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Influence of Vitamin D Levels on Oral Lichen Planus: A Meta-Analysis

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Abstract
Background: Oral lichen planus (OLP) is a chronic inflammatory mucocutaneous disease of autoimmune nature. Low serum vitamin D levels have been associated with an exaggerated inflammatory response in OLP.
Objective: To assess the influence of vitamin D levels in OLP.
Search and selection methods: A search for studies on vitamin D and oral lichen planus was performed in the following databases: PubMed (MEDLINE, Cochrane Library), Web of Science (WoS) and Scopus.
Data analysis: For continuous outcomes, the estimates of effects of an intervention were expressed as mean differences (MD) using the inverse variance (IV) method, and for dichotomous outcomes, the estimates of effects of an intervention were expressed as odds ratios (OR) using Mantel-Haenszel (M-H) method, both with 95% confidence intervals.
Results: 16 studies with 1405 participants (727 OLP patients and 678 controls) were included in this meta-analysis. OLP patients had significantly lower mean vitamin D concentrations ($p<0.001$) and an increased risk (OR:2.45) of having deficient vitamin D levels ($p<0.01$) compared to controls. In contrast, controls were 2.79 times more likely to have normal vitamin D levels than patients with OPL ($p<0.001$). Finally, non-erosive OLP patients were ten times more likely to have normal vitamin D levels than erosive OLP patients ($p<0.01$).
Conclusions: Vitamin D levels might influence the evolution of OLP.

Keywords: Immunomodulating Agents, Inflammation, Lichen Planus, Oral, Vitamin D

1. Introduction

Oral lichen planus (OLP) is a chronic inflammatory disease of an autoimmune nature with mucosal and/or cutaneous involvement. It affects approximately 2% of the general population and typically presents with lesions of long duration, with episodes of exacerbation and remission [1]. However, its etiology is not yet fully understood. A cytotoxic activity of T-lymphocytes against epithelial keratinocytes has been suggested by the stimulation of defensive cells that recognize certain surface epithelial antigens as foreign [2]. Currently, OLP is considered an oral potentially malignant disorder (OPMD) with a malignant transformation rate ranging from 0.44% to 2.28% according to the literature. This risk of malignancy is higher in erosive and/or atrophic OLP lesions, in patients with heavy tobacco/alcohol consumption, and in the presence of concomitant hepatitis C virus infection [3]. Vitamin D is a micronutrient that regulates serum calcium and phosphorus metabolism. It also has antiproliferative, anti-angiogenic, pro-differentiating, and pro-apoptotic activities. Its anti-inflammatory and immunomodulatory effects regulate keratinocyte proliferation and differentiation [4]. Vitamin D plays a key role in maintaining homeostasis. This includes bone metabolism and, more recently, the immunomodulatory role of vitamin D on leukocytes. Low serum vitamin D levels have been associated with an exaggerated inflammatory response present in several diseases of an autoimmune nature such as rheumatoid arthritis, lupus erythematosus, or OLP [5]. This study aimed to analyse the influence of vitamin D levels on oral lichen planus.

2. Material and Methods

All the research steps (search, study selection, and data extraction) were developed independently by both authors (ARA and IC). Potential discrepancies in the article selection were resolved by consensus.

2.1 Search strategy
A search was conducted for studies on vitamin D and oral lichen planus up to March 2024 in the following databases: PubMed (MEDLINE, Cochrane Library), Web of Science (WoS), and Scopus. Search strategies were developed for each database using a combination of Medical Subjects Headings (MeSH) and free text terms. The search terms were: ('lichen planus, oral' [MeSH Terms] OR 'oral lichen planus') AND ('vitamin d' [MeSH Terms] OR 'vitamin D'); 'oral lichen planus' AND 'vitamin D'; TITLE-ABS-KEY ('oral lichen planus' AND 'vitamin D'). The inclusion criteria were as follows: a) all types of articles related to our purpose, b) articles without relevant risk of bias (score ≥6 stars on the Newcastle-Ottawa methodological quality assessment scale) [6], and c) articles written in any language and with no restrictions on publication date. The exclusion criteria were: a) articles with no full-text availability, b) articles with no clinical data, and c) articles with unusable data.

2.2 Data extraction
Mean vitamin D concentrations (ng/mL) were analyzed in patients with oral lichen planus and controls without the disease. Similarly, in both population groups (oral lichen planus/controls) the degree of vitamin D deficiency was established according to the following classification: deficiency (<20 ng/mL), insufficiency (20-29 ng/mL), and normal vitamin D levels (≥30 ng/mL). Finally, vitamin D concentrations and the degree of vitamin D deficiency were assessed considering erosive and non-erosive clinical subtypes of oral lichen planus.

2.3 Assessment of methodological quality
The methodological quality of the articles was evaluated using the Newcastle-Ottawa (NOS) methodological quality assessment scale [6] composed of eight items that evaluate three dimensions (selection, comparability, and exposure). Considering the score obtained, the studies are classified as high quality (≥7 stars), moderate quality (4-6 stars), and low quality (1-3 stars).

2.4 Statistical analysis
For the meta-analysis, data were processed with RevMan 5.4 software (The Cochrane Collaboration, Copenhagen, Denmark). For continuous outcomes, the inverse variance (IV) for the mean difference (MD), and for dichotomous outcomes, the odds ratio (OR) with the Mantel-Haenszel Chi-square formula (M-H) was used, both with 95% confidence intervals (95%CI). Heterogeneity was determined according to the Higgins statistic (I^2). In cases of high heterogeneity (I^2>50%), the random-effects model was applied. A p-value below 0.05 was considered the minimum level of significance.

3. Results
3.1 Study selection
The literature search yielded 98 articles (26 in PubMed, 32 in WoS, and 32 in Scopus) between the years 2013 and 2024, 20 of them duplicates, leaving 68 articles for eligibility. 52 articles were excluded due to: a) articles with no full-text availability (n=18), b) articles without clinical data (n=15), and c) studies with non-usable data (n=19). After applying these criteria,16 studies were included in this meta-analysis (Fig 1).

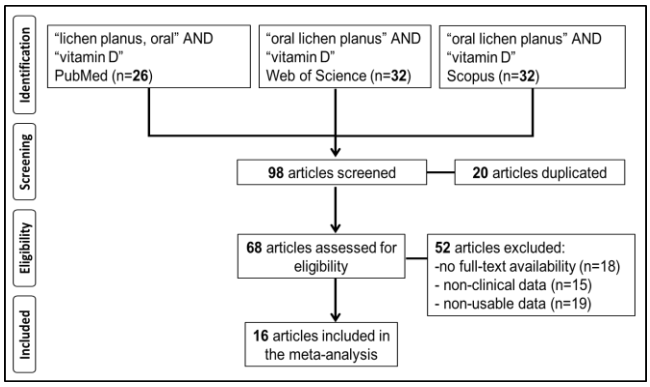

Fig 1: Study selection flowchart

Table 1 presents the main descriptive characteristics and the methodological quality according to the NOS scale of the sixteen studies [7-22] included in this meta-analysis. A total of 1,405 participants, 727 patients (51.7%) with OLP, and 678 (48.3%) healthy controls were considered in these articles. Among OLP patients, 53.8% were female and 46.2% were male, and among controls without the disease, 51.7% were female and 48.3% were male. The studies were conducted in the following countries: Iran (6 studies), India (3 studies), Kingdom of Saudi Arabia (2 studies), Turkey (2 studies), Iraq (1 study), Egypt (1 study), and China (1 study). According to the NOS quality scale, six articles (37.5%) had 6 stars, eight articles (50.0%) got 7 stars, and two articles (12.5%) reached 8 stars.

Table 1: Characteristics and methodological quality assesment of the sixteen articles included in this meta-analysis.

First author, year	Country	Study population	Vitamin D* detection method	Other parameters analyzed	NOS
Gupta, 2017 [7]	India	102 OLP (66F, 36M; 37.1y) 102 cont (66F, 36M; 37.1y)	ELFA	Age; gender; OLP clinical subtypes; psychological profile; residence; diet; socio-economic status.	8
Tak, 2017 [8]	India	20 OLP (14F, 6M; 47.8y) 20 cont (14F, 6M; na)	ECLIA	Age; gender; OLP clinical subtypes.	6
Bahramian, 2018 [9]	Iran	18 OLP (11F, 7M; 44.1y) 18 cont (14F, 4M; 49.9y)	ECLIA	Age; gender.	6
Mulayim, 2018 [10]	Turkey	40 OLP (23F, 17M; 35.9y) 40 cont (21F, 19M; 33.4y)	HPLC	Age; gender; location; Ca; P; PTH; ALP	8
Seif, 2018 [11]	Iran	66 OLP (45F, 21M; 55.0y) 30 cont (24F, 6M; 50.1y)	ELISA	Age; gender; OLP clinical subtypes.	7
Ahmed, 2019 [12]	Iraq	40 OLP (31F, 9M; 51.7y) 40 cont (29F, 11M; 49.2y)	ECLIA	Age; gender; OLP clinical subtypes; location.	7
Arica, 2020 [13]	Turkey	48 OLP (31F, 17M; 50.8y) 46 cont (32F, 14M; 46.6y)	ECLIA	Age; gender; OLP clinical subtypes; Ca; P; PTH.	7

