Cell. Mol. Biol. (ISSN: 1165-158X)

Journal Homepage: www.cellmolbiol.org

Cellular and Molecular Biology

Original Article

Effect of periodontal therapy on serum and salivary Interleukin-1 beta (IL-1β) and malondialdehyde levels in chronic periodontitis

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Article Info

Article history:

Received: May 16, 2024
Accepted: September 04, 2024
Published: October 31, 2024

Use your device to scan and read the article online

Abstract

Chronic periodontitis (CP) is distinguished by an inflammatory reaction and the presence of oxidative stress (OS), which has consequences for overall health. Interleukin-1β (IL-1β) and malondialdehyde (MDA) serve as markers of inflammation and OS, respectively. Analyzing the alterations in their reaction to periodontal therapy can provide valuable insights into the management and monitoring of CP progression. The current study aimed to evaluate the impact of non-surgical periodontal therapy (NST) on IL-1β and MDA levels in the serum and saliva of CP patients and explore their correlation with clinical periodontal indices post-therapy. There were 60 participants in this research, aged 33 to 50, equally split between thirty periodontally healthy controls and 30 patients with CP. Measures were taken of the clinical periodontal parameters, including the bleeding index, probing pocket depth, gingival index, and plaque index. Saliva and blood samples were collected for IL-1β and MDA analysis using ELISA and spectrophotometrically. CP patients received scaling and root planning (SRP) as part of phase I periodontal therapy, and after six weeks, we reevaluated clinical parameters and IL-1β and MDA levels. In CP patients, both saliva and serum IL-1β and MDA levels significantly increased alongside worsening clinical periodontal parameters compared with periodontally healthy individuals. phase I periodontal therapy led to a notable decrease in both saliva and serum IL-1β and MDA levels, accompanied by improvements in clinical parameters. Additionally, following six weeks of scale and root planning treatment, our data showed a strong positive relationship between salivary IL-1β and MDA levels with PPD and CAL. SRP therapy is effective in managing periodontal health, as evidenced by a significant decrease in clinical parameters and biomarker levels after treatment for CP patients. This suggests that salivary IL-1β and MDA may be useful biomarkers for indicating the severity of periodontal disease and the effectiveness of treatment.

Keywords: Chronic periodontitis, Interleukin-1β, Malondialdehyde, Non-surgical periodontal therapy, Saliva, Serum.

1. Introduction

Periodontitis is a form of inflammation that affects the tissues that support the enamel of the teeth. Pathogenic bacteria are the main cause of it. The intricate relationship between the bacteria and the body's defensive systems causes it. It may cause pocket development and gum recession by progressively destroying the alveolar bone and periodontal ligament. This common oral condition, second only to tooth decay, affects 5-30% of adults. Its course often alternates between periods of activity and dormancy, affecting the progression and severity of the disease [1, 2].

Periodontopathic bacteria significantly amplify the susceptibility to periodontitis by inducing immune responses and triggering the subsequent release of proinflammatory cytokines, pivotal to the destruction of periodontal tissue [3]. Periopathogens like *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*, collectively identified as the “red complex” along with Aggregatibacter actinomycetemcomitans, are recognized as principle etiological agents in periodontitis. These disease-causing microorganisms stimulate proinflammatory molecules called cytokines, including IL-1β, tumor necrosis factor-(TNF-), and prostaglandins. These cytokines possess potent proinflammatory and deleterious characteristics and are crucial in the process of periodontal tissue degradation and bone loss [4].

IL-1β is particularly important because of its obvious pro-inflammatory and bone resorption capabilities. It is mainly secreted by activated macrophages and lymphocytes as well as fibroblasts, endothelial cells and mast cells. It plays a role in coordinating inflammatory responses and affecting cells. Key role. , differentiation and apoptosis, which are closely related to the pathophysiology of periodontitis. Clinical studies substantiate that periodontitis properly amplified IL-1β production both locally (in gingival crevicular fluid (GCF) and saliva) and systematically

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Doi: http://dx.doi.org/10.14715/cmb/2024.70.10.22

(in serum). Furthermore, as a suggestive biomarker for the advancement of periodontal disease (PD), its level is favorably related to both clinical attachment loss (CAL) and increased probing depth. Notably, IL-1β is not merely a marker but also a functional player in disease pathology, and its levels have been observed to diminish following periodontal treatment, underscoring its potential role in monitoring disease activity and treatment efficacy [5, 6].

