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# The Interleukin-17 (IL-17) Concentration in Saliva of Patients with Oral Lichen Planus

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ABSTRACT

***Background:*** The aim of the present study was to measure the clinical and pain score in these patients and to measure the level of IL-17 in saliva of patients having different forms of Oral lichen planus lesions (OLP).

***Subjects and methods:*** According to sample size calculation, the present study was done on a total of 40 subjects divided into 3 groups Group (I) Twenty patients having erosive/atrophic OLP. Group (II) Ten patients having reticular OLP and Group (III) Ten healthy control patients. Salivary samples were collected from the subjects of the three groups to evaluate the levels of IL-17 using enzyme-linked immunosorbent assay (ELISA).

***Results:*** The values of the clinical and pain score were statistically significantly higher in the erosive/atrophic group than both the reticular and healthy control subjects. The levels of IL-17 in saliva of patients with erosive/atrophic OLP were statistically significantly higher than in patients with the reticular OLP and healthy control subjects, and there was a high statistically significant difference between the reticular group and the healthy control subjects $p<0.001$.

***Conclusions:*** According to the results, the salivary levels of IL-17 are higher in the erosive/ atrophic type of OLP than the reticular type and both are higher than the healthy control subjects. This suggested that IL- 17 has a great role in the immune-pathogenesis of OLP and may be of diagnostic value for the severity of the condition of the erosive/atrophic OLP.

## 1. INTRODUCTION

Oral lichen planus is an immune mediated chronic disease which affects the oral mucous membranes. It tracks acyclic pattern of exacerbations or flares followed by periods of remission, contrasting lichen planus of the skin, which has been reported to have a high rate of spontaneous remission. [(1)] It usually presents asymmetrical and bilateral lesions, where it may also present as multiple lesions in the mouth. The clinical presentation of the oral lesions is present in six forms: papular, reticular and plaque-like lesions, atrophic, erosive/ ulcerative and bullous lesions. The papular, reticular and plaque- like lesions are asymptomatic while the atrophic, erosive/ ulcerative and bullous lesions are esymptomatic with symptoms ranging from soreness to severe burning pain [(2)].

The reason of OLP is not completely known. Many etiological factors have been suggested for the etiology like genetic predisposition, bacterial and viral infections, autoim- mune diseases, immunodeficiency, stress, trauma and systemic diseases such as diabetes, hypertension, malignant neoplasms and bowel disease [(3)].

T helper 17 (Th17) cells were recognized as a new subclass of CD4+ T helper cells in 2005. The Th17 differentiation requires both inflammatory cytokines which are: IL-6, IL- 21 and transforming growth factor β (TGF- β) to efficiently induce the lineage- specific transcription factor retinoic-acid-receptor- related orphan nuclear receptor γt (RORγt) a key regulator of Th17 differentiation as well as IL-17 production. T helper 17 cells are critically involved in host defense, inflammation and autoimmunity [(4)].

The role of interleukin-17 (IL-17) in the immune- pathogenesis of OLP has been emerged. A huge development in this field occurred with the acknowledgment that IL-17- producing CD4+ T cells are developed as a population distinct from the classic T helper type 1 (Th1) and T helper type II (Th2) cells [(5,6)].

Interleukin-17 (IL-17) is one of the cytokines produced by Th17. Interleukin-17 and other Th17 cytokines are related to the pathogenesis of diverse autoimmune and inflammatory diseases. It is also important for host defense against many microbes, particularly extracellular bacteria and fungi. IL-17 induces chemokine release from various cell types of the skin, including endothelial cells, macrophages, and keratinocytes leading to tissue remodeling and the recruitment of pro- inflammatory effector cells of the oral mucosa which denotes its critical role in the pathogenesis of OLP [(7)].

In 2014, **Shen et al.,** conducted a study on 42 patients having OLP and 38 patients having skin LP and 10 normal control patients having no lesions and found that IL-17 levels expression in the oral tissues of patients with LP

and OLP was significantly higher compared to the healthy patients who had no lesions [8]. Another study by **Kun et al.,** on 45 patients, 15 were having erosive/atrophic OLP patients, 15 were having reticular OLP patients and 15 healthy volunteers, and they studied the levels of salivary IL-17 in the three groups. They found a statistically significant difference between the erosive/atrophic group and the reticular group and between the erosive/atrophic group and the healthy control group [9].

## 2. AIM OF THE STUDY

To measure the clinical and pain score in these patients and to measure the level of IL-17 in saliva of patients having different forms of Oral lichen planus lesions (OLP).

## 3. SUBJECTS AND METHODS

In this study forty patients were selected; twenty of them were having erosive-atrophic OLP,ten were having reticular OLP and ten healthy volunteers. These patients were evaluated for their eligibility for this study. All subjects were chosen from the out- patient clinic of Oral Medicine, Periodontology, Oral Diagnosis and Radiology department Faculty of Dentistry Ain Shams University and Oral Medicine, periodontology and oral Diagnosis department Faculty of Dentistry Future University.

## 4. STATISTICAL ANALYSIS

Categorical data were presented as frequencies and percentages and were analyzed using chi square test. Numerical data were tested for normality using Shapiro Wilk test and were presented as mean and standard deviation values. Para- metric data were analyzed using one-way ANOVA followed by Tukey's post hoc test for intergroup comparisons. Non- parametric data were analyzed using Kruskal wallis test followed by pairwise comparisons utilizing Mann Whitney U test with Bonferroni correction for intergroup comparisons. The significance level was set at p 0.05 within all tests. Statistical analysis was performed with IBM3® SPSS® Statistics Version 26 for Windows.

At the first visit before the initiation of the study information including: age, gender, disease process, medical history, drug history, family history, and clinical signs and symptoms were documented for each patient.

Patients having OLP were examined clinically by magnifying mirror using spot light for the oral lesions, the distribution of the lesions and the affected areas were recorded, also their skin was examined and there were no extra-oral manifestations. A punch biopsy was taken to confirm the diagnosis of OLP by histological examination.

**Inclusion criteria:**

Subjects of both genders were selected, their age from 30 to 60 years and didn't suffer from any systemic, infectious and allergic diseases. They were also selected having no oral lesions except OLP, and had no history of any treatments which can affect OLP from less than two weeks for topical medications and four weeks for systemic medications prior to starting the study [10].

**Exclusion criteria:**

Pregnant/breast-feeding mothers, vulnerable group of patients (prisoners, handicapped and mentally retarded patients.

**Ethical procedures:**

All subjects were provided with full verbal and written in- formation on the protocol of this study and a written informed consent was taken from each subject. The study was approved by the ethical committee of faculty of dentistry Ain Shams University and took the number FDAsuRecIM021824.

**The forty subjects were divided into three groups in which:**

Group I consisted of twenty patients with atrophic/erosive OLP. Group II consisted of ten patients with reticular OLP. Group III consisted of ten healthy control volunteers with no OLP or any other oral or skin lesion.

Sampling: The un-stimulated whole saliva (UWS) was collected between 9:00 a.m. and 11:00 a.m., and 90 minutes after the last drinking any drinks or eating any food. It is collected by asking the patients to swallow then tilt their head forward, and the salivary sample was taken by aspiration using sterile sterile syringe and stored in Eppendorf tubes at once, and put to freeze at or under -20ºC to avoid the growth of any bacteria and preserve the saliva samples from degradation. IL-17 levels were measured using Human IL-17 (ELISA) kits delivered from BMS2017/BMS2017TEN supplied from eBioscience, Affymetrix (Vienna, Austria).

The clinical and pain score values were measured and the samples of saliva were taken from patients of the three study groups Clinical scoring (CS) was measured in which the marker lesion in each patient was assessed for areas of reticulation, erosion, and ulceration by visual examination and the scoring was recorded as following:

0: Represented no lesion/normal mucosa.

1: Mild white striae/no erythematous area.

2: White striae with atrophic area less than 1 $cm^2$

3: White striae with atrophic area more than 1cm2 4: White striae with erosive area less than 1 $cm^2$

5: White striae with erosive area more than 1 $cm^2$ [11].

Pain visual Analog Scale (P-VAS) was measured in which the pain VAS consisted of a 10-cm horizontal line marked 0–10 (0 no pain; 10 most severe pain experienced). Patients marked the scale at each visit, and the all P-VAS were included on one sheet of paper allowing the patient to think in terms of change instead of absolutes. The P-VAS was then scored by measuring from the patient's mark to the beginning of the scale in cm [12].

## 5. CASE PRESENTATION

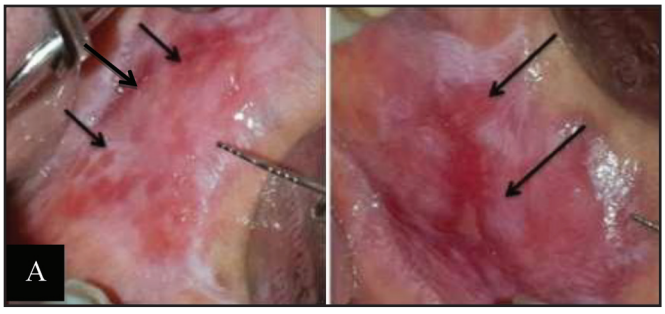


**Figure A — A photograph showing atrophic erosive form of oral lichen planus occupying nearly the whole right and left buccal mucosa presented as a large shallow atrophy surrounded by wickham's striae radiating from their periphery in a female patient of 52 years old.**

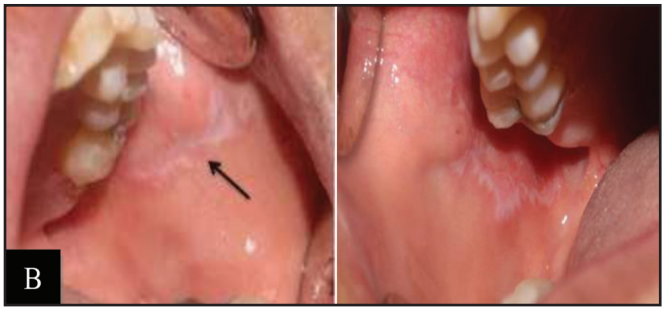


**Figure B — A photograph showing reticular form of oral lichen planus presented as a white keratotic lesion with fine lines "wickham's striae" on the right and left buccal mucosa in a female patient of 45 years old.**

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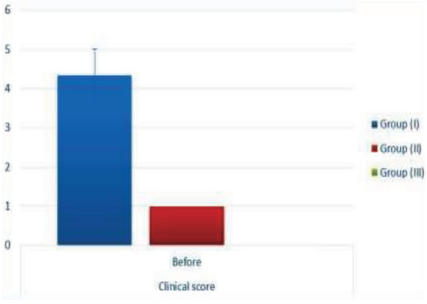
## 6. RESULTS

**Table (1) & figure (1) showing Mean and (SD) values for (CS) in the three groups. (Group I: erosive/atrophic group, Group II: the reticular group and Group III: the healthy control subjects)**

| Follow up | (CS) (Mean±SD) | | | p-value |
|---|---|---|---|---|
| | Group I | Group II | Group III | |
| | $4.37\pm0.69^{A}$ | $1.00\pm0.00^{B}$ | $0.00\pm0.00^{B}$ | **<0.001*** |




There was a highly statistically significant difference ($p<0.001$) in the mean and SD values of the CS between group one and each of group II and III where the mean and SD value in group I was (4.37±0.69) and in group II it was (1.00±0.00) and group III it was (0.00±0.00).

