

**MINISTRY OF HIGHER EDUCATION AND
SCIENTIFIC RESEARCH
BABYLON UNIVERSITY _ FACULTY OF
DENTISTRY**

ASSOCIATION OF VITAMIN "D" DEFICIENCY AND INCIDENCE OF ORAL LICHEN PLANUS

A research submitted to the department of oral medicine, in the Faculty of Dentistry Babylon University as a partial requirement of degree of bachelors (B.D.S.)

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We thank God Almighty, who has enabled us to complete this scientific research, and who grants us health, wellness and determination

We extend our sincere thanks and appreciation to Dr. Suha for all the guidance and valuable information she provided us with, which contributed to enriching the subject of our study in its various aspects.

We also extend our thanks to the members of the esteemed discussion committee, and not to forget the good Dr. Ammar

Special thanks to our families, brothers, sisters and friends who made every effort to reach what we are

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ (١) خَلَقَ الْإِنْسَانَ مِنْ عَلَقٍ (٢)
اقْرَأْ وَرَبُّكَ الْأَكْرَمُ (٣) الَّذِي عَلَّمَ بِالْقَلَمِ (٤) عَلَّمَ الْإِنْسَانَ مَا لَمْ
يَعْلَمْ (٥)

صدق الله العلي العظيم
سورة العلق

ABSTRACT

Introduction:

Lichen planus is a rather common chronic inflammatory disease of skin and mucous membranes, which probably arises due to an abnormal immunological reaction and have some tendency to undergo malignant transformation . It mainly affects patients of middle age or older and is slightly more common in females.(1&2)

The oral lesions have a characteristic but not entirely specific appearance and distribution.

Depending on the balance between destruction and resolution, the disease presents with a range of appearances. Like; Reticular lichen planus, Atrophic lichen planus, Ulcerated lichen planus, Plaques lichen planus, Desquamative gingivitis and Bullous lichen planus.

Vitamin D, It is also called as 'sunshine vitamin'. Although vitamin D belongs to the category of vitamins, it chemically behaves like a hormone or pro-hormone in many instances. Vitamin D is fat soluble and it can be produced in the sun-exposed skin or it can be absorbed in the intestine as dietary vitamin D. The active form of vitamin D is known as 1-25 dihydroxycholecalciferol (2&4)

Objective: To study the relation between Vitamin D deficiency and occurrence of oral Lichen planus.

Material and Methods: the study deals with surveying about previous studies that searching about the correlation between the deficiency of vitamin D and development of oral lichen planus.

Results: Many researches were included in this study that searching about the relationship between vitamin D deficiency and development of oral lichen planus, and all studies found significant correlation between vitamin D deficiency and incidence of oral lichen planus.

Conclusion: From the above different studies we conclude that Vit. D deficiency play an important role in the development of oral lichen planus, and correction the level of serum Vit. D, may play a major role in curing of the disease.

So as a conclusion, Vit. D supplementation may be considered as a an adjuvant line of treatment for such chronic un curable disease.

Keyword :

1- lichen planus

2- vitamin D

INTRODUCTION

1- LICHEN PLANUS

Lichen planus is a rather common chronic inflammatory disease of skin and mucous membranes, which probably arises due to an abnormal immunological reaction and have some tendency to undergo malignant transformation . It mainly affects patients of middle age or older and is slightly more common in females.(1&2)

1.1. Aetiology and pathogenesis:

The etiology of lichen planus remains unknown, however psychological stress often aggravates the condition. In contrast, the pathogenesis is relatively well understood.

- It is believed that an abnormal recognition and expression of basal keratinocytes of the epithelium as foreign antigens by the Langerhans cells, induces an autoimmune reaction in the body, which results in the initiation of this disease.
- Initially, Langerhans cells recognize an antigen, which is similar to the antigens on the epithelial keratinocytes of the susceptible patient with certain classes of major histocompatibility antigens (MHA).
- Thereafter, during the processing of antigens and subsequent stimulation of the T-lymphocytes by the Langerhans cells, some lymphocytes which are cytotoxic to the epithelial keratinocytes are produced .
- These cytotoxic T-lymphocytes accumulate in the sub-basilar connective tissue region of the epithelium and interact with the basal keratinocytes and eventually cause 'liquefaction degeneration' of these cells.(2)