Gholizadeh, 2020 [14]	Iran	64 OLP (na, na; na) 45 cont (na, na; na)	ELISA	Salivary and serum vitamin D levels.	6
Mahmoud, 2020 [15]	Egypt	30 OLP (15F, 15M; 42.0y) 30 cont (18F, 12M; 39.9y)	ELISA	Age; gender; BMI; IL-17.	7
Sadeghi, 2020 [16]	Iran	35 OLP (20F, 15M; 41.8y) 70 cont (35F, 35M; 40.8y)	ELFA	Age; gender.	6
Hu, 2021 [17]	China	67 OLP (na, na; 41.3y) 54 cont (na, na; 39.2y)	ECLIA	Age; BMI; TAC; IL-6; TNF-α; hs-CRP.	6
Rezazadeh, 2021 [18]	Iran	34 OLP (23F, 11M; 48.0y) 43 cont (25F, 18M; 48.7y)	HPLC	Age; gender; vitamin A; vitamin B_{12}; vitamin C; vitamin E.	7
Lama, 2022 [19]	KSA	60 OLP (49F, 11M; 47.9y) 30 cont (24F, 6M; 47.1y)	ELISA	Age; gender; OLP clinical subtypes; IL-17; IL-6.	7
Pawar, 2022 [20]	India	20 OLP (9F, 11M; na) 30 cont (na, na; na)	ECLIA	Age; gender; OLP clinical subtypes; location.	6
Saeed, 2022 [21]	KSA	33 OLP (21F, 12M; 35.1y) 30 cont (16F, 14M; 39.7y)	ECLIA	Age; gender; OLP clinical subtypes; location; BMI.	7
Nosratzehi, 2023 [22]	Iran	50 OLP (33F, 17M; 53.0y) 50 cont (33F, 17M; 51.0y)	ELISA	ANA.	7

***25-hydroxy vitamin D [25(OH) vit D]; **KSA:** Kingdom of Saudi Arabia; **OLP:** patients with oral lichen planus; **cont:** controls without the disease; **F:** female; **M:** male; **y:** mean age in years; **ELFA:** enzyme-linked fluorescent assay; **ECLIA:** electro-chemiluminescence immunoassay; **HPLC:** high pressure liquid chromatography method; **ELISA:** enzyme-linked immunosorbent assay; **na:** data not available; **Ca:** Calcium; **P:** Phosphorus; **PTH:** parathyroid hormone; **ALP:** alkaline phosphatase; **BMI:** body mass index; **IL-17:** interleukin 17; **TAC:** total antioxidant capacity; **IL-6:** interleukin 6; **TNF-α:** tumor necrosis factor alpha, **hs-CRP:** high-sensitivity C-reactive protein; **ANA:** antinuclear antibody; **NOS:** Newcastle-Ottawa methodological quality scale.

3.2 Vitamin D concentrations (oral lichen planus *vs.* controls)

Thirteen studies [7, 9, 10, 12-16, 18-22] compared serum vitamin D concentrations between OLP patients and controls without the disease (Fig 2). OLP patients had mean vitamin D concentrations 5.67 ng/mL lower than those of controls, with a highly statistically significant association (MD=-5.67; 95% CI: -8.84 to -2.50; p<0.001).