Also there was a highly statistically significant difference ($p<0.001$) in the mean and SD values of (P- VAS) between group I and each of group II and III where the mean and SD values in group I was (7.27±0.92) and for group II and III it was (0.00±0.00).

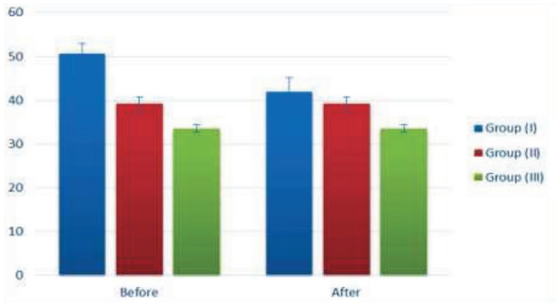
**Table (2) showing Mean and (SD) values for (P-VAS) in the three groups. (Group I: erosive/atrophic group, Group II: the reticular group and Group III: the healthy control subjects)**

| Follow up | (CS) (Mean±SD) | | | p-value |
|---|---|---|---|---|
| | Group I | Group II | Group III | |
| Baseline | $7.27\pm0.92^{A}$ | $0.00\pm0.00^{B}$ | $0.00\pm0.00^{B}$ | **<0.001*** |

Concerning the IL-17 levels in saliva, there was a highly statistically significant difference between the mean and SD values of salivary IL-17 levels between group (I) and each of group (II) and group (III) and between group (II) and group (III) ($p<0.001$). Where the mean and SD values of IL17 levels in saliva in group (I) was (50.66±2.30 pg./ml) and for group (II) it was (39.23±1.57 pg/ml) while for group (III) it was (33.52±0.84pg/ml).

**Table (3) and figure (2) showing the mean and (SD) values for IL-17 salivary concentration between the three groups.**

| Follow up | (CS) (Mean±SD) | | | p- value |
|---|---|---|---|---|
| | Group I | Group II | Group III | |
| Baseline | $50.65\pm2.29^{A}$ | $39.24\pm1.56^{B}$ | $33.51\pm0.83^{C}$ | **<0.001*** |




## 7. DISCUSSION

In this study, the clinical and pain visual analogue scores was evaluated and there was a highly statistically significant difference for the clinical score between the erosive/atrophic group and both the reticular and control groups ($p<0.001$). These results were in accordance with the results of Chainani et al., where they found that there was a statistically significant difference between the erosive patients of OLP and the reticular patients of OLP ($p<0.001$) [13].

Also the results of the present study regarding the clinical score were in accordance with another study by Siponen et al., they measured the clinical score and they found that there was a statistically significant difference between the erosive/atrophic OLP group and reticular group [14].

The results of the present study regarding the (P- VAS) were in accordance with Suzan and Hadir, where they found that there was an highly statistically significant difference between the erosive/atrophic group and reticular group ($p<0.001$) [15].

Regarding the levels of IL-17 in saliva there was a highly statistically significant difference in the values of IL-17 salivary levels between the erosive/atrophic group and both the reticular and control groups, and there was a statistically significant difference in the values of IL-17 salivary levels between the reticular group and control group. These results were in accordance with the results of the study conducted by Kun et al as they found a statistically significant difference between the erosive/atrophic group and both the reticular and the healthy control group, but they found that there was no statistical significant difference between the reticular group and the healthy control group [9].

Another study by El-Refai et al., as they measured the concentration of IL-17 in patients having OLP compared to healthy control groups, They found that there was a high statistically significant difference in the concentration of IL-17 in saliva in the OLP than in the healthy control individuals [16].

## 8. CONCLUSION

This study verified that the clinical score values in patients with erosive/atrophic form of OLP are higher compared to patients with either reticular form or healthy controls. Also the concentration of IL-17 in saliva in patients with erosive/atrophic form of OLP are higher than in patients with the reticular form and both are higher than the healthy control subjects. According to these results, we concluded that IL-17 has a great role in the immune-pathogenesis of OLP and could be used as a salivary diagnostic marker for OLP conditions.

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