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Correlation between salivary IL-10 and clinical features in patients with periodontitis

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Abstract

Introduction: Periodontitis is an inflammatory condition that leads to the destruction of the tooth-supporting tissues. Its pathogenesis is driven by imbalance in cytokines. Interleukin-10 (IL-10), an anti-inflammatory cytokine, may regulate periodontal inflammation by antagonizing proinflammatory mediators. However, the precise correlation of this polymorphism with disease severity and clinical profiles is unknown.

Objectives: The present study sought to determine the salivary levels of IL-10 in periodontitis patients and healthy controls, and investigate the possible associations between IL-10 concentrations and major clinical periodontal parameters: PPD (Probing Pocket Depth), CAL (Clinical Attachment Loss), BOP (Bleeding on Probing), PI (Plaque Index) and GI (Gingival Index).

Methods: A case-control study tested at Al-Najaf Center for Dentistry clinics from April 2024 to February 2025 on (65) diagnosed periodontitis cases and (45) healthy controls matched with age and gender. Unstimulated whole saliva was collected in the morning under standardized conditions and tested for IL-10 with a commercial enzyme-linked immunosorbent assay (ELISA) kit. Clinical periodontal data were also collected and severity-classified. The statistical analyses were conducted using SPSS version 25 and t–test, ANOVA, and the Pearson's correlation tested for group differences and associations between IL-10 levels with clinical symptoms. Results: The mean salivary IL-10 level in patients with periodontitis was significantly higher (42.35 ± 11.68 pg/mL) than that of controls (35.27 ± 9.84 pg/mL) ($p = 0.023$). Levels of IL-10 were significantly correlated with the severity of PPD and CAL ($F = 3.71$, $p = 0.03$; $F = 7.89$, $p = 0.001$; respectively). Correlation analysis showed moderate to strong positive correlations of IL-10 with PPD ($r = 0.45$, p 0.02).

Conclusion: High salivary IL-10 levels are related to periodontitis and reflect positively with parameters of tissue destruction, especially PPD and CAL. These results imply that, as a marker of disease severity, IL-10 could be a non-invasive useful biomarker for the progression of periodontal diseases.

Keywords: Interleukin-10, periodontitis, PPD, CAL, BOP, PI, GI

Introduction

Periodontal disease is one of the most common chronic inflammatory oral conditions and continues to be a significant public health issue globally. Moderate to severe periodontitis is believed to affect a substantial proportion of adult individuals and provides major contributions to tooth loss, reduced quality of life and global disability-adjusted life years; the burden of periodontal diseases in terms of socioeconomic and

health impact has been emphasized in several global reports and position papers (1). Periodontitis is more than a local infection and not just a colonization of

bacteria that leads to formation of inflammation but a dysregulated host–microbe interaction in which the host immune response—not only the presence of microorganisms—causes progressive loss of tooth-supporting structures (2).

Molecularly, periodontitis is a complex cascade of innate and adaptive immune mediators that coordinate inflammation and tissue recovery (3). Pro-inflammatory cytokines, in particular interleukin-1β (IL-1β), tumor necrosis factorα (TNF-α) and interleukin-17 (IL-17) induce leukocyte recruitment, matrix degradation, and osteoclast formation leading to connective tissue destruction and alveolar bone resorption (4). Opposing these effects are a cascade of regulators, anti-inflammatory cytokines that limit tissue injury and selectively influence the immune environment; among them, IL-10 is a critical regulator cytokine with pleiotropic activity against innate as well as adaptive cells (5).

IL-10 is secreted by a variety of cell types in periodontal lesions, including regulatory T cells (7), B regulatory (B10) cells and macrophages, and act by inhibiting pro-inflammatory cytokine production and antigen presentation while blocking osteoclast formation that eventually leads to bone resorption. Preclinical studies demonstrate that IL-10 can inhibit IL-17–driven inflammatory networks in the periodontium and consequently limit tissue damage; lack of IL-10 or defects in its signaling lead to exacerbated inflammation and enhanced bone resorption (7). However, the complexity of IL-10 function in human periodontitis must also be considered, since its anti-inflammatory effects may prevent excessive tissue destruction but an overly efficient local immunosuppression might facilitate bacterial colonization and chronic disease (8).

As periodontitis is the outcome of complex interactions between microbial challenge and host response, quantifying biomarkers derived from hosts has become a promising strategy to enhance diagnosis, staging, and monitoring disease activity (9). Of the body fluids available for diagnostic purposes. We have already reported elsewhere that increasing surface tension has been shown to produce VDS-like signs in various hydrogels so far tested (13). Thus, we have taken human saliva as an example of a non-blood fluid in which higher-surface-tension conditions are known to be associated with clinical inflammation05-08 and applied it here to VDS detection justifying our choice by its practicality of collection; point-of-care suitability on selectivity introduced by aggregation. Cytokine saliva studies Certain cytokines—for example, IL-1β (8), IL-6 (9), and IL-10 (10) —are altered in subjects with periodontitis or healthy controls have been detected by means of those systematic reviews and meta-analyses on salivary cytokine tests, as well as that the levels changed after periodontal therapy had provided support for their usage as biomarkers (11-14).

The goal of this work is, to clarify the correlation between salivary IL-10 concentrations and periodontitis clinical representation with respect to disease pathogenesis mechanism and possible diagnosis following biomarker.

Patients and Methods

Study Design and Setting

Methods: The present case–control study was carried out at Al-Najaf Center for Dentistry Clinics, Al-Najaf, Iraq between April 2024 and February 2025. One hundred and ten subjects were recruited comprising 65 patients diagnosed clinically as having periodontitis and 45 systemically healthy controls. Periodontitis diagnosis and classification were made by clinical evaluation done by trained dental specialists according to the 2018 Classification of Periodontal and Peri-Implant Diseases and Conditions.

Subjects were adults, between the ages of 20 and 65 years. Patients with periodontitis had levels of clinical attachment loss (CAL), probing pocket depth (PPD) and radiographic bone loss compatible with the diagnosis of periodontitis. The control subjects had healthy gingiva, no clinical attachment loss, and probing pocket depth ≤3 mm. Exclusion criteria were: subjects suffering from systemic or chronic diseases (e.g. diabetes mellitus, cardiovascular diseases, and autoimmune disorders), recent infections, being pregnant or breastfeeding history of periodontal therapy in the past four months; use of antibiotics and/or anti-inflammatory drugs during the previous three months; smoker attitudes.

Clinical Examination

Comprehensive periodontal examinations were carried out for all participants by calibrated dental examiners using a standardized periodontal probe. The following

clinical parameters were assessed and recorded for each participant:

1. **Probing Pocket Depth (PPD):** measured in millimeters at six sites per tooth and categorized as:

- 1–3 mm: *Normal*
- 4–5 mm: *Moderate*
- ≥6 mm: *Severe*

2. **Clinical Attachment Loss (CAL):** categorized as:

- 0–2 mm: *Normal*
- 3–4 mm: *Moderate*
- ≥5 mm: *Severe*

3. **Bleeding on Probing (BOP):** expressed as a percentage of bleeding sites and classified as:

- <10%: *Low*
- 10–30%: *Moderate*
- 30%: *High*

4. **Plaque Index (PI):** assessed according to the Silness and Löe criteria and classified as:

- 0–0.9: *Good*
- 1.0–1.9: *Fair*
- ≥2.0: *Poor*

5. **Gingival Index (GI):** evaluated as:

- 0.1–1.0: *Mild*
- 1.1–2.0: *Moderate*
- 2.1–3.0: *Severe*

All measurements were recorded using a mouth mirror and periodontal probe under adequate lighting conditions. Calibration sessions were conducted before the study to ensure inter- and intra-examiner reliability.

Sample Collection and Processing

Unstimulated whole saliva samples were collected from all participants under standardized conditions in the morning hours (between 9:00 and 11:00 a.m.) to minimize diurnal variation. Participants were instructed to refrain from eating, drinking, or performing oral hygiene for at least 90 minutes prior to collection. Approximately 5 mL of unstimulated saliva was collected by passive drooling into sterile tubes while participants sat upright. Samples were immediately transported to the laboratory on ice and centrifuged at 3000 rpm for 10 minutes to remove debris and cells. The clear supernatant was aliquoted and stored at –80°C until biochemical analysis.

Estimation of Salivary Interleukin-10 (IL-10)

Salivary IL-10 levels were quantified using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (e.g., Human IL-10 ELISA Kit, [Manufacturer, Country]) following the manufacturer's instructions. All samples were analyzed in duplicate to ensure accuracy and reproducibility. The mean concentration (pg/mL) from duplicate wells was used for statistical analysis.

Ethical Considerations

The study protocol was conducted in accordance with the Declaration of Helsinki (2013). Ethical approval was obtained from the Institutional Review Board (IRB) of Al-Najaf Center for Dentistry Clinics before initiation. All participants were informed about the purpose, procedures, and potential risks of the study and provided written informed consent. The confidentiality of all personal and medical data was strictly maintained throughout the study.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA). Descriptive statistics (mean ± standard deviation, frequency, and percentage) were used to summarize demographic and clinical data. Normality of distribution was assessed using the Shapiro–Wilk test. Differences in mean salivary IL-10 levels between periodontitis patients and controls were analyzed using the independent-samples t-test, as appropriate. Correlations between IL-10 levels and periodontal parameters (PPD, CAL, BOP, PI, GI) were evaluated using Pearson's or Spearman's correlation coefficients depending on data distribution. A p-value < 0.05 was considered statistically significant (15).

Results

The demographic distribution of the participants demonstrated no statistically significant difference between patients' periodontitis and healthy controls regarding age and gender. The greater percentage (38.5%) of participants in both groups fell within the age bracket of 34-43 years. The gender distribution exhibited (58.5%) for male, and (41.5) for female. Chi-square

analysis gave P-values of 0.78 for age and 0.89 for gender meaning that the two groups are demographically well-matched. (Table 1).

Table 1. Age and gender distribution of both OSCC patients and control

Indicators		`Patients (No. = 65)		Control (No. = 45)		Chi Square	P value (Sig.)
		Freq.	%	Freq.	%		
Age/Years	14-23	5	7.7	6	13.3		0.22 (NS)
	24-33	15	23.1	12	26.7		
	34-43	25	38.5	16	35.6		
	≥ 44	20	30.7	11	24.4		
Gender	Male	38	58.5	23	51.1		0.18 (NS)
	Female	27	41.5	22	48.9		

Table 1 demonstrates the distribution of key clinical periodontal parameters among patients with periodontitis and healthy controls. The results reveal a clear and statistically significant difference between the two groups across all evaluated indicators. Most patients with periodontitis exhibited moderate to severe probing pocket depth (PPD) and clinical attachment loss (CAL), reflecting advanced periodontal destruction. In contrast, the majority of controls showed normal or mild readings for both parameters. Similarly, bleeding on probing (BOP), plaque index (PI), and gingival index (GI) values were substantially higher among periodontitis patients, indicating greater gingival inflammation and poor oral hygiene status. The Chi-square analysis showed significant ($p < 0.05$) to highly significant ($p < 0.01$) differences.

Table 2. Clinical features for Periodontitis patients and control

Indicators		`Patients (No. = 65)		Control (No. = 45)		Chi Square	P value (Sig.)
		Freq.	%	Freq.	%		
PPD	(Normal)	10	15.4	33	73.3	7.98	0.02 (S)
	(Moderate)	25	38.5	9	20		
	(Severe)	30	46.1	3	6.7		
CAL	(Normal)	8	12.3	30	66.7	14.22	0.001 (HS)
	(Moderate)	20	30.8	10	22.2		
	(Severe)	37	56.9	5	11.1		
BOP	(Low)	12	18.5	25	55.6	6.97	0.03 (S)
	(Moderate)	20	30.8	12	26.7		
	(High)	33	50.7	8	17.7		
PI	Good	10	15.4	22	48.9	6.45	0.04 (S)
	Fair	22	33.8	14	31.1		

	Poor	**33**	**50.8**	**9**	**20**		
GI	**Mild**	**13**	**20**	**24**	**53.3**	**8.26**	**0.01 (S)**
	Moderate	**25**	**38.5**	**13**	**28.9**		
	Severe	**27**	**41.5**	**8**	**17.8**		

Table 3 shows that the mean salivary IL-10 level in patients with periodontitis (42.35 ± 11.68 pg/mL) was significantly higher than that of healthy control participants (35.27 ± 9.84 pg/mL), with a p-value of 0.023, indicating a statistically significant difference between the two groups.

Table 3. Assessment of IL-10 levels between patients and control participants

Groups	**No.**	**IL-10 (pg/ml) Mean ± SD**	**T Test (P Value)**
Patient	65	42.35 ± 11.68	2.34 (0.023)
Control	45	35.27 ± 9.84	

Table 4 shows that salivary IL-10 concentrations vary significantly among periodontitis patients when classified by clinical severity. Patients with severe probing pocket depth (PPD) and greater clinical attachment loss (CAL) exhibited the highest IL-10 levels, with statistically significant differences ($F = 3.71$, $p = 0.03$; $F = 7.89$, $p = 0.001$). This indicates a strong relationship between disease severity and increased IL-10 expression, possibly reflecting an intensified anti-inflammatory response aimed at modulating chronic inflammation in advanced cases. In contrast, differences in IL-10 according to bleeding on probing (BOP) and plaque index (PI) were not statistically significant ($p > 0.05$), suggesting that short-term inflammatory or hygiene-related changes may have less impact on systemic IL-10 levels than tissue destruction parameters. However, IL-10 levels were significantly higher among patients with severe gingival inflammation (GI) ($p = 0.04$), supporting the notion that IL-10 plays an immunomodulatory role in the local inflammatory process.

Table 2. Differences in IL-10 among patients' subgroups classified according to clinical features

Indicators		**No.**	**IL-10 (pg/ml) Mean ± SD**	**F Test**	**P value (Sig.)**
PPD	**(Normal)**	**10**	**33.42 ± 7.85**	**3.71**	**0.03 (S)**
	(Moderate)	**25**	**41.58 ± 9.62**		
	(Severe)	**30**	**45.97 ± 10.21**		
CAL	**(Normal)**	**8**	**32.76 ± 8.04**	**7.89**	**0.001 (HS)**
	(Moderate)	**20**	**40.35 ± 9.11**		
	(Severe)	**37**	**47.24 ± 10.48**		
BOP	**(Low)**	**12**	**39.10 ± 8.56**	**1.12**	**0.33 (NS)**
	(Moderate)	**20**	**42.22 ± 9.37**		
	(High)	**33**	**44.68 ± 10.95**		

PI	**Good**	**10**	**38.67 ± 8.42**	**2.02**	**0.14 (NS)**
	Fair	**22**	**41.53 ± 9.75**		
	Poor	**33**	**44.90 ± 11.23**		
GI	**Mild**	**13**	**38.74 ± 8.11**	**3.42**	**0.04 (S)**
	Moderate	**25**	**42.58 ± 9.82**		
	Severe	**27**	**46.30 ± 10.54**		

The correlation analysis revealed that salivary IL-10 levels were positively associated with key indicators of periodontal tissue destruction. Specifically, probing pocket depth (PPD) and clinical attachment loss (CAL) showed moderate to strong positive correlations with IL-10 (r = 0.45 and 0.52, respectively; p < 0.01), indicating that higher IL-10 levels are observed in patients with more severe periodontal destruction. In contrast, IL-10 exhibited weaker and non-significant correlations with bleeding on probing (BOP) and plaque index (PI). Gingival index (GI) showed a moderate positive correlation (r = 0.30; p = 0.02).

Table 5. Correlation between IL-10 and clinical features among patients

		IL-10	**P value**
Clinical Features	**PPD**	**0.45**	**0.001 (HS)**
	CAL	**0.52**	**<0.001 (HS)**
	BOP	**0.18**	**0.12 (NS)**
	PI	**0.21**	**0.08 (NS)**
	GI	**0.3**	**0.02 (S)**

Discussion

The aim of the present study was to evaluate the correlation between salivary IL-10 concentration and clinical status of periodontitis in our population. Salivary levels of IL-10 were significantly higher in the periodontitis group than controls, and they were positively correlated with PPD and CAL among various clinical manifestations and other confounding factors. These results add support to the involvement of IL-10 in host response to periodontal inflammation and tissue destruction.

The observed elevation of salivary IL-10 in patients with periodontitis is analogous to other recent studies that have found similarly high levels of the anti-inflammatory cytokine and further provide evidence for their deregulated immune response, where increased anti-inflammatory mediators may act as a compensatory mechanism to counter excessive pro-resolving mediator activity in chronic periodontitis (16,17). IL-10 predominantly secreted by T regulator cells, B monocytes and macrophages has a strong anti-inflammatory action inhibiting production of tissue damaging proinflammatory cytokines IL-1β, -6 and TNF-α in the periodontal tissues (18). Thus, elevated IL-10 observed in patients with disease may represent a protective response geared toward minimizing excess tissue damage following prolonged bacterial exposure and inflammation.

In line with findings in the present study, Mohammed et al. (7) found that there were significant higher levels of salivary IL-10 in moderate and severe periodontitis patients than in healthy subjects. Similarly, Leira et al. (14) found a positive association between high IL-10 levels and PPD and CAL and suggested that the up-

regulation of IL-10 may constitute an attempt by the host to control continuous tissue damage. Moreover, Teles et al. (13) showed that salivary and gingival crevicular fluid IL-10 levels gradually elevated in accordance with the severity of disease, indicating a possibility that IL-10 may contribute as an indicator associated to chronicity and severity of periodontal inflammation. This homogeneity of results between studies from different population groups confirms that salivary IL-10 levels are dynamically regulated with the evolution of periodontal disease.

Nevertheless, although an increase in IL-10 within the context of periodontitis can be seen as a compensatory anti-inflammatory reaction, excessive IL-10 production has also been proposed by some investigators to participate in impaired bacterial elimination and disease exacerbation by down-regulation of effective immune responses (19). This dual and context-dependent function of IL-10 has been well described in autoimmune regulation, where the cytokine simultaneously favors resolution of inflammation but mechanism that supports pathogen survival under chronic conditions (20). Sun et al. (5) showed IL-10 to temper the IL-17–induced inflammatory response in a model of experimental periodontitis, which would ameliorate tissue destruction but hamper antibacterial defenses. Thus, increased levels of IL-10 in late stages of the disease characterized by uncontrolled inflammation as found here could reflect a host effort to counteract unrestrained pro-inflammatory responses although not enough to completely restore tissue homeostasis.

A high positive relation has been found between IL-10 and clinical indices of tissue destruction as PPD and CAL in the present study as well which further confirm that expression of IL-10 tends to be higher, when disease progresses. This is in good agreement with Relvas et al. (4) In which anti-inflammatory cytokine IL-10 like IL-1β and IL_6, increased in a dose-response relationship with the severity of periodontitis mild to moderate and then severe. These findings are also in agreement with those of Chen et al. (12), IL-10 levels were positively associated with clinical attachment level, but poorly correlated with bleeding on probing and plaque (IL-10 is mainly related to chronic tissue breakdown than to the level of acute inflammatory markers or oral hygiene). Likewise, in our study no association was found between IL-10 and BOP or PI, which further suggests that systemic anti-inflammatory responses may not correlate with short-term modulations of plaque accumulation or superficial inflammatory status.

It is interesting to note, that the moderate positive relationship observed between IL-10 and GI in the present study indicates that local gingival inflammation may still stimulate IL-10 secretion, although less efficiently. This result is in line with the findings of AlMoharib et al. (13) that IL-10 expression is higher with increasing disease severity, however PR DCL's associations are relatively weak with surface level markers such as BOP or GI. Thus, the salivary presence of the cytokine seems to represent a mix of chronic tissue destruction and local inflammation influences, and is suggested to act as a useful parameter for complete disease evaluation.

First, the finding of the present study may have implications for the possible use of salivary IL-10 as a non-invasive biomarker in periodontitis monitoring. Saliva sampling has major advantages compared to serum or tissue collection in terms of simplicity, patient convenience, and low cost. A number of recent reviews have suggested that evaluation of salivary cytokines, including salivary IL-1β, IL-6, and IL-10, might provide a promising diagnostic method for differentiating healthy and gingivitis and periodontitis periodontal conditions. Arias-Bolzmann et al. found that salivary IL-10 had a large area under the curve for periodontitis diagnosis and used it in combination with proinflammatories. Thus, the present study may contribute important evidence to this view. Salivary IL-10 was identified as statistically significantly high, and it was associated with clinical markers of disease, suggesting its potential importance in the monitoring of periodontal disease (11). Nonetheless, our results show that different studies have variations in expression that could be explained by differences in disease classification criteria, patient demographics, patient smoking and sampling designs. Finally, IL-10 is a pleiotropic cytokine that is modulated by environmental and genetic factors. Polymorphisms in these molecules might therefore likely define some interindividual variations (21). More research with genetic facilities and larger sample sizes could explore that fact.

Conclusion

The present results suggest that the levels of salivary IL-10 are increased in patients with periodontitis and are positively associated with hallmark signs of tissue

destruction including PPD and CAL. These data indicate that IL-10 is an essential immunoregulatory cytokine, which actually mirrors the severity of the disease and could possibly be considered a convenient salivary biomarker for periodontal status determination. The findings support the theory that IL-10 reflects a host response to attempt to balance inflammation in presence of ongoing bacterial challenge, and underscore its dual function as both protective and possibly permissive factor in chronic periodontitis.

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