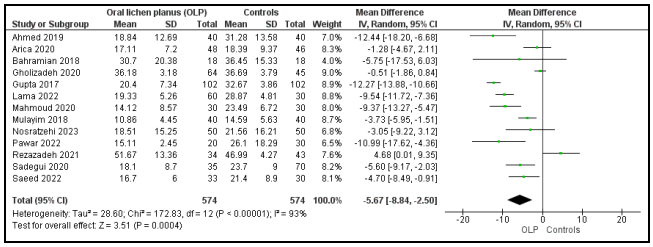

Fig 2: Study data and forest plot for vitamin D concentrations in patients with oral lichen planus and controls. **Mean±SD:** mean±standard deviation

The evaluation of different parameters related to vitamin D levels in oral lichen planus (OLP) patients also considering their clinical subtype and controls without the disease is shown in Table 2.

Seven studies [7, 11-13, 17, 19, 21] investigated vitamin D deficiency (<20 ng/mL) in OLP patients and controls. OLP patients were 2.45 times more likely to have vitamin D deficiency compared to controls. In the statistical analysis, a significant relationship was found (OR=2.45; 95% CI: 1.30 to 4.63; p<0.01).

Eight studies [7, 8, 11-13, 17, 19, 21] analyzed vitamin D insufficiency (20-29 ng/mL) in subjects with and without OLP. Oral lichen planus had no relevant influence on vitamin D insufficiency, with no statistical significance observed (OR=1.20; 95% CI: 0.76 to 1.89; p=0.44).

Seven studies [7, 8, 12, 13, 17, 19, 21] examined normal vitamin D levels (≥30 ng/mL) in OLP patients and controls. Controls without the disease increased 2.79-fold the probability of having normal vitamin D levels compared to OLP patients. After statistical analysis, highly significant differences were found (OR=2.79; 95% CI: 1.90 to 4.10; p<0.001).

Four studies [12, 13, 18, 20] determined the mean concentrations of vitamin D between patients with erosive and non-erosive OLP. Although OLP erosive patients had lower mean vitamin D concentrations than patients with non-erosive OLP subtypes, the results were not statistically significant (MD=-1.02; 95% CI: -2.97 to 0.92; p=0.30).

Two studies [8, 19] focused on low levels (insufficient or deficient) of vitamin D according to the erosive and non-erosive OLP clinical subtypes. Although erosive OLP patients were more likely to have low vitamin D levels, no statistical significance was found (OR=5.86; 95% CI: 0.16 to 210.63; p=0.33). These same two studies [8, 19] investigated normal vitamin D levels in patients with non-erosive and erosive OLP subtypes. Non-erosive OLP patients multiplied ten-fold their probability of presenting normal levels of vitamin D compared to erosive OLP patients, with a statistically significant relationship (OR=10.47; 95% CI: 2.15 to 50.97; p<0.01).

Table 2: Evaluation of different parameters related to vitamin D levels in oral lichen planus patients (OLP) and controls without the disease (Cont)

Parameter	Ref.	Outcome	OR/MD	(95% CI)	I^2	*P*-value
OLP vs. Controls						
Vitamin D deficiency (<20 ng/mL)	[7, 11-13, 17, 19, 21]	OLP	OR: 2.45	(1.30 to 4.63)	71%	<0.01*
Vitamin D insufficiency (20-29 ng/mL)	[7, 8, 11-13, 17, 19, 21]	Cont	OR: 1.20	(0.76 to 1.89)	47%	0.44
Vitamin D normal levels (≥30 ng/mL)	[7, 8, 12, 13, 17, 19, 21]	Cont	OR: 2.79	(1.90 to 4.10)	40%	<0.001*
OLP clinical subtypes						
Vitamin D mean concentrations (ng/mL)	[12, 13, 18, 20]	eOLP	MD: -1.02	(-2.97 to 0.92)	44%	0.30
Vitamin D low levels (<20 ng/mL)	[8, 19]	eOLP	OR: 5.86	(0.16 to 210.63)	82%	0.33

Vitamin D normal levels (≥30 ng/mL)	[8, 19]	neOLP	OR: 10.47	(2.15 to 50.97)	0%	<0.01*

Ref.: references; **OR:** Odds Ratio; **MD:** mean difference; **(95% CI):** 95% confidence interval; I^2**:** Higgins statistic for heterogeneity (percentage); **eOLP:** erosive OLP; **neOLP:** non-erosive OLP; *****statistically significant.

4. Discussion

In the present meta-analysis, data from 16 studies on the concentrations and deficiency degree of vitamin D in patients with oral lichen planus (OLP).

In this study, OLP patients had lower mean vitamin D concentrations than those of healthy controls, with a highly statistically significant relationship (p<0.001). Of the thirteen studies that compared vitamin D concentrations, twelve of them [7, 9, 10, 12-16, 19-22] agreed that these vitamin D levels were lower in patients with OLP; while only one [18] found lower levels in the control group.

Vitamin D exerts its biological function through its binding to specific vitamin D receptors called VDRs, whose presence has been demonstrated in the immune cells including T-lymphocytes, B-lymphocytes, and antigen-presenting cells. Vitamin D regulates cell proliferation and differentiation, modulating the expression of cytokines, both pro- and anti-inflammatory [21]. This vitamin promotes a negative feedback of several inflammatory mediators such as interleukin-1 beta (IL-1β), interferon-gamma (IFN-γ), interleukin-17 (IL-17) [19], and especially IL-6 and IL-8, whose serum concentrations are usually high in OLP patients [23]. Vitamin D stimulates the cellular differentiation of Th2 lymphocytes, while it inhibits Th1 and Th17 lymphocytes involved in the inflammatory processes of OLP. It also reduces the antigen presentation to T lymphocytes, inhibiting their activation. All these action mechanisms of vitamin D could explain the decrease in its concentrations in OLP patients, inducing an exaggerated and impaired immune response [19]. Patients with diabetes mellitus, another autoimmune disorder such as OLP, often present vitamin D deficiencies. Diabetic patients are up to 2.5 times more likely to have OLP, suggesting the association between these two diseases [24].

In the present study, OLP patients were more likely to suffer from vitamin D deficiency than controls, with a statistically significant association (p<0.01). Of the seven studies that focused on this parameter, six of them [7, 11, 12, 17, 19, 21] agreed to point out vitamin D deficiency among OLP patients; while one study [13] did not confirm this finding. Vitamin D deficiency in OLP patients could be due to the absence of the immunomodulatory role of this vitamin and, consequently, a disturbance of the immune response [25]. The relationship between vitamin D deficiency and a series of autoimmune diseases (diabetes mellitus, multiple sclerosis, rheumatoid arthritis, etc.) and mucocutaneous diseases such as pemphigus vulgaris or OLP has been demonstrated [12, 19, 26, 27]. However, a study carried out in Turkey [13] found no association between vitamin D deficiency and lichen planus, with vitamin D deficiency being observed more frequently in the control group. Although sun exposure could be adequate for the geographical place where the study was conducted, other factors must be involved in this frequent vitamin D deficiency in that population. It should also be taken into account that this study was carried out with patients with cutaneous lichen planus and not only OLP [13].

In this work, vitamin D insufficiency was not affected by having or not having OLP, without reaching statistical significance (p=0.44). Of the seven studies that evaluated this parameter, five of them [7, 11, 12, 17, 21] confirmed this vitamin D insufficiency in the controls; one study [19] reported a neutral finding and the remaining two ones [8, 13] observed more vitamin D insufficiency in OLP patients. Low levels (insufficient or deficient) of vitamin D constitute a global problem that frequently affects the general population. This may be due to little sun exposure, fewer outdoor activities, and an insufficient vitamin D supply through the diet [13]. All of these factors produce a decrease in vitamin D concentrations to inadequate levels. The development of OLP is related to various factors such as a genetic predisposition, emotional state, some infectious causes [22], and any triggering factor that alters the immune response [19]. Arica *et al.* [13] found more vitamin D insufficiency in OLP patients compared to controls, although a higher vitamin D deficiency in healthy patients, as previously indicated. Inadequate levels of vitamin D are commonly found not only in subjects with diseases but also in the general population. OLP is a disease especially prevalent in women between 30 and 60 years, where many of them are in the pre-menopausal or menopausal stages, which in parallel is associated with lower vitamin D levels [29].

In the present work, individuals without OLP had normal levels of vitamin D more frequently than OLP patients, with highly statistically significant differences (p<0.001). All studies [7, 8, 12, 13, 17, 19, 21] that analyzed this variable corroborated these normal levels of vitamin D among controls. Vitamin D plays an important role in the modulation and control of the immune response [27].

In this study, erosive OLP patients had lower concentrations and levels of vitamin D, although no statistically significant differences were found (p>0.05) according to the OLP clinical subtype. All studies [12, 13, 18, 20] that focused on vitamin D concentrations confirmed these lower levels in erosive OLP patients. The atrophic-erosive OLP clinical subtypes are those that are associated with a greater vitamin D deficiency. The presence of erosive oral lesions indicates greater severity of the lesions, with very intense autoimmune aggression by T-lymphocytes against basal keratinocytes [13]. Lower levels of vitamin D imply a greater lack of control of the autoimmune response and greater inflammation due to the release of pro-inflammatory cytokines, and consequently, the appearance of more severe OLP lesions [13].

Finally, non-erosive OLP patients were more likely to have normal (adequate) levels of vitamin D with a highly statistically significant association (p<0.01). All the studies [8, 19] that analyzed this parameter reinforced this finding. The vast majority of non-erosive OLP patients have asymptomatic reticular subtypes. These characteristics would indicate a lower severity of the disease with better biological behavior. Some authors consider pharmacological treatment unnecessary, limiting themselves to follow-up with periodic check-ups [25]. In these cases, the presence of normal levels of vitamin D would allow better control of the immune response in the OLP, preventing the erosive OLP forms [20]. The administration of vitamin D in OLP patients has been suggested as a possible therapeutic option since it induces improvement in lesions, especially erosive ones where healing is improved [23, 28, 29]. Nevertheless, the results

found regarding the therapeutic value of vitamin D are still inconsistent.

This study has some limitations. 1) The results of this meta-analysis should be interpreted with caution due to the high heterogeneity observed in some comparisons. 2) The possible relationship between vitamin D levels and OLP requires new research to establish more solid results and make decisions regarding whether or not to include it in the treatment of this disease.

5. Conclusions

In this meta-analysis, OLP patients had significantly lower mean vitamin D concentrations ($p<0.001$) and a higher risk (OR: 2.45) of having vitamin D deficient levels ($p<0.01$) compared to controls. On the contrary, controls increased 2.79-fold the probability of having normal vitamin D levels compared to OLP patients ($p<0.001$). Finally, non-erosive OLP patients multiplied ten-fold the probability of presenting normal levels of vitamin D compared to erosive OLP patients ($p<0.01$).

6. References

1. Alrashdan MS, Cirillo N, McCullough M. Oral lichen planus: A literature review and update. Arch Dermatol Res. 2016; 308(8):539-551.
2. Astorga MJ, Fuentes G, Quitral R, Cordero K. Relationship between vitamin D and oral lichen planus. Exploratory systematic review. Int J Odontostomat. 2022; 16(2):267-272.
3. Idrees M, Kujan O, Shearston K, Farah CS. Oral lichen planus has a very low malignant transformation rate: A systematic review and meta-analysis using strict diagnostic and inclusion criteria. J Oral Pathol Med. 2021; 50(3):287-298.
4. Sakthivel S, Gunasekaran S, Castelino RL, Babu GS, Ajila V, Buch SA. Serum vitamin D levels in patients with oral lichen planus: A systematic review and meta-analysis. Gulhane Med J. 2021; 63(4):267-273.
5. Saeed S, Choudhury P, Ahmad SA, Alam T, Panigrahi R, Aziz S, *et al.* Vitamin D in the Treatment of Oral Lichen Planus: A Systematic Review. Biomedicines. 2022; 10(11):2964.
6. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses [Internet]. Ottawa (Canada): The Ottawa Hospital. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
7. Gupta A, Sasankoti Mohan RP, Kamarthi N, Malik S, Goel S, *et al.* Serum vitamin D level in oral lichen planus patients of north India-A case-contro study. J Dermatol Res Ther. 2017; 1(3):1-17.
8. Tak MM, Chalkoo AH. Vitamin D deficiency- A possible contributing factor in the aetiopathogenesis of oral lichen planus. J. Evolution Med Dent Sci. 2017; 6(66):4769-4772.
9. Bahramian A, Bahramian M, Mehdipour M, Falsafi P, Khodadadi S, Dabaghi Tabriz F, *et al.* Comparing Vitamin D Serum Levels in Patients with Oral Lichen Planus and Healthy Subjects. J Dent (Shiraz). 2018; 19(3):212-216.
10. Mülayim MK, Nazik H, Öztürk P. Evaluation of vitamin D levels in patients with lichen planus. Turk Klin J Dermatol. 2018; 28(3):123-127.
11. Seif S, Jafari AZ, Mardani M, Hamidizadeh N. Evaluation Of Serum Vitamin D Level In Oral Lichen Planus Patients. J Mashhad Dental School. 2018; 42(1):49-58.
12. Ahmed SA. The role of serum vitamin D deficency in oral lichen planus case control study. Diyala J Med. 2019; 17(2):189-198.
13. Arica DA, Selçuk LB, Örem A, Ural ZK, Yayli S, Bahadir S. Evaluation of serum vitamin D levels in patients with lichen planus. Turk Arch Dermatol Venereol 2020; 54(4):138-142.
14. Gholizadeh N, Pirzadeh F, Mirzaii-Dizgah I, Sheykhbahaei N. Relationship between salivary vitamin D deficiency and oral lichen planus. Photodermatol Photoimmunol Photomed. 2020; 36(5):384-386.
15. Mahmoud SB, Anwar MK, Shaker OG, El Sharkawy DA. Possible Relation between Vitamin D and Interleukin-17 in the Pathogenesis of Lichen Planus. Dermatology. 2021; 237(6):896-901.
16. Sadeghi M, Zarabadipour M, Azmodeh F, Mirzadeh M, Golezari AS. Association of serum level of 25-hydroxy vitamin D with Oral Lichen Planus. A case-control study. J Oral Res. 2020; 9(5):400-404.
17. Hu Y. The relationship between serum vitamin D level with inflammatory markers and Total Antioxidant Capacity in Oral lichen planus. Cell Mol Biol (Noisy-le-grand). 2022; 67(5):227-232.
18. Rezazadeh F, Haghighat S. Serum Vitamin Profile in Oral Lichen Planus Patients in Southwest of Iran. Biomed Res Int. 2021; 8627435.
19. Lama H M, Hussein F, Sadek H, Abdelghany W. Serum vitamin D level in healthy individuals versus patients with symptomatic and asymptomatic oral lichen planus. Cell Mol Biol (Noisy-le-grand). 2022; 68(2):19-25.
20. Pawar V, Krishna S, Deepak TA, Prarthana GA, Vyavahare S, Jujare R. Association of vitamin D serum concentration and oral lichen planus: A randomized controlled clinical trial. J Indian Acad Oral Med Radiol. 2022; 34(4):414.
21. Saeed AHM, Alfataih MTBA, Al Adainan BMM. vitamina D deficiency among patients with lichen planus in najran KSA. Egypt J Hosp Med. 2022; 89(2):6556-6560.
22. Nosratzehi T. Serum vitamin D and antinuclear antibody level in oral lichen planus patients: A cross-sectional study. Ann Med Surg (Lond). 2023; 85(2):136-139.
23. Delavarian Z, Dalirsani Z, Mousavi Z, Shakeri MT, Rafatpanah H, Seif F, *et al.* Evaluation of the efficacy of vitamin D in the treatment of oral lichen planus: A double-blind randomized clinical trial. J Oral Health Oral Epidemiol. 2021; 10(2):107-115.
24. Dave A, Shariff J, Philipone E. Association between oral lichen planus and systemic conditions and medications: Case-control study. Oral Dis. 2021; 27(3):515-524.
25. Gonzalez-Moles MA, Warnakulasuriya S, Gonzalez-Ruiz I, Gonzalez-Ruiz L, Ayen A, Lenouvel D, *et al.* Worldwide prevalence of oral lichen planus: A systematic review and meta-analysis. Oral Dis. 2021; 27(4):813-828.
26. Gupta J, Aggarwal A, Asadullah MD, Khan MH, Agrawal N, Khwaja KJ. Vitamin D in the treatment of

oral lichen planus: A pilot clinical study. J Indian Acad Oral Med Radiol. 2019; 31:222-227.
27. Nazeer J, Singh S, Jayam C, Singh R, Iqubal MA, Singh R. Assessment of the Role of Vitamin D in the Treatment of Oral Lichen Planus. J Contemp Dent Pract. 2020; 21(4):390-395.
28. Motahari P, Pournaghi Azar F, Rasi A. Role of Vitamin D and Vitamin D Receptor in Oral Lichen Planus: A Systematic Review. Ethiop J Health Sci. 2020; 30(4):615-622.
29. Razi A, Mohiuddin S, Karim AA, Iqbal A. Vitamin D as an adjuvant therapy to cure oral lichen planus in peri-menopausal women. Pakistan Oral Dental J. 2018; 38(4):399-403.