Malondialdehyde (MDA), a prevalent byproduct of the oxidation of lipids, is extensively used to evaluate oxidative stress (OS) and has been regularly investigated for studies related to periodontitis. There is a notable direct relationship between MDA levels and periodontal parameters, showing that MDA relates strongly to the severity of the disease [7]. Interestingly, MDA levels may decrease after periodontal therapy. The role of OS in periodontitis, represented by markers like MDA, is quite clear: it stimulates immunological reactions, leading to the secretion of cytokines such as IL-1β. This, subsequently, boosts inflammation and further periodontal tissues, forming a continuous cycle of damage and inflammation throughout the progression of periodontal illness [8].

Mostly comprising scaling and root planning (SRP), non-surgical periodontal treatment (NSPT) seeks to reduce the bacterial load and change circumstances inside microbial habitats, therefore reducing the host inflammatory reaction [9]. Notably, previous studies have reported a resolution of inflammation and improvement in clinical parameters among periodontitis patients following NSPT. Histological evaluation indicates a reduction, although not a complete eradication, in inflammatory infiltrate within the connective tissue and a sustained presence of proinflammatory cytokines such as IL-1β post-therapy [10]. Furthermore, after treatment, a slight elevation in IL-1β concentration has been observed in the GCF. Incorporating the detection of molecular biomarkers like IL-1β in clinical practice can potentially offer insights into the efficacy of treatment outcomes post-NSPT [11]. Nevertheless, there have been few investigations on the impact of NSPT on local clinical indicators, systemic inflammatory markers, as well as systemic and oxidative stress markers. Therefore, the present study aims to evaluate the impact of SRP treatment on the levels of IL-1β, an inflammatory marker, and MDA, a measure of oxidative stress, in patients suffering from chronic periodontitis (CP).

2. Materials and Methods

2.1. Study population

This study was a controlled clinical trial with an intervention, involving a total of 60 participants (33-50 years old) of both sexes (32 males and 28 females). The participants were randomly selected from patients who were accepted into the Department of Periodontics, College of Dentistry/Hawler Medical University for treatment of periodontal issues. All patients provided written informed permission after a comprehensive description of the study's objective. The study received ethical approval from the Ethical Committee of the College of Dentistry, Hawler Medical University.

The patients were categorized into two groups based on their periodontal well-being. Group I: Thirty participants (n=30) with healthy periodontium were enrolled and considered a control group (CG). Group II: Thirty participants (n=30) with CP received treatment, including SRP, and were considered a test group. The patients underwent clinical and radiological assessment for CP based on the criteria established by the American Academy of Periodontology in 1999 [12]. In at least 30% of the teeth examined, participants with at least two interdental regions with CAL ≥ 3mm and probing pocket depth (PPD) ≥ 5mm were considered to have CP [13].

Inclusion criteria for the CG were participants with at least 20 natural teeth periodontal pockets < 3m, loss of attachment< 2 (or with no attachment loss), and no radiographic evidence of bone loss with < 20% sites. Furthermore, for the test group, the participants had to have generalized chronic PPD ≥ 5 mm in at least 30% of the teeth examined and CAL ≥ 3 mm with radiographic evidence of alveolar bone loss. The exclusion criteria encompassed patients who had undergone periodontal treatment in the previous six months, a record of medication usage such as antibiotics and anti-inflammatory drugs in the last six months, any systemic ailment that could potentially impact the advancement of periodontal illness, and the existence of any observable oral mucosal lesions. Furthermore, those who were pregnant or breastfeeding, smokers, or drinkers were also excluded.

2.2. Sample collection and analysis

2.2.1. Saliva collection and analysis

Each participant provided a sample of un-stimulated whole saliva measuring three milliliters. The collection took place between 8:00 a.m. and 11:00 a.m., following the methodology outlined by Navash and Kumar in their 2008 publication [14]. The participants were given explicit instructions to abstain from consuming food or beverages, chewing gum, and engaging in oral hygiene practices for a minimum of two hours before the collection of saliva samples. The participants were directed to repeatedly rinse their mouths with distilled water in order to remove any food debris, followed by five minutes of relaxation in an upright posture [14]. Saliva samples were obtained before periodontal treatment and clinical assessment, and again after six weeks of NSPT. The saliva samples were gathered into 5mL aseptic plastic test tubes, promptly put on an ice pack, and conveyed to the laboratory. They were centrifuged at a speed of 3500 rotations per minute for 10 min. The transparent liquid remaining after sedimentation was promptly poured into a plastic container marked with the individual's name, date, and visit sequence, and thereafter preserved at a temperature of -40 ˚C until the time of analysis.

A volume of five ml of blood was obtained from each individual during the early morning hours (8:00-11:00 a.m.) and promptly transported to the laboratory. The specimen was let to coagulate at ambient temperature for one hour, followed by centrifugation at a speed of 3000 revolutions per minute for 10 min. Serum samples were collected and preserved in Eppendorf tubes at a temperature of -40 º C until the test was conducted. Saliva and blood samples were obtained on two occasions: first, at the beginning of the study, and then again after six weeks for patients in group II. However, people in group I only had their samples collected once. The levels of IL-1β in serum and saliva were tested using an ELISA kit given by My Biosource International Inc., USA (catalog# MBS763691), following the manufacturer's instructions. The accepted range was 1-20 ng/L. The MDA concentration in both sa-

liva and serum was measured using a spectrophotometric technique.

2.2.2. Measurement of MDA

The levels of MDA in both serum and saliva were assessed using the methodology described by Jain et al. [15]. This method was dependent on the interaction between MDA and thiobarbituric acid (TBA) to produce a molecule that can be quantified using spectrophotometry. To conduct the analysis, 0.2 ml of the collection was thoroughly combined with 0.8 ml of phosphate-buffered saline (pH 7.4) and 0.025 ml of a 0.88% solution of butylated hydroxytoluene. After adding 0.5 mL of a solution containing 30% trichloroacetic acid, the samples were refrigerated for two hours. Subsequently, they were subjected to centrifugation at a speed of 2000 x g at a temperature of 25 °C for 15 min. A volume of 1 ml of supernatant was combined with 0.075 ml of 0.1 M EDTA and 0.25 ml of 1% thiobarbituric acid in a solution of 0.05 N NaOH. The specimens were immersed in a vigorously boiling water bath for 15 min and thereafter allowed to cool down to the ambient temperature. The wavelength at which the absorbance was measured was 532 nm.

2.2.3. Calculation

The optical density of the test samples exhibits a clear correlation with the concentration of MDA in the sample. The optical density values are derived by plotting them against a standard graph and then multiplying them by the applicable dilution factors. The highest level of concentration is shown as µM/L.

2.3. Clinical Parameters

The periodontal condition of all participants was assessed by measuring the Gingival Index (GI), Plaque Index (PI) [16], PPD, Bleeding on probing (BOP), and CAL [17] using a UNC-15 probe at six locations per tooth. Using full-mouth periapical images, the degree of loss in periodontal bone was assessed [18]. The data were documented and the therapy was conducted by a single proficient periodontist after the collection of blood and saliva samples. In order to form Group III (post-treatment) all clinical measures were assessed at the start of the trial in both groups and six weeks after treatment.

2.4. Non-surgical periodontal therapy

The patients in group II had NSPT, which included SRP as well as advice on maintaining oral hygiene. Patients were taught to maintain good oral hygiene by using proper brushing techniques, flossing, and using interdental brushes. The SRP was conducted by a skilled periodontologist with the use of a local anesthetic, to minimize discomfort during periodontal debridement. This was achieved by using ultrasonic equipment (Electro Medical System, Switzerland) and Gracey curettes (Hu-Friedy, Chicago, IL, USA). The procedure was performed until the surface of the root was seen as smooth using a metallic explorer probe (MEDESY, Italy). Following the completion of SRP, the teeth were polished using a rubber cup. Root planning was performed when needed, 15 days following the first assessment, at two additional appointments. There were no prescriptions for antibiotics, anti-inflammatory drugs, or chemical aids to manage plaque following the therapy after six weeks of SRP, the evaluation of gum health, gathering of more blood and saliva samples, and the examination of IL-β and MDA were conducted once again. The CG did not receive any periodontal therapy during the trial and was assessed just once.

2.5. Statistical analysis

The data that was gathered was analyzed using the SPSS 21 software tool. The findings, which followed a normal distribution, were presented as the mean ± standard deviation (Mean ± SD) of several variables (IL-1β, MDA, GI, PPD, CAL, BOP) in both subgroups of the test group (at the beginning and after six weeks of treatment) and the CG. The analysis of variance (ANOVA) was used to compare the groups. The pre-and post-data were compared with a paired t-test. Spearman's correlation value was used to look at the relationship between clinical data and IL-1β and MDA levels. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical findings

Table 1 contains clinical parameter values. When comparing CP patients (Group II) to healthy controls (Group I), the baseline clinical periodontal parameters were considerably higher ($p < 0.001$) in Group II patients. All clinical indices improved as a result of periodontal treatment. After receiving SRP treatment for six weeks, every clinical parameter in Group II showed a substantial reduction ($p < 0.001$) when compared to its baseline levels.

3.2. Laboratory findings of biomarkers

The statistical analysis of biomarkers assessed between the two research groups is shown in Table 2 and Figure 1. The levels of IL-1β in both serum and saliva were considerably elevated ($p < 0.01$) in group II as compared to group I. After undergoing SRP treatment, the concentrations of IL-1β in both the bloodstream and saliva reduced signi-

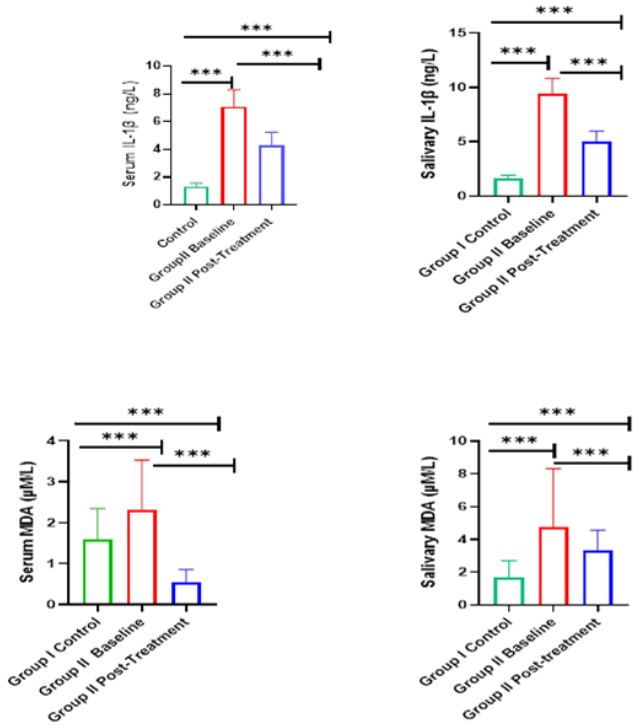

Fig. 1. Comparison of mean values of the biomarkers between groups I and II. ****: P- value≤ 0.0001 significant.

Table 1. Comparative analysis of the mean of clinical parameters between two groups.

Clinical Parameters	group I (n=30)	Group II (n=30)		p-value[a] group Ivs group II (baseline)	p-value[b] group II baseline vs Post-treatment	p-value[a] Group I vs GII (post-treatment)
		Baseline	Post-treatment			
PI	0.51 ± 0.16	1.66 ± 0.35	0.58 ± 0.19	0.001	0.001	0.001
GI	0.4 ± 0.37	2.27 ± 0.51	1.22 ± 0.53	0.001	0.001	0.001
PPD (mm)	1.31 ± 0.47	5.1 ± 0.63	2.61 ± 0.52	0.001	0.001	0.001
CAL(mm)	0.00 ± 0.00	3.98 ± 0.82	1.94 ± 0.45	0.001	0.001	0.001
BOP	4.21 ± 3.01	56.13 ± 21.67	24.44 ± 6.59	0.001	0.001	0.001

Values are mean± SD; Standard deviation; [a]p-values for mean ± SD by independent sample 't' test; [b]p-values for mean± SD obtained by paired 't' test.

Table 2. Comparison of biomarkers between both groups.

Parameters	group I (n=30)	Group II (n=30)		p-value[a] group Ivs group II (baseline)	p-value[b] group II baseline vs post-treatment	p-value[a] Group I vs GII (post-treatment)
		Baseline	Post-treatment			
Serum IL-1β (ng/L)	1.32 ± 0.25	7.10 ± 1.21	4.27 ± 0.97	0.00	0.00	0.001
Salivary IL-1β (ng/L)	1.59 ± 0.33	9.44 ± 1.38	5.06 ± 0.90	0.00	0.00	0.001
Serum MDA (µM/L)	1.59 ± 0.75	2.30 ± 1.23	0.53 ± 0.31	0.001	0.00	0.001
Salivary MDA (µM/L)	1.69 ± 0.99	4.76 ± 3.55	3.34 ± 1.21	0.00	0.00	0.001

Values as mean± SD; [a]p values for mean± obtained by independent sample "t" test; [b]p values for mean obtained by paired "t" test.

Table 3. Correlation between clinical periodontal parameters and biomarkers in patients with CP using Spearman's correlation before therapy.

Clinical Parameters	IL-β				MDA			
	Serum		Salivary		Serum		Salivary	
	rho	*P*	rho	*P*	rho	*P*	rho	*P*
PI	0.296	0.113	-0.218	0.248	0.015	0.939	-0.210	0.265
GI	0.018	0.926	0.019	0.919	-0.030	0.873	0.212	0.260
PPD (mm)	-0.040	0.832	0.335	0.040*	0.186	0.325	0.556	0.001*
CAL(mm)	0.51	0.788	0.356	0.050*	0.103	0.589	0.496	0.005*
BOP	-0.326	0.079	0.75	0.694	0.004	0.983	0.043	0.821

r= Spearman' s correlation Coefficient; *Statistically significant p< 0.05.

ficantly compared to the initial values (p <0.01). Just like MDA, the initial levels of MDA in the blood and saliva were considerably greater in group II compared to the CG (p <0.01). Following SRP, there was a substantial drop (p <0.01) in the levels of IL-1β in both blood and saliva compared to the initial values in Group II. These levels returned to values similar to those of the CG following treatment.

A correlation between clinical periodontal parameters and biomarkers was assessed using Karl Pearson″s correlation test, as indicated in Table 3. Initially, salivary IL-1β levels exhibited a significant positive correlation with both PPD and CAL at baseline (r=0.335, p=0.004 and r=0.356, p=0.05, respectively). Similarly, salivary MDA also showed positive correlations with PPD and CAL (r=0.556, p=0.001 and r=0.496, p=0.005). After six weeks of SRP therapy, salivary IL-1β and MDA levels continued to exhibit positive correlations with PPD and CAL (r=0.959, p=0.026 and r=0.377, p=0.045) (r=0.386, p=0.035 and r=0.378, p=0.055), respectively. However, no notable relationships were observed between serum IL-1β and MDA levels with clinical parameters (p >0.05%).

4. Discussion

Periodontal disorders arise from inflammation caused by pathogenic microorganisms in the subgingival biofilm, along with a weakened immune response and degradation of connective tissue. The presence of bacteria increases the synthesis of cytokines by the gingival epithelium, causing uncontrolled inflammation, which ultimately leads to missing teeth in adults from various groups [19]. Elevated OS and diminished antioxidant capacity are believed to play pivotal roles in developing periodontitis [20, 21]. This indicates that patients suffering from periodontal illnesses are more susceptible to an imbalance between antioxidants and oxidative stress [22]. The involvement of OS makers, notably MDA, is crucial since they not only arise from inflammation but also can enhance continuing tissue damage by sustaining a state of inflammation. Therefore, considering both cytokine and OS markers is vital for a comprehensive understanding and management of periodontal inflammation more effectively through influencing systemic inflammatory and oxidative status [23].

Previous research has mainly focused on elucidating the utility of IL-1β and MDA measurements in either saliva, serum, or GCF in individuals diagnosed with CP. They have been likened to those who are in good health [24–27]. However, no studies have investigated the changes in blood and salivary IL-1β and MDA levels pre- and post-periodontal therapy in patients with CP, and their correlation with measures in persons without PD.

The clinical indicators (GI, PI, PPD, CAL, and BOP) were shown to demonstrate improvement after SRP in the present investigation. This favorable reaction to SRP is consistent with the results of previous research [28–31], which have also reported similar improvements in clinical parameters following SRP.

The current study found that individuals who had CP had considerably higher levels of IL-1β in both their saliva and blood compared to healthy persons (P< 0.01). Additionally, after periodontal treatment, a significant reduction in IL-1β levels was seen in the CP group in comparison to the CG (P <0.01). Notably, salivary IL-1β concentrations exceeded those in serum across all groups, possibly due to localized secretion from periodontal tissue cells in response to inflammation.

Several studies have highlighted the significance of IL-1β in CP. Al-Taweel et al. [25] reported significantly elevated serum IL-1β levels in CP patients, suggesting its relevance to the disease's pathogenesis. Zhu et al., [32] found increased IL-1β levels in both serum and GCF in CP patients than those in the CG, emphasizing its role as a potential biomarker in disease progression. Research conducted by Aleksandrowicz et al. [24] found that individuals with severe periodontitis had the highest mean level of IL-1β in their GCF. In addition, Miller et al. [33] discovered elevated levels of IL-1β in saliva among individuals with CP, suggesting its potential as a biomarker for periodontitis in saliva. IL-1β is well acknowledged as a crucial mediator of inflammation in chronic local inflammatory disorders. It promotes the breakdown of bone in the alveolar process. It enhances the production of collagenolytic enzymes, namely Matrix Metalloproteinase, which play a role in breaking down the extracellular matrix. This process leads to bone loss and tissue damage [34].

In individuals with CP, the present research showed a meaningful decrease in IL-1β levels in both blood and saliva after periodontal treatment. This reduction significantly correlated with clinical improvement, particularly in PPD and CAL, aligning with findings from previous studies [5, 28]. These studies also reported decreased IL-1β in GCF post-scaling root planning reduced IL-1β levels and disease severity. Sexton et al. [35] performed a longitudinal evaluation of several salivary biomarkers linked to periodontitis in a cohort of 68 persons with CP. The aim was to examine the correlation between periodontal treatment and the state of the illness. They measured salivary cytokine levels, including IL-1β, IL-8, MIP-1α, MMP-8, OPG, and TNF-α, and observed that salivary IL-1β were indicative of disease severity and treatment response. This suggests that IL-1β may hold promise as a valuable marker for monitoring PD status. These findings strengthen the hypothesis that cytokines like IL-1α, IL-1β, and IL-6 play a role in the pathogenesis of periodontitis, as previously suggested [11]. These studies collectively underscore the utility of IL-1β as a valuable biomarker for assessing the effectiveness of periodontal therapy and tracking disease progression. However, it is worth noting that our results contrast with another study [3, 36, 37] that did not detect differences in GCF levels of IL-1β and IL-6 following SRO. These discrepancies may arise from variations in sampling protocols, participant inclusion criteria, and disease severity, as mentioned in the introduction. Therefore, when interpreting and comparing these methodological differences [8, 38].

The findings of the current study indicate that individuals with CP exhibited elevated levels of MDA in both saliva and serum, which is consistent with the findings reported OS biomarkers, particularly MDA in saliva, serum, and GCF, were higher in patients with CP than controls [26, 27, 39]. Moreover, after phase I periodontal treatment, there was a notable reduction in salivary and serum MDA levels, which aligns with the study results [22]. Additionally, Significant improvements in clinical indicators were seen after the completion of phase I periodontal treatment. According to Chaplle et al. [40] NSPT may enhance the antioxidant defense in individuals with chronic pancreatitis by improving clinical indicators.

The current study revealed a significant disparity between the amounts of MDA in saliva and serum. This finding suggests that there is a localized increase in lipid peroxidation (LPO) within the periodontal region of CP, which appears to be more significant in terms of the pathology of PD than the systematic increase. The significant reduction in MDA levels following therapy also implies that successful NSPT may help restore local total antioxidant capacity in individuals with CP to levels comparable to those in CG.

This study revealed a positive correlation between the increase of salivary IL-1β and MDA levels with an increase in PPD and CAL at baseline. Also, there was a positive correlation between decreased salivary IL-1β and MDA levels and decreased PPD and CAL after six weeks of SRP therapy. The findings indicate a substantial correlation between the levels of biomarkers (IL-1β and MDA) and the degradation of periodontal tissue. Therefore, the detection of increased concentrations of IL-1β and MDA in the saliva of individuals with CP, along with the strong association with clinical evaluations of periodontal tissue damage, indicates that IL-1β and MDA levels could serve as a highly responsive and dependable biomarker for assessing chronic inflammation activity and subsequent tissue destruction. IL-1β and MDA are considered significant indicators in the development of periodontal disorders [4]. This conclusion is also in line with the findings of previous investigations [25, 28]. The data suggests a clear relationship between the levels of IL-1β and the severity of PD.

5. Conclusion

Given the limitations of the present investigation, it may be concluded that measuring IL-1β and MDA levels in saliva can be useful for detecting the active phase of PD and predicting the effectiveness of phase I periodontal therapy. Future research with a larger sample size and varying durations of IL-1β and MDA estimation in saliva should be conducted.

Conflict of interests

The authors do not have any disagreements or disputes with any stage of the article preparation.

Consent for publications

The authors reviewed and authorized the final article for publication.

Ethics approval and consent to participate

The study has received ethical approval from the Ethical Committee of the College of Dentistry, Hawler Medical University.

Informed consent

All participants provided written informed consent.

Availability of data and material

The corresponding author can provide the study's data upon reasonable request.

Authors' contributions

The Authors contributed in this research work equally.

Funding

Non.

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