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Elevated Salivary TNF-α Levels and Clinical Severity of Oral Lichen Planus

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Abstract

This study aimed to evaluate salivary TNF-α levels in patients with OLP compared to healthy controls and to assess correlations with clinical subtypes. A cross-sectional study was conducted on 35 participants (20 OLP patients and 15 controls) recruited from Al-Farabi University College of Dentistry. Saliva samples were collected and analyzed using ELISA to quantify TNF-α concentrations. TNF-α levels were significantly higher in OLP patients (48.9 ± 9.8 pg/mL) compared to controls (18.5 ± 8.1 pg/mL; $p < 0.000001$). Within the patient group, ulcerative lesions exhibited markedly elevated TNF-α levels (59.9 ± 2.0 pg/mL) compared to reticular lesions (46.3 ± 7.8 pg/mL; $p = 0.024$). No significant differences in age or gender distribution were observed between groups. Elevated salivary TNF-α levels in OLP patients, particularly in erosive forms, highlight the cytokine's pivotal role in disease progression and severity. TNF-α may serve as a potential biomarker for monitoring OLP activity and guiding therapeutic strategies.

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Introduction

Oral lichen planus (OLP) is a chronic inflammatory disorder of the oral mucosa, with a reported prevalence of approximately 1–2% in the general population (1). The condition demonstrates a marked predilection for middle-aged and elderly women, with female-to-male ratios ranging from 1.3:1 to 2.5:1, thereby confirming its higher incidence among females [1]. Accumulating evidence indicates that OLP represents a localized autoimmune disease driven by T-cell dysfunction [2].
Clinically, oral lichen planus (OLP) typically presents as white reticular changes [3], which may coexist with or progress to erosive forms that are considered more aggressive. The morphological spectrum of OLP lesions is broad, encompassing reticular, papular, erythematous, erosive, and ulcerative variants, each associated with distinct symptomatic profiles [4]. The buccal mucosa is the most frequently affected site, although the gingiva, tongue, lips, and palate may also be involved. These clinical manifestations are characterized by periods of relapse and remission [5], underscoring the importance of regular oral examinations for effective disease monitoring [6]. However, secondary prevention strategies remain largely dependent on frequent dental visits, which are often impractical in remote or underserved regions [7]. Consequently, individuals with limited financial resources are disproportionately excluded from adequate care in healthcare systems where dental services are not fully subsidized [8].
Pro-inflammatory cytokines, which act as central regulators of the tumor microenvironment, are critical mediators of chronic pro-tumorigenic inflammation. These molecules exert diverse effects on cellular processes, including growth, differentiation, and functional activity. It is well established that their physiological roles become dysregulated during both inflammatory states and carcinogenesis. Among these, tumor necrosis factor-alpha (TNF-α) is considered the most significant cytokine. TNF-α is a pleiotropic mediator involved in inflammation, angiogenesis, apoptosis, and cellular proliferation, thereby positioning it as a key contributor to malignant transformation [9]. Furthermore, TNF-α, as a multifaceted pro-inflammatory cytokine, has been recognized for its pivotal role in the pathogenesis and prognosis of a wide spectrum of diseases, including cancer and diabetes mellitus [10].

Tumor necrosis factor-alpha (TNF-α) plays a central role in innate inflammatory responses and has been implicated in the pathogenesis of several chronic autoimmune-mediated inflammatory disorders, including psoriasis [11] and systemic lupus erythematosus. In such conditions, both serum and salivary TNF-α concentrations have been shown to correlate with disease activity and severity, supporting its potential utility as a prognostic biomarker. Accordingly, the present study was designed to evaluate serum and salivary TNF-α levels in patients with oral lichen planus in comparison with healthy controls [12].

Material and Methods

A cross-sectional study was conducted on 35 subjects recruited from the dental clinics of Al-Farabi University College of Dentistry. Participants were divided into two groups: patients diagnosed with oral lichen planus (OLP) and healthy controls. Histopathological confirmation was performed for all OLP cases. Ethical approval was obtained from the institutional review board, and written informed consent was secured from each participant prior to enrollment.

All patients included in the study were free from systemic diseases and had not received medications known to induce lichenoid reactions within the preceding six months. Additionally, none of the patients had amalgam restorations that could elicit lichenoid contact reactions. Control subjects were systemically healthy and exhibited no evidence of oral inflammatory lesions.

To minimize diurnal variation, saliva samples were collected in the morning. From each subject, 5 mL of unstimulated whole saliva was obtained and transferred into sterile centrifuge tubes. Following centrifugation, the clarified salivary supernatant was aliquoted into disposable storage vials and preserved at −80°C until analysis. The salivary concentration of tumor necrosis factor-alpha (TNF-α) was quantified using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (RayBio Human TNF-α enzyme immunoassay).

