The Egyptian Journal of Hospital Medicine (October 2022) Vol. 89 (2), Page 6556- 6560

Vit D Deficiency Among Patients with Lichen Planus in Najran KSA

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ABSTRACT

Background: Lichen planus (LP) is a chronic inflammatory autoimmune skin disorder that commonly affects the skin, oral mucosa, genital mucosa, scalp, and nails. Vitamin D has properties of anti-inflammatory with immunomodulatory effects and some antioxidant effects.

Objectives: This research aimed to assess the level of serum vitamin D among patients with Lichen Plans and also to do a comparison with the healthy control group

Subjects and Methods: A case-control study was carried out. Thirty-three patients with Lichen planus and 30 normal healthy controls were involved in this study. The blood samples were taken and collected to assess the serum levels of 25-hydroxy vitamin D, from all the patients and the control subjects.

Results: The Mean serum level of Vitamin D in patients with LP was 16.7 ± 6.0, which was significantly lower than that of normal subjects (21.4 ± 8.9), with P value = 0.029.

Conclusion: Our research showed a lower level of Vit D among patients with LP. Also, there may be other factors that play roles in provoking LP and its immunopathogenesis.

Keywords: Lichen planus, Vitamin D, Etiology, Pathogenesis, Oral lichen planus.

INTRODUCTION

Lichen planus (LP) is a chronic skin disorder characterized by inflammatory processes involving the skin and to some extent, the mucosal membrane, nails, and hair with the prevalence of one percent of the whole population. The onset of the disease can occur at any age, but the disease usually starts in middle-aged adults. The precise etiology of Lichen Planus and its pathophysiology is still not fully understood. An immunological mechanism including activated CD8+ T cells, directed against the lowermost layer (basal keratinocytes) of the epidermis, which leads to changes in keratinization of the skin has been proposed. Regarding the Previous reports which elicited upregulation of ICAM-1 with the association of helper T cell cytokines and type 1 (Th1) - driven immune response [1, 2].

The T-helper1/T-helper2 ratios in patients with LP are high, this supports the idea that T-helper1 may have a dominant role in the pathogenesis of LP [3].

The effect of cytotoxic CD8+ T lymphocytes that are provoked during MHC class II antigen presentation of Langerhans cells to CD4+ T-helper cells is responsible for the toxicity toward keratinocyte antigens in the lower layer of the epidermis (basal layer), which lead to degeneration of this layer [4].

Vitamin D is a hormone that mainly controls the regulation of calcium and phosphorus homeostasis [4, 5]. It is also responsible for some antiangiogenic properties in addition to pro-differentiating, anti-proliferative, and pro-apoptotic effects. Vitamin D receptor (VDR) which is a specific nuclear hormone receptor is the main responsible part of vitamin D's biological function [6].

Regarding the physiological effects, vitamin D is responsible for the regulation of proliferation and differentiation of keratinocytes, also to some extent for skin immune system homeostasis, besides the apoptotic procedure in the skin [6, 7]. Vitamin D also has a clear role in the way of the response of immune reaction with some anti-inflammatory possessions [8, 9, and 10]. Vitamin D also has effects on embarrassment of T-helper 1 explosion, motivation of adjusting T cells, with some conquest of B lymphocyte diversity, and also shares in reserve of the proclamation of immunoglobulin. It likewise inhibits the antigen exhibition and leads to modulation of dendritic cells maturation [11].

On the other hand, Vitamin D also down-regulates the construction of cytokines, such as interleukin (IL)-1β, TNF-alpha, IL-6, and IL-8 [12]. For these factors, the immunomodulatory properties, and decreased vitamin D level may affect the regulatory T cell numbers, and other T lymphocytes, such as T-h1 that play a role in a number of inflammatory diseases, notably LP. Consequently, lack of vitamin D could put people at risk for developing Th1-dominant immunological diseases as LP [13, 14].

Limited research has examined the amount of blood vitamin D in individuals experiencing lichen planus to yet, and indeed the results are conflicting [15, 16, 17].

The aim of this study was to investigate the association between lichen planus and Vitamin D deficiency. We measured the level of vitamin D in the serum of lichen planus patients and to do a comparison with that of the control group.

PATIENTS AND METHODS

Study design and groups

A case-control study design was conducted. We involved all patients with lichen planus diagnosed at the Dermatology Clinic in Najran University Hospital over the past two years from Feb. 2019 to Dec. 2021. All the cases with the typical presentation were diagnosed clinically while in the suspected cases the diagnosis was

Received: 01/07/2022
Accepted: 07/09/2022

confirmed by clinicopathological correlation. Thirty-three patients were diagnosed with lichen planus during these two years. We also included 30 healthy matched control group. They were volunteers from the hospital staff and university students from the same geographic population of LP patients group, all cases and control group had skin Fitzpatrick phenotype three to five.

Exclusion criteria: People less than 18 years old, patients with any medications that influence the level of Vit D like patients on any type of systemic corticosteroid treatment, calcium channel blockers, those with calcium and Vit D supplements, or high doses of corticosteroid during the last five months and any provocative oral agents in the case of oral LP like amalgam or gold. Also, patients with any history of hepatic, kidney, bone metabolic diseases and other diseases like intestinal malabsorption, any history of malignancies, hyperthyroidism, hypothyroidism, parathyroid diseases, diabetes mellitus, pregnant women, all were excluded from study and control groups.

We used questionnaires for all subjects that demonstrate demographic properties, body weight (BMI), and any medical or pharmacological profiles. Specific clinical features of LP, type, and duration of illness were also involved.

Blood samples collection and interpretation:

The best indicator of Vit D (25-hydroxyvitamin) deficiency is its serum level, which was our way of evaluation from samples taken from the blood of all patients and control subjects, we collected the samples from Feb 2019 to Dec. 2021, the sample tubes labeled by the information of the subject, name, age, type of LP in the patient's group. We consider the level of Vitamin D deficient if the serum level of Vit D was less than 20 ng/mL, from 20 to 30 ng/mL were we considered as insufficient, and sufficient for serum level over 30 to 100 ng/mL [7]. The time of blood sample collection was from 9.00 to 12 AM, after fasting period from midnight. All the tubes were collected then placed into separated tubes then left for thirty minutes to clot, then ten minutes on a centrifuge at 3000 RPM. The serum level of Vit D was assessed by chemiluminescence immunoassay procedure.

Ethical considerations:

The study was approved by The Research Ethical Committee of Najran University. All the participants of the study provided fully informed consents. Data confidentiality was confirmed, collected data were totally de-identified since names and specific address of the participants were not included. Data were safeguarded on the PI computer that was password protected till group statistical analysis and publication. This work was performed according to the code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Through using statistical programme for social sciences. The gathered information was categorized and examined (SPSS Inc., Chicago, Illinois, USA). For both the qualitative and quantitative data, descriptive statistics were utilised. A P value of 0.05 or even less was employed to determine whether discrepancies were substantial when using the X^2-test and Mann Whitney test.

RESULTS

Table (1 & 3) showed the Mean levels of BMI, age and Vit. D in cases and control. Mean age of thirty-three patients (21 women and 12 men) was 35.1 ± 8.9 years and 30 controls (16 women and 14 men) mean age was 39.7 ± 7.8 years. The Mean serum level of Vitamin D in patients with LP was 16.7 ± 6.0, which was lesser than that of healthy subjects (21.4 ± 8.9 ng/ml, P value = 0.029). The body mass index was mildly higher in Lichen planus patients than in the healthy individuals. The Mean BMI was 25.7 ± 3.7 for LP cases and 25.3 ± 3.6 for control group with insignificant difference (P value = 0.576).

Table (2) Type of LP, duration of the Illness and presence of/or family history of autoimmune diseases among the studied cases. Showed that the cutaneous disease was present in 18 patients, mucocutaneous disease in 9, and mucosal lesions only in 6. Wickham striae or reticular lesions were present in 9 of the 15 patients with mucocutaneous and oral mucosa involvement in 11. The lichen planus patients were with lower serum vitamin D levels compared to the control group. Vitamin D levels were statistically significantly lower in mucosal LP patients compared to those with cutaneous LP. The level of serum vitamin D less than 20 ng/mL was considered deficient, 20-30 ng/mL was regarded as insufficient, and the level of 30-100 ng/mL as sufficient. The deficient and also the insufficient were shown in a part of the patient and the control groups as well. The level of serum vitamin D was sufficient in only one patient with LP in total. The toxic levels of serum Vit D (more than 100 ng/mL) were neither found in a group of patients, nor in the controls group.

Table (1): Mean ± SD of age, Vit. D and BMI levels in cases and control groups

Parameter	Mean ± SD of cases	Mean±SD of control	P value
Age (years)	35.1 ± 8.9	39.7 ± 7.8	0.014*
Vit. D level (ng/mL)	16.7 ± 6.0	21.4 ± 8.9	0.029*
BMI (kg/m^2)	25.7 ± 3.7	25.3 ± 3.6	0.576*

*Mann Whitney test was used

Table (2): Type of LP, duration of the Illness and presence of/or family history of autoimmune diseases among the studied cases (n=33)

Type of LP	**No.**	**%**
Cutaneous LP	11	3.33
Mucocutaneous	9	27.2
Mucosal LP	3	9.09
Mucosal ulcerative LP	2	6.06
Cut. LP, Nail LP	2	6.06
Cut Penile LP	2	6.06
Cut LP Hypertrophic	1	3.03
Cut LP Pigmentosa	1	3.03
Cut. Actinic LP	1	3.03
Mucosal Ulcerative oral LP	1	3.03
Duration of the Illness (in years)		
1-2	18	54.5
3-4	11	33.3
>4	4	12.1
Presence of/or family history of autoimmune diseases		
Family history of vitiligo	3.03	1.6
Hypothyroidism	3.03	1.6
NO	93.94	49.2

Table (3): Gender, age group and Vit. D level in cases and control

Parameter		Cases and control		Total	P value
		Case (n=33)	Control (n=30)		
Gender	Female	21	16	37	0.451*
		63.6%	53.3%	58.7%	
	Male	12	14	26	
		36.4%	46.7%	41.3%	
Age group (in years)	<20	2	3	5	0.07*
		6.1%	10.0%	7.9%	
	20-30	8	16	24	
		24.2%	53.3%	38.1%	
	31-40	14	7	21	
		42.4%	23.3%	33.3%	
	>40	9	4	13	
		27.3%	13.3%	20.6%	
Vit. D serum level	<20 ng/mL	23	17	40	0.278*
		69.7%	56.7%	63.5%	
	20 - 30 ng/mL	9	9	18	
		27.3%	30.0%	28.6%	
	30 to 100 ng/mL 7	1	4	5	
		3.0%	13.3%	7.9%	

*Chi-square test was used

DISCUSSION

The deficiency of Vitamin D is a known health problem throughout the whole world involving more than fifteen percent of the population, the prevalence is higher in the kingdom of Saudi Arabia (up to 80%) even though the ultraviolet B radiation is high, it involves also the other middle east countries [17, 18]. The high incidence may be attributed to a variety of factors like inadequate intake of Vit D supplements, low time of sun exposure, traditional country uniforms which cover most body parts of the body among males and females as well, long time of indoor activities with decreased times of outdoor works and increased level of obesity [19]. We employed in our research the best easy method to assess the level of Vitamin D by measurement of 25 OH D metabolite, because this metabolite have a longer half-life (from 20 to 30 days), and it offers a suitable assessment of vitamin D store level [19,20].

1, 25 dihydroxycholecalciferol is the most active metabolite of vitamin D but with a four to fourteen hours half-life. The level of vitamin D sufficient is a subject of debate, but we considered it sufficient if the level of vitamin D is above 30 ng/mL, insufficient if the level is between 20-30 ng/mL, and deficient if the level is below 20 ng/mL, [21]. We exclude in this study any patient with autoimmune diseases like inflammatory bowel disease, Behcet's disease, or autoimmune CTD and autoimmune thyroid diseases because some studies noted vitamin D deficiency in these patients' groups [22-26]. Numerous research have been conducted in Saudi Arabia on the country's citizenry's vitamin D levels, most of these studies demonstrated deficiency of vitamin D among the population in a percentage range from 60-95%. This widespread deficiency of vitamin D may make the result of this study inconsistent.

Varma *et al.* [27] from India was the first who recognizes the relationship between lichen planus and vitamin D deficiency, they reported vitamin D deficiency among those patients and reported complete improvement of cutaneous LP and partial improvement of oral LP, but it was so problematic to trait this enhancement to vitamin D.

Regarding the case-control study of **Gupta *et al.* [17]** that was issued in India, they reported a significantly lower level of vitamin D in patients with oral lichen planus in comparison with control group. But also they noted insufficient vitamin D levels in the control group and they suggested vitamin D deficiency was a significant problem in the study population. The study also recognized that the severity of oral lichen planus proportionally increased with the level of vitamin D deficiency, although still, the difference was insignificant.

In comparison of the oral erosive lichen planus with other types of lichen planus, we noted a lower level of vitamin D in oral LP but the difference was not statistically significant. The deficiency of vitamin D besides being associated with disease severity of lichen planus, but this needs further studies to support that association [17]. **Du *et al.* [5]** published a study in China, they reported a lower level of vitamin D in patients with oral lichen planus, and on the oral biopsy, they noted a downregulation of VDR expression in the patient group, which supports the pathogenesis of T- helper 1 inflammatory response in lichen planus. But the low number of patients in that study makes the result effectively insufficient. Another study by **Bahramian *et al.* [16]** from Iran reported a lower level of vitamin D in 18 patients with oral lichen planus in comparison with 18 healthy control group, but still the difference was statistically insignificant. The season in that study was not determined, but maybe there is a difference of vitamin D level in different seasons [26].

In our study, the patients collected from different seasons through two years, also from India there was another study reported a high incidence of oral lichen planus in summer in comparison with winter [27]. This difference in the results between the level of vitamin D and seasonal incidence makes the lichen planus development not directly associated with the level of vitamin D.

In our study, we noted that the body mass index is significantly associated with a high incidence of lichen planus. This may support that the BMI may be a suggested finding in LP patients as reported in some studies [28].

And some evidence emphasized an association between vitamin D deficiency and increased BMI [29]. Another study from Iran by **Motahari *et al.* [30]** reported vitamin D deficiency in patients with LP, the deficiency was more with oral LP, and they reported also an association of vitamin D deficiency with increased BMI, but all the results were statistically inconsistent.

We found the result of our study is inconsistent with some studies. This may be attributed to the lichen planus heterogeneity either cutaneous or mucosal or mucocutaneous, and disease activity. Also, other factors may influence vitamin D level like the season the sample was taken, duration of sunlight exposure, the level of body mass index, and nutritional status of the patients [16.30], the polymorphism of vitamin D related genes like single nucleotide, VDR, and the gene of CYT P450 may have roles in the metabolism of vitamin D [30,31].

CONCLUSION AND RECOMMENDATIONS

In our study, the level of vitamin D in patients with lichen planus was lower than in the control group and the difference between the two groups was statistically significant. To determine the relationship between vitamin D deficiency and the pathogenesis of lichen planus, the assessment of vitamin D alone was not enough.

We need more information related to the vitamin D gene-related polymorphism and its relationship with the types and severity of the disease and larger study group of patients.

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