Original Article

Correlation Between Different Salivary Interleukins and Clinical Periodontal Parameters

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Abstract

Background: Periodontitis is a multifactorial disease that affects tooth-supporting structures which consequently lead to loss of tooth support and tooth loss. Interleukins showed an important role in periodontal destruction. **Objectives:** The current study aimed to determine if there is a possible correlation between different interleukins and periodontal clinical parameters. **Materials and Methods:** Participants of the present study were divided according to periodontal conditions into periodontitis group (40 patients) and periodontally healthy group (40 subjects). All participants were male and systemically healthy. Salivary samples were taken from each participant before recording periodontal parameters and stored till being assessed for interleukin-6, interleukin-8, interleukin-12, and interleukin-17 by using an enzyme-linked immunosorbent assay technique. **Results:** All interleukins were lower in healthy group than periodontitis group. There were significant correlations between probing pocket depth and interleukin-6 and interleukin-17 (r = 0.31, P value = 0.05) and (r = 0.5, P value = 0.001) respectively. As well as a significant correlation was found between clinical attachment loss and interleukin-8 (r = 0.36, P value = 0.02). **Conclusion:** Correlation could be found between clinical attachment loss and interleukin-8, also it was found between probing pocket depth and interleukins (6 and 17).

Keywords: Clinical periodontal parameters, interleukin-6, interleukin-8, interleukin-12, interleukin-17

Introduction

Periodontitis is an inflammatory disease with a chronic nature, it affects the structure that support the teeth; it is associated with a composite interaction between the host defense system and the pathogens.[1,2] In recent years, the multifactorial etiologies of periodontal diseases have been emphasized. One of the most destructive causes of periodontium is the inflammatory mediator including cytokines. Cytokines participate with great effect on the immune reaction in periodontal conditions.[3,4] In both immunity and homeostasis, cytokines act as messengers and mediators.[5]

Nowadays, different factors in saliva including protein, enzymes, cytokines, and immunoglobulins considered biomarkers for diagnosing and monitoring cases of periodontitis.[6]

Being a plentiful biological fluid, ease in collection, and noninvasive procedures made saliva a targeted biological diagnostic fluid in screening periodontal diseases.[7]

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Interleukin (IL)-6 is a cytokine with multifunctional activity including stimulation of the production of immunoglobulin (Ig)G and IgA and final maturation of B-lymphocytes to plasma cells as well.[8]

One of the chemokines is IL-8, which has potent chemotactic actions not only for granulocytes but also for macrophages and lymphocytes. It is a powerful moderator of polymorphonuclear leukocyte aggregation at the sites of inflammation.[9]

Macrophages, monocytes, and neutrophils produced IL-12 in humans.[10] Interleukins 12 and 4 are key mediators in the differentiation of CD4 lymphocytes to Th1 or Th2 T cells. Interleukin-12 aids in the production of Th1 lymphocytes which produce interferon-gamma (IFN).

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Another interleukin is IL-17 which is a T-lymphocyte-produced cytokine, this cytokine is formed by several cells including macrophages, dendritic cells, mast cells, and natural killer cells too.[11] Interleukin-17, in a combination with additional cytokines, like IFN, IL-1B, Onkostatin-M, and tumor necrosis factor-alpha exacerbated a strong intracellular biologic consequences.[12]

Different studies have been shown that IL-6, IL-8, IL-12, and IL-17 increased in periodontal diseases.[13,14]

The current study aimed to find the correlation between clinical periodontal parameters and salivary (IL-6, IL-8, IL-12, and IL-17) biomarkers if ever present.

Materials and Methods

Patients

The current study is a case–control study. The study population involved 80 male individuals, with age range of 30–60 years. Study groups included periodontitis patients group (40 patients) and healthy group (40 subjects), periodontitis is diagnosed according to the most recent classification of periodontal diseases and conditions.[15] The sample size was calculated according to Sharma *et al*.[16] Learned consents were given to all participants to join in the present study; the study was conducted after being approved by the ethics team and Periodontics Department in College of Dentistry, Babylon University.

Inclusion criteria

(I) No periodontal therapy for the last 3 months,
(II) No utilization of anti-inflammatory medications or antibiotics for 3 months preceding the study,
(III) No smoking history, and
(IV) No systemic diseases.

Exclusion criteria

(I) Female gender;
(II) Patients with systemic diseases or subjects with smoking history;
(III) Patients who underwent periodontal treatment or who have taken antibiotics in the last 3 months; and
(IV) Number of the remaining teeth <20 teeth.
(V) Subjects who refuse to participate in the study.

Clinical evaluation

After the collection of salivary samples from each participant, clinical periodontal parameters were taken from six sites of each tooth (mesobuccal, central buccal, distobuccal, mesolingual-palatal, central lingual-palatal, and distolingual-palatal). Periodontal parameters included bleeding on probing (BOP),[17] plaque index (PI),[18] clinical attachment loss (CAL), and probing pocket depth (PD). Records were performed with a periodontal probe (Michigan O probe with Williams's markings).

Salivary sampling

Participants were prohibited from eating and drinking for 1 h and a half, also brushing was prevented for 12 h proceeding to the collection of samples. Subjects were instructed to droll 1–2 mL of nonstimulated saliva into a sterile container. After centrifugation of the samples, the supernatant was stored at (−80°C) till needed for analysis. The levels of IL-6, IL-8, IL-12, and IL-17 were estimated using an enzyme-linked immunosorbent assay (ELISA) kit (Elabscience Biotechnology Inc., Houston, TX, USA).

Statistical analysis

Data were analyzed using SPSS 20. The data are shown as means and standard deviation. The means of the two groups were compared by using an independent *t* test. Correlations between clinical periodontal parameters and salivary biomarkers were performed by means of Pearson's correlation. The results were regarded as significant statistically when *P* value was less than 0.05.

Ethical approval

The current study was performed in agreement with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' analytical and verbal approval before the sample was taken. The study protocol and the subject information and the consent form were reviewed and approved by a local ethics committee according to document number (2 on June 11, 2023) to get this approval.

Results

Descriptive statistics including mean and standard deviation of age, teeth number, BOP, PD, CAL, IL-6, IL-8, IL-12, and IL-17 for both groups (periodontitis and healthy) were shown in Table 1. It was found that BOP, PD, and CAL means were 0.37 ± 0.29, 4.57 ± 0.91, and 6.2 ± 1.83 in periodontitis group, respectively. Also, the levels of IL-6, IL-8, IL-12, and IL-17 were 162.38 ± 57.61, 215.27 ± 101.004, 433.1 ± 179.72, and 81.05 ± 32.53, respectively. Also, the levels of these interleukins were higher in periodontitis group than in healthy group with statistically significant differences as shown in Table 1.

Statistical analysis found that there was a statistically significant correlation between IL-6 and PD, whereas it failed to find significant correlations between this biomarker and other periodontal parameters as shown in Table 2.

It was established that there was a significant correlation between IL-8 and CAL, but there were no significant correlations with BOP, PI, and PD as shown in Table 3.

Regarding IL-12 and IL-17, the current study failed to find any significant correlations between IL-12 and clinical periodontal findings as shown in Table 4; whereas it found a statistically significant correlation between IL-17 and PD as shown in Table 5.

Table 1: Means and standard deviations of age, teeth number, BOP, PI, PD, CAL, IL-6, IL-8, IL-12, and IL-17 for both groups

Criteria	Group 1	Group 2	*P* value
Age	35.5 ± 11.42	40.8857 ± 13. 09	0.087
Teeth number	25.00 ± 5.68	24.23 ± 5.3	0.476
BOP	0.0007 ± 0.0005	0.37 ± 0.29	0.000
PI	0.67 ± 0.2	1.03 ± 0.45	0.000
PD	1.25 ± 0.44	4.57 ± 0.91	0.000
CAL	—	6.20 ± 1.83	—
IL-6	119.14 ± 21.7	162.38 ± 57.61	0.000
IL-8	164.35 ± 75.98	215.27 ± 101.004	0.006
IL-12	301.72 ± 128.09	433.1 ± 179.72	0.001
IL-17	17.32 ± 4.97	81.05 ± 32.53	0.000

Group 1 = healthy group, group 2 = periodontitis group

Table 2: Correlation of IL-6 with BOP, PI, PD, and CAL

Clinical parameters	*r*	*P* value
BOP	0.09	0.57
PI	0.02	0.89
PD	0.31*	0.05
CAL	0.10	0.53

*Significant

Table 3: Correlation of IL-8 with BOP, PI, PD, and CAL

Clinical parameters	*r*	*P* value
BOP	0.29	0.07
PI	0.17	0.30
PD	0.26	0.11
CAL	0.36*	0.02

*Significant

Table 4: Correlation of IL-12 with BOP, PI, PD, and CAL

Clinical parameters	*r*	*P* value
BOP	0.22	0.17
PI	0.18	0.27
PD	0.24	0.14
CAL	0.01	0.97

Table 5: Correlation of IL-17 with BOP, PI, PD, and CAL

Clinical parameters	*r*	*P* value
BOP	0.14	0.37
PI	0.12	0.48
PD	0.50**	0.001
CAL	0.04	0.82

**Highly significant

Discussion

Progressive damage of periodontium, with the development of gingival recession and periodontal pockets are clinical features of periodontitis which is defined as an inflammatory disease of periodontium caused by a specific microorganism.[19] The severity of periodontitis is significantly affected by different etiological factors.[20]

The progression of periodontal diseases including periodontitis resulted from complex interactions between bacterial, environmental, host-derived immune-inflammatory mediators and even genetic factors. The current study dealt with an important part of inflammation which is cytokines specifically the interleukins family. In the last three decades, several studies targeted the function of interleukins in pathogenesis of periodontitis and periodontal diseases and a lot of them succeeded in finding that function.[21,22]

The results of the current study found that all of the selected salivary biomarkers including IL-6, IL-8, IL-12, and IL-17 were higher in periodontitis group than healthy group with statistically significant differences. These results were in agreement with several previous studies.[21-26]

Teles *et al.*[27] failed to find statistically significant differences in salivary cytokines between healthy and periodontitis groups and they explained this insignificant result as that human buccal and gingival epithelial cells were able to produce cytokines, which could afford a supplementary or another resource of these mediators in whole saliva.

Presence of putative inhibitors in saliva is another potential confounder in the analysis of records depended on the concentrations of cytokines in saliva. Wozniak *et al.*[28] investigated the retarding property of parotid and whole saliva on the amounts of numerous cytokines. They accomplished that the majority of cytokines levels were significantly depressed in whole as compared with parotid saliva.

Fokkema *et al.*[29] showed that untreated patients with periodontitis released lesser levels of IL-12p70 (a heterodimer of IL-12 with a biological activity) in comparison to controls.

The current study found that there was a significant correlation between IL-6 and PD, this result was in

agreement with Isola *et al*.,[26] who found a significant and proportional relation between salivary IL-6 levels and PD, CAL, and bleeding sites.

It had been advocated to consider salivary IL-6 as an established indicator of past and recent contact with periodontal pathogens as salivary IL-6 has been documented to be a confidential biomarker of active inflammation in periodontal sites.[30,31]

Kurgan *et al*. found that there was no significant correlation between IL-6 and PD before and after periodontal therapy which is inconsistent with our finding; however, patient inclusion criteria for the two studies were not the same as the previous study included patients with rheumatoid arthritis.[32]

The current study found a statistically significant correlation between IL-8 and CAL, this result is consistent with Ertugrul *et al*.,[24] who established a statistically significant correlation between IL-8 and CAL in subjects with different periodontal conditions ranging from periodontally healthy to generalized periodontitis conditions.

On the other hand, this finding was inconsistent with Pandey *et al*.[33] Konopka *et al*.[34] failed to find a statistically significant correlation between CAL and IL-8 before and even after scaling and root planning.

Regarding IL-12, the current study found that there were no significant correlations with all periodontal parameters. This result was in concordance with Tarannum and Faizuddin.[25]

Sharma *et al*.[35] found that IL-12 had no significant correlation with all selected the clinical periodontal parameters before and after nonsurgical periodontal therapy.

The current study found that there was a significant correlation between IL-17 and PD only. This result was consistent with Yang *et al*.,[23] who established a statistically significant correlation between IL-17 and all clinical periodontal parameters. Similar results were found by Abdulmajeed and Mahmood.[36]

Conclusion

From the current study, we can summarize that there is a considerable shift in levels of IL-6, IL-8, IL-12, and IL-17 from healthy to periodontitis states. Although not all periodontal parameters showed a statistically significant correlation with all interleukins but significant correlations were found between PD and IL-6 and IL-17. Also, a significant correlation was found between IL-8 and CAL.

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Conflicts of interest

There are no conflicts of interest.

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