The data were analyzed using statistical software (SPSS version 29.0.2). Descriptive statistics, including means and standard deviations, were computed for each group. To determine the significance of differences in salivary TNF-alpha mean values between the control and patient groups, Student's independent t-test was employed. A probability value (p) of ≤ 0.05 was established as the threshold for statistical significance.

Results

A total of 35 participants (20 patients and 15 controls) were included. There was no significant difference in age (51.6 ± 7.6 vs 50.9 ± 6.6 years; p = 0.77) or gender distribution (p = 0.30) between patients and controls (Table 1).

Table 1. Baseline characteristics of study participants.

Variable	Patients (n = 20)	Controls (n = 15)	Test	p-value
Age (years), mean ± SD	51.6 ± 7.6	50.9 ± 6.6	Welch's t-test	0.77
Female, n (%)	14 (70%)	8 (53.3%)	Fisher's exact test	0.3
Male, n (%)	6 (30%)	7 (46.7%)		

Data are presented as mean ± standard deviation (SD) or number (percentage). Continuous variables were analyzed using Welch's t-test. Categorical variables were analyzed using Fisher's exact test. A p-value < 0.05 was considered statistically significant.

TNF-α levels in patients and controls

TNF-α levels were significantly higher in patients (48.9 ± 9.8 pg/mL) compared with controls (18.5 ± 8.1 pg/mL) (p < 0.000001) (Table 2).

Table 2. TNF-α levels in patients and controls.

Group	TNF-α (pg/mL) mean ± SD	Test	Statistic	p-value
Patients	48.9 ± 9.8	Welch's t-test	t = 9.05	<0.000001
Controls	18.5 ± 8.1			

TNF-α levels are presented as mean ± standard deviation (SD). Group comparisons were performed using Welch's t-test. A p-value < 0.05 was considered statistically significant.

TNF-α levels according to lesion subtype

Within the patient group, TNF-α levels were significantly higher in ulcerative lesions (59.9 ± 2.0 pg/mL) compared with reticular lesions (46.3 ± 7.8 pg/mL) (p = 0.024) (Table 3).

Table 3. TNF-α levels by lesion type.

Subtype	TNF-α (pg/mL) mean ± SD	Test	Statistic	p-value
Ulcerative	59.9 ± 2.0	Welch's t-test	t = 3.45	0.024
Reticular	46.3 ± 7.8			

TNF-α levels are presented as mean ± standard deviation (SD). Comparisons between lesion types were performed using Welch's t-test. A p-value < 0.05 was considered statistically significant.

Discussion

Oral lichen planus (OLP) is a skin-mucus chronic disorder which is relatively common and is often concerned with oral mucosae. Its etiology has not been completely clarified; however, it is known that the immunology system plays an important role in its incidence. Despite the different available cures, this disease has a long-term clinical treatment period [13].

Various studies have suggested that immunological mechanism play an important role in the pathogenesis of oral lichen planus but the exact cause remain unclear [14].

The immunological mechanism results in the vacuolar degeneration of the basal cells but histochemical studies have identified T lymphocytes as a predominant cell in this lesion. The major cells responsible for the damage of basal keratinocytes are CD8+ T cells [15].

The exact etiology of OLP is unclear, but the immunologic system plays a significant role [16]. Nuclear factor-kB (NF-kB) as a primary transcription factor controls the expression of a series of cytokines, including tumor necrosis factor-a (TNF-a) [17], and as a major mediator of inflammatory actions directed toward both tissue destruction and recovery. TNF-a also stimulates fibroblast growth while inducing death of diseased cells at the site of inflammation [18].

Our study found that the mean age of affected patients was 51 years, which aligns with the findings of Nosratzehi et al. (2023), who concluded that oral lichen planus (OLP) most commonly occurs during the fifth and sixth decades of life [19]. Furthermore, 70% of the patients in our cohort were female, consistent with the observations of Al-Nasser et al. (2013), who reported that females are more frequently affected than males, with a female-to-male ratio of 2.2:1 [20].

The results demonstrated significantly elevated levels of tumor necrosis factor-alpha (TNF-α) in patients compared to controls, consistent with the findings of Malarkodi T and Sathasivasubramanian S [21].

Erosive forms of oral lichen planus exhibit significantly higher salivary TNF-α levels than reticular forms, and TNF-α concentrations correlate positively with disease severity in our study.

The findings of our study are consistent with those reported in both studies.

Salivary TNF-α levels were significantly increased in patients with OLP compared with healthy subjects. The presence of TNF-α showed positive correlation to clinical forms of OLP, being significantly higher in the erosive/atrophic type than in the reticular type of disease [22].

Salivary TNF-α levels were higher in erosive OLP than in reticular OLP and were positively correlated with lesion severity [23].

Conclusion

Salivary TNF-α level was significantly higher in oral lichen planus patients when compared to control. The research highlights that TNF-α, a proinflammatory cytokine, plays a pivotal role in the development and progression of oral lichen planus.

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