1.2. Types :

Skin lesions

During the course of the disease, about one-third of patients have skin lesions only, one-third have oral lesions only and the remaining third have

both. Skin lesions are typically purplish papules, 2–3 mm across with a glistening surface marked by minute fine ‘Wickham’s striae’* and are usually itchy. Typical sites are the flexor surface of the forearms and especially the wrists, shins and small of back. Skin lesions help in diagnosis if present but can be identical in drug-induced lichenoid reactions. Skin lesions are relatively easy to treat with steroids, and many patients only suffer them for a few years.(1)

Oral lesions

The oral lesions have a characteristic but not entirely specific appearance and distribution. Lesions are usually bilateral and very often symmetrical, sometimes strikingly so. The buccal mucous membranes, particularly posteriorly, are by far the most frequently affected site, but lesions may spread forward almost to the commissures. The next most common site is the tongue, either the lateral margins or, less frequently, the dorsum. The gingivae are often affected, at least focally, by desquamative gingivitis, and this is fairly frequently the only oral site involved. Only gingiva around teeth is affected; lichen planus resolves on extraction of teeth and rarely affects edentulous ridges. The floor of the mouth and palate are usually uninvolved and apparent extension to floor of mouth should raise suspicion of either misdiagnosis (of a potentially malignant dysplastic process) or a drug reaction. Depending on the balance between destruction and resolution, the disease presents with a range of appearances. These are not different types of lichen planus, only presentations or phases of disease. Any one patient may have several presentations that change from one pattern to another over time. The patterns help determine treatment need but have no other significance. Unlike skin lesions, oral lesions are difficult to treat, and Most patients will suffer oral lesions for life, although severity may wane with age.(2)

1 Reticular lichen planus comprises a meshwork pattern of Striae, fine white lines caused by keratinization, between 0.1–2 mm wide that criss-cross randomly. They are sharply defined snowy white and form lacy, radiating or annular patterns . They may occasionally be interspersed with minute, white papules. If the keratinization is thick, striae may be felt as slightly raised and patients feel them as roughening or a ‘dry’ area (Fig. 1). (1)



(Fig. 1)

2 Atrophic lichen planus produces red areas of epithelial thinning , often combined with striae. The inflamed sub-mucosa is visible through the thin epithelium, appearing red (Fig. 2) . (1)



(Fig. 2)

3 Ulcerated lichen planus The ulcers are shallow and irregular and covered by a smooth, slightly raised yellowish layer of fibrin .Ulcers are usually surrounded by atrophic areas, and striae may be seen around the margins (Fig. 3) .(1)



(Fig. 3)

4-Plaques lichen planus are solid areas of keratinization and often affect the dorsum of the tongue or the buccal mucosa. They are clinically indistinguishable from other leukoplakias. clinically presents a raise or flattened, white area on the mucous membrane (Fig. 4) .(2)



(Fig. 4)

5 Desquamative gingivitis is most commonly caused by lichen planus. The gingivae appear shiny, inflamed and smooth across the full width of the attached gingiva . The gingivae are occasionally the only site of lichen planus (Fig. 5) . (1)



(Fig. 5)

