# "SALIVARY MACROPHAGE INFLAMMATORY PROTEIN-1 ALPHA: DYNAMIC BIOMARKER IN CHRONIC PERIODONTITIS SUBJECTS PRE AND POST SCALING AND ROOT PLANING"

**Dr. Apeksha Annigeri B[1]., Dr. Trijanya Gowda[2], Dr. Apoorva G[3]**
[1]Lecturer, Department of Periodontics, KAHER's VK Institute of Dental Sciences, Belagavi, India
[2]Assistant professor, Department of Periodontics, HKE's S Nijalingappa Dental College and Hospital, Kalaburagi, India.
[3]Lecturer, Department of Periodontics, KAHER's VK Institute of Dental Sciences, Belagavi, India

Corresponding author: Dr. Apeksha Annigeri B[1]
Email : apekshaannigeri@gmail.com

**Abstract**
**Background:** Chronic Periodontitis is characterized by chronic inflammation and progressive destruction of periodontal tissues mediated by various cytokines and chemokines. Macrophage Inflammatory Protein-1 Alpha is crucial in recruiting inflammatory cells and in resorbing alveolar bone. The present study aimed to assess the salivary MIP-1α levels between the periodontal health and chronic periodontitis and its variation after non-surgical periodontal therapy.
**Materials and Methods:** This was a comparative pre–post clinical study conducted on 40 subjects consisting of healthy controls and chronically affected periodontitis group. The clinical periodontal parameters such as Probing Pocket Depth (PPD), Clinical Attachment level (CAL), Periodontal Inflamed Surface Area (PISA), Gingival Index (GI), Gingival Bleeding Index (GBI), and Plaque Index (PI) were measured at baseline and after 3 months following Scaling and Root Planing (SRP). Saliva samples were taken and salivary Macrophage Inflammatory Protein - 1 alpha (MIP-1α) levels were then estimated using ELISA analysis.
**Results:** The clinical periodontal, PISA parameters and the level of salivary MIP-1α were all significantly higher in chronic periodontitis patients than the healthy controls ($p<0.05$). Periodontal and/or clinical parameters, PISA and salivary MIP-1α levels were found to be significantly decreased after non-surgical periodontal therapy ($p<0.001$). There was a positive correlation for salivary MIP-1α levels with probing pocket depth, clinical attachment level and PISA.
**Conclusion:** There is a strong correlation between salivary MIP-1α and periodontal inflammation and destruction. The significant decrease after periodontal treatment indicates that it could be a useful non-invasive diagnostic and monitoring tool for chronic periodontitis.
**Keywords:** Chronic Periodontitis; Saliva; Macrophage Inflammatory Protein-1 alpha; Scaling and Root Planing; Biomarker
**How to cite this article:** Annigeri BA, Gowda T, Apoorva G. Salivary Macrophage Inflammatory Protein-1 Alpha: Dynamic Biomarker in Chronic Periodontitis Subjects Pre and Post Scaling and Root Planing. Int J Drug Deliv Technol. 2026;16(49s): 449-455. DOI: 10.25258/ijddt.16.49s.47
**Source of support:** Nil.
**Conflict of interest:** None

**Introduction:**

It is known that oral health is a major part of general systemic health, and that Periodontal Disease is one of the most prevalent chronic inflammatory diseases in the world. Progressive destruction of gingiva, periodontal ligament, cementum and alveolar bone resulting in tooth loss if untreated. The disease occurs as a result of multifactorial involvement of pathogenic microorganisms and host immune-inflammatory response. A group of gram-negative anaerobic bacteria, specifically Porphyromonas gingivalis Pg, are recognized as important pathogens associated with tissue destruction during periodontal disease [1].

Periodontal disease development and progression is strongly controlled by inflammatory and immune pathways. As part of an inflammatory response against a bacterial challenge, host cells produce several inflammatory mediators that play a part in the connective tissue destruction and in the loss of alveolar bone [2]. The chemokines are small proteins of chemotactic activity which are responsible for the migration and activation of leukocytes at inflammation sites [3]. They are key in achieving inflammatory responses in periodontal tissues and regulating immune cell trafficking [4].

Pro-inflammatory chemokine Macrophage Inflammatory Protein-1 Alpha plays an important role in the progression of periodontal disease. Binds to CCR1 and CCR5 receptors, expressed on monocytes, macrophages and lymphocytes, and is involved in the recruitment of inflammatory cells into periodontal tissues [5]. In addition, MIP-1α

can activate the release of inflammatory cytokines and increase the activity of osteoclasts, causing alveolar bone destruction [6].

Previous studies have demonstrated increased levels of MIP-1α in inflamed periodontal tissues, gingival crevicular fluid, and saliva of periodontitis patients. Gemmell et al. (2001) reported that chemokine positive cells in diseased gingival tissues were increased [7] and Kabashima et al. (2002) reported a rich amount of MIP-1α positive cells in inflamed periodontal tissues. [8] Shea et al. (2005) found an increase in Gingival crevicular fluid levels of MIP-1α in patients with periodontal disease as well [10].

Saliva is becoming an interesting diagnostic fluid due to the ease, cost-effectiveness and non-invasive nature of its collection. Salivary biomarkers can be reflective of local and systemic inflammatory changes in the body and can be beneficial in early detection and monitoring of periodontal disease [10]. Al-Sabbagh et al., 2012, showed that a significant difference in the level of salivary MIP-1α was seen between patients with periodontal disease and those with periodontal health and it can differentiate between the two conditions [11]. Likewise, de Lima et al. (2016) proposed salivary biomarkers as having a high potential for diagnosis in periodontal disease [12].

Non-surgical periodontal therapy, particularly deep pocket cleaning (scaling and root planing) is the main treatment for chronic periodontitis. Periodontal therapy is used to decrease the amount of microorganisms and inflammation in the area and, consequently, further improves the clinical parameters of periodontal tissue health. However, few studies have investigated the periodontal therapy-induced changes in the level of salivary MIP-1α and reported results to date have been conflicting [13].

This is the reason the following study was carried out to determine the levels of Macrophage Inflammatory Protein-1α in periodontal health and disease condition and to see the changes in the level of Macrophage Inflammatory Protein-1α after non-surgical periodontal treatment. The study proposes to identify the possible use of salivary MIP-1α as a biomarker for periodontal inflammation and as a therapeutic target.

**Materials and methods**

This clinical pre–post study involved a comparison of two groups of subjects who presented themselves for periodontal evaluation and treatment in the Department of Periodontics, and comprised of subjects who were attending the department for other evaluations and treatments. Forty subjects were selected who were healthy as regards any underlying disease and had given their informed written consent and institutional ethical clearance.

The study population was split in three groups. The first 20 subjects in the study were those who were periodontally healthy (Gingival Index (GI) score <1, probing pocket depth (PPD) <4 mm, and no clinical attachment loss (CAL). The 20 subjects with moderate to severe chronic periodontitis with ≥3 to 4 mm PPD and ≥3 mm CAL were the ones included in group 2, but re-evaluated 3 months after the non-surgical periodontal therapy in group 3.

The following subjects were excluded from the study: Systemic diseases that impact the periodontal status; Gum disease therapy in the past two months; Smokers; Pregnant women or lactating women; subjects using anti-inflammatory medication.

Clinical periodontal examination involved determination of Plaque Index (Silness and Loe, 1964), Gingival Index (Loe and Silness, 1963), Gingival Bleeding Index (Ainamo and Bay, 1975), probing pocket depth and clinical attachment level. The surface area of the periodontal pockets that were inflamed was determined by using Microsoft Excel software and the formula proposed by Nesse et al., 2008 for quantifying periodontal inflammatory burden [14].

Unstimulated whole saliva (2 mL) was collected in the morning from 9 AM until 11 AM by spitting technique. The participant was asked to wash his or her mouth thoroughly with water before collecting the sample. Chronic periodontitis subjects had saliva samples taken also before and three months after scaling and root planning (SRP), while healthy subjects' saliva was taken at baseline. Samples collected were refrigerated at – 80 °C till biochemical analysis.

Chronic periodontitis patients received non-surgical periodontal treatment using ultrasonic scalers and Gracey curettes until the surfaces of the roots were smooth and deposits were absent. All participants were given oral hygiene instructions.

The level of Macrophage Inflammatory Protein-1 Alpha in the saliva was measured via a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Raybiotech ELISA kit) following the manufacturer's instructions. Optical density was determined by microplate reader at 450 nm with concentrations reported in pg/mL.

The data was analyzed statistically by SPSS version 22.0. Data were shown as mean ± SD and number with percentage. Intergroup comparison was done by applying one-way ANOVA and Tukey's multiple comparison test to the clinical parameters. For non-parametric variables, Kruskal–Wallis and Mann–Whitney U tests were used. Correlations between clinical periodontal parameters, PISA and salivary MIP-1α were analyzed using Spearman rank correlation test. Multiple linear regression analysis was conducted

to look for predictors for salivary MIP-1α and PISA levels. A p value <0.05 was determined to be statistically significant.

**Results**:

Demographic and baseline data of participants in the study are presented in Table 1. The mean age of the subjects having chronic periodontitis was significantly higher than the mean age of healthy controls (40.25 ± 9.93 years vs. 24.25 ± 2.77 years; $p < 0.001$). No significant difference between the gender of groups was found ($p = 0.11$). The patients with chronic periodontitis showed increased PISA, gingival index, gingival bleeding index, CAL, PPD, and MIP-1α in comparison to healthy patients, which revealed that the periodontal inflammatory burden and tissue destruction were significantly increased in the chronic periodontitis group.

**Table 1. Demographic and Baseline Characteristics of Study Participants**

| Characteristic | Healthy Controls (Group 1) n = 20 | Chronic Periodontitis (Group 2) n = 20 | p-value |
|---|---|---|---|
| Age (years) | 24.25 ± 2.77 | 40.25 ± 9.93 | <0.001* |
| Male, n (%) | 6 (30.0) | 11 (55.0) | 0.11 |
| Female, n (%) | 14 (70.0) | 9 (45.0) | |
| Plaque Index | 0.83 ± 0.33 | 1.60 ± 0.35 | <0.001* |
| Gingival Index | 0.81 ± