannopoulou EZ, Schneider S, Warncke K, Krasmann M, Winkler C, Ziegler AG. Prevalence of vitamin D deficiency in pre-type 1 diabetes and its association with disease progression. *Diabetologia.* 2014;57(5):902-8.
21. Thum-Tyzo K, Petkowicz B, Tyzo B, Pedowska M, Dziedzic M. OI0378 Vitamin D3 and oral health in patients with lichen planus. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2014;117(5):e385.
22. Beena Varma R, Valappila NJ, Pai A, Channavir Saddu S, Mathew N. Oral Lichen Planus: Is Vitamin D Deficiency a Predisposing Factor? A Case Report. *Int J Sci c Study.* 2014;2(7).
23. Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr.* 2008;87(4):1080s-6s.
24. Chirumbolo S, Björklund G, Sboarina A, Vella A. The Role of Vitamin D in the Immune System as a Pro-survival Molecule. *Clin Ther.* 2017;39(5):894-916.
25. Gupta A, Mohan RPS, Kamarthi N, Malik S, Goel S, Gupta S. Serum Vitamin D Level in Oral Lichen Planus Patients of North India- A Case-Control Study. *Journal of Dermatological Research and Therapy.* 2017;1(3):1-17.
26. Altieri B, Muscogiuri G, Barrea L, Mathieu C, Vallone CV, Mascitelli L, Bizzaro G, Altieri VM, Tirabassi G, Balercia G, Savastano S, Bizzaro N, Ronchi CL, Colao A, Pontecorvi A, Della Casa S. Does vitamin D play a role in autoimmune endocrine disorders? A proof of concept. *Rev Endocr Metab Disord.* 2017;18(3):335-46.