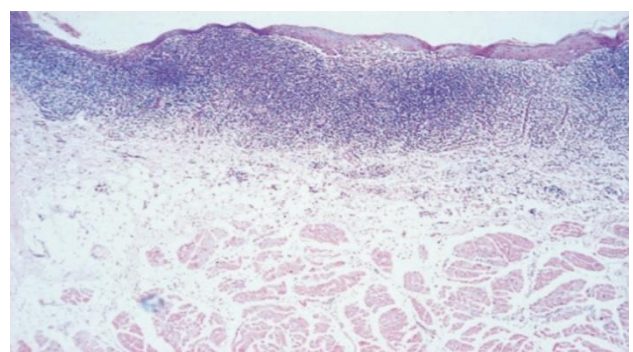
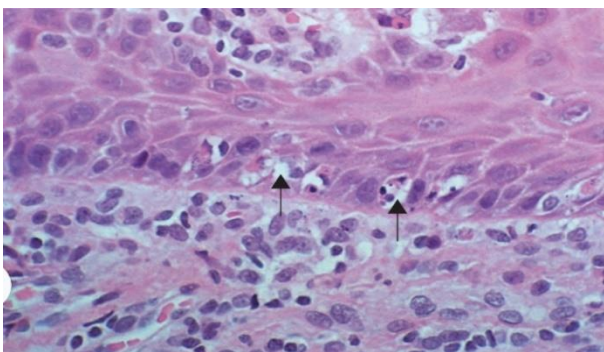
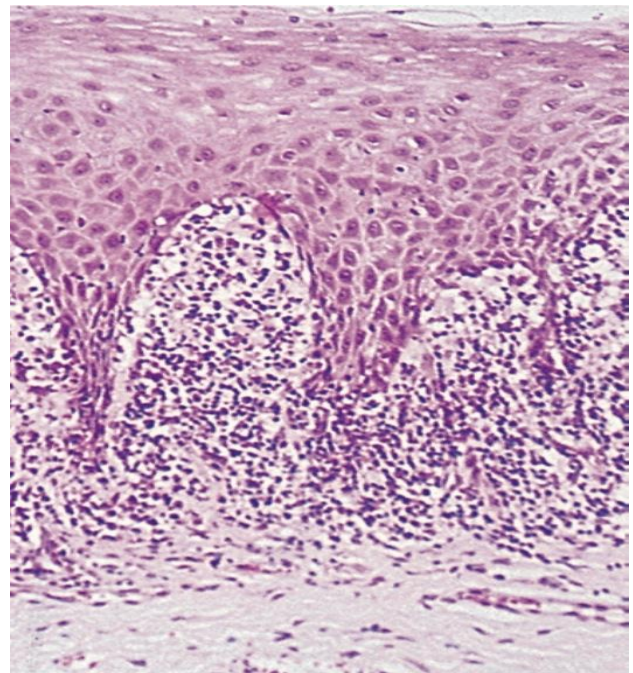
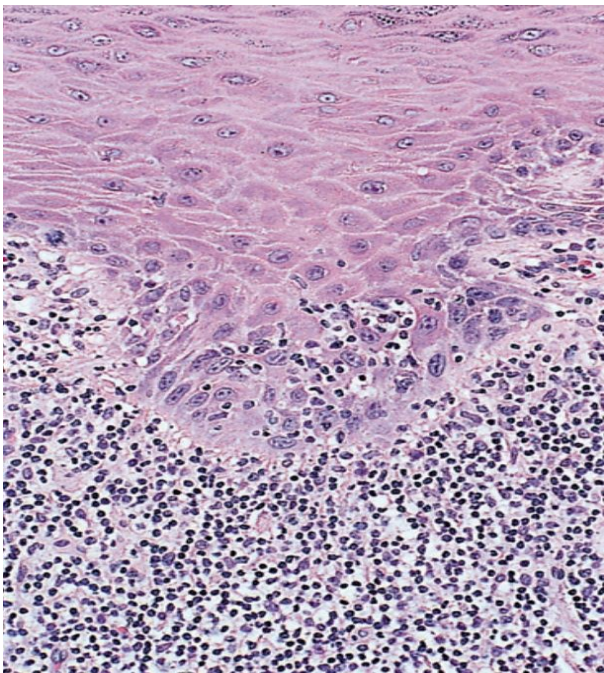
6 Bullous lichen planus This is a rare type and vesicles or bullae may occur from time to time. It is very important to differentiate this type from pemphigus or mucous membrane pemphigoid (Fig. 6) . (3)



(Fig. 6)

1.3. Pathology

Histologically, a series of common features are seen in varying proportions matching the clinical presentations. There is usually a dense sharply defined band-like infiltrate of lymphocytes running along beneath the epithelium. Smaller numbers of lymphocytes infiltrate the basal cell layers and are seen adhering to basal cells undergoing apoptosis. Apoptotic bodies are seen along the basement membrane, and where they cluster there are 'holes' in the epithelium from loss of basal cells (liquefaction degeneration is a historical term for this: there is no liquefaction) (Fig. 7). (1)



(Fig. 7)

1.4. Diagnosis :

The diagnosis can usually be made on the history, the appearance of the lesions and their distribution, ideally confirmed by biopsy. Biopsy is required in plaque-type lesions or when lesions are in any other way unusual. (1)

1.5. Treatment

Small lesions of lichen planus are treated well with topical steroids, e.g. fluocinonide. In more resistant cases, systemic administration of methyl prednisolone is effective either alone or in combination with topical steroids. Intra-lesional injections of steroid have been used with some degree of success but are often not well tolerated by the patient. Patient's psychological balance must be restored. (2)

2-VITAMIN D

It is also called as 'sunshine vitamin'. Although vitamin D belongs to the category of vitamins, it chemically behaves like a hormone or pro-hormone in many instances. Vitamin D is fat soluble and it can be produced in the sun-exposed skin or it can be absorbed in the intestine as dietary vitamin D. The active form of vitamin D is known as 1-25 dihydroxycholecalciferol (2&4)

2.1.Functions of vitamin D

- Vitamin D helps in the absorption of calcium and phosphorus from the foods in intestine by stimulating the calcium binding proteins in the GI tract.
- It helps in calcium and phosphorous metabolism.

- It promotes the calcification or mineralization of bone, cartilage and teeth; however very high levels of vitamin D can cause bone resorption.
- Vitamin D acts on immune system by promoting phagocytosis and by inducing immunomodulatory functions.
- It antagonistically acts against the action of parathyroid hormone.
- It increases the renal reabsorption of calcium. (2)

2.2.Forms

1- A nine-carbon, monounsaturated (i.e., containing one double bond) side chain. Vitamin D-active compounds with this structure are derivatives of ergocalciferol, is also called vitamin D₂. This vitamin can be produced synthetically by the photolysis of plant sterols.

2- An eight-carbon, saturated (i.e., containing no double bond) side-chain. Vitamin D-active compounds with this structure are derivatives of cholecalciferol, also called vitamin D₃, which is produced metabolically through a natural process of photolysis of 7-DHC on the surface of skin exposed to ultraviolet irradiation, e.g., sunlight. The metabolically active vitamers are side chain-substituted, open-ring steroids with a cistriene structure with hydroxylated carbons at ring position 1 and side chain position 25.(5)

2.3.VITAMIN D DEFICIENCY

Signs of Vitamin D Deficiency

Vitamin D deficiency affects several systems, most prominently skeletal and neuromuscular

1-Primary causes involve:

- inadequate vitamin D supply
- inadequate exposure to sunlight
- insufficient consumption of foods containing vitamin D

2-Secondary causes relate to impaired absorption, metabolism, or nuclear binding of the vitamin

- gastrointestinal diseases (e.g., small bowel disease, gastrectomy, pancreatitis), involving mal-absorption of the vitamin
- hepatic diseases (biliary cirrhosis, hepatitis), that reduce activity of the 25-hydroxylase
- renal diseases—that reduce the activity of the 1-hydroxylase (nephritis, renal failure) or cause loss of 25-OH-D₃ into the urine (nephrotic syndrome)
- exposure to drugs (e.g., the anticonvulsants pheno-barbital, diphenylhydantoin), that induce the catabolism of both 25-OH-D₃ and 1,25-(OH)₂-D₃
- hypoparathyroidism, impairs the ability to respond to hypocalcaemia by increasing activity of the 1-hydroxylase
- cyp27b1 mutations, resulting in loss of 25-OH-D₃ 1-hydroxylase activity in vitamin D-dependent rickets type I
- VDR mutations, impair transcription of vitamin D-regulated genes in vitamin D-dependent rickets type II
- PTH resistance, results in pseudo-hypoparathyroidism, i.e., hypocalcaemia without compensating renal retention or bone mobilization of Ca, despite normal PTH secretion

- vitamin D resistance, impairments in both enteric absorption and renal tubular reabsorption of phosphate, hypersensitivity to PTH, and reduced 1-hydroxylation of 25-OH-D3 (5)

2.4.VITAMIN D TOXICITY

Overdose of vitamin D can cause the following problems:

- Hypercalcaemia due to increased absorption of calcium.
- Can cause high blood pressure.
- Anorexia, nausea, vomiting followed by poly-urea and polydipsia.
- Weakness, nervousness, pruritus (itching), renal failure and increased risk of ischemic heart disease.(2)

Aim of Study: To study the relation between Vitamin D deficiency and occurrence of oral Lichen planus.

Material and Methods: the study deals with surveying about previous studies that searching about the correlation between the deficiency of vitamin D and development of oral lichen planus.

Results and Discussion

Oral lichen planus mostly affect middle age female, the most common type of oral lichen planus was reticular type (95%) followed by erosive (57.5%) and atrophic oral lichen planus (45%). Mostly oral lichen planus appears on buccal mucosa bilaterally (95%). (ef)

The present study searching about the relationship between the deficiency of vitamin D and occurrence of oral lichen planus...

There are several studies illustrated the relationship between Vitamin D deficiency and development of oral Lichen planus:

Delavarian, et. al., studied on patients with clinical presentation of OLP. The patients were divided into three different groups depending on factors such as stress, low vitamin D levels, or a combination of the above factors. Patients with severe vitamin D deficiency were supplemented with vitamin D. They found a marked improvement and long-term remission in the symptoms in vitamin D-deficient patients after restoration of normal vitamin D level suggests its role in pathogenesis of OLP like other autoimmune diseases.(6)

Motahari, et.al, in 2020, studied a group consisted of 65 oral lichen planus patients and 100 healthy blood donors in the control group. Single nucleotide polymorphisms were genotyped by real time PCR or PCR-restriction fragment length polymorphism (RFLP) method. Heterozygous as well as mutated genotype of vitamin D receptor (VDR) FokI (rs2228570) polymorphism was associated with increased oral lichen planus risk in comparison with wild type genotype.(7)

Another study were done by Shoukheba in 2020, who studied on patients group of 30 women, their ages ranged from 45 to 65 years, with oral lichen planus and they observed that the incidence of oral lichen planus most commonly reported among the female population of peri and postmenopausal age . OLP in peri and postmenopausal women can be mediated by the declined level of estrogen and Progesterone directly or indirectly through causing depression that can trigger LP. Estrogen increases the activity of the enzyme responsible for activating Vit. D, so declining estrogen levels during the menopausal transition could lead to symptoms of

Vit D deficiency. Hence, there is a strong correlation between Vit.D deficiency and the incidence of lichen planus.(8)

Ahmed in 2019, studied the serum level Vit. D in patients affected with oral LP in comparism to healthy patients and found that Vitamin D deficiency was significantly higher in patients with oral lichen planus (60%) and (22.5%) in control group, and they conclude that the deficiency in serum vitamin D level was not only related to the development of oral lichen planus, but it was also related to the symptoms, and types of oral lichen planus.(9)

Gupta, et. Al, in 2019, involved (28) patients with OLP with vitamin D deficiency or insufficiency, in their study. The intervention and control groups were given one capsule of 50000 units of vitamin D and one placebo capsule weekly for 8 weeks, results showed that the severity of lesions was significantly reduced in the intervention group . After the treatment, They concluded that, Vitamin D reduced the severity of OLP lesions. Vitamin D can be suggested as adjuvant therapy for patients with OLP. (10)

Bahramian, et. al, in 2018, made a study included, (18) patients suffering from oral lichen planus and (18) healthy people were chosen as the control group. Vitamin D serum levels were assessed with a Vitamin D total (25-hydroxy vitamin D) by employing the Electrochemiluminescence technique. They found that, the level of Vitamin D in the serum of patients suffering from oral lichen planus are lower than healthy individuals but not significant.(11)

Razi, et .al, in 2018 searching about the relationship between Vitamin D deficiency and development of Lichen planus. The purpose of their study is to investigate Vitamin D supplementation as an adjunctive method in curing the progression of lichen planus among peri-menopausal women.

So Vitamin D deficiency is mostly common in peri menopausal women and is associated with Oral Lichen Planus cases.(12)

Gupta, et.al, in 2017 are studied venous blood samples of 102 clinically diagnosed oral lichen planus patients and 102 age and sex matched controls were obtained for the study and serum vitamin D levels were estimated. They found, Vitamin D 3 deficiency was more in OLP cases (70.6%) as compared to controls. Vitamin D deficiency was found more in OLP cases pointing towards the possible co-relation of vitamin D and OLP.(13)

Tak, and Chalkoo in 2016 studied on a group of patients who were previously diagnosed as Oral lichen planus patients. 25-Hydroxyvitamin D [25 (OH) D] Levels were measured by ECLIA (Electrochemiluminescence immunoassay) method and found Statistically Significant Association of serum vitamin D levels in patients with Oral lichen planus. The results of this study suggest that Vitamin D levels may have an important role in the etio-pathogenesis of the disease or may be one of the contributory factors that determines the progression and prognosis of the disease.(14)

Conclusion:

From the above different studies we conclude that Vit. D deficiency play an important role in the development of oral lichen planus, and correction the level of serum Vit. D, may play a major role in curing of the disease.

So as a conclusion, Vit. D supplementation may be considered as a an adjuvant line of treatment for such chronic un curable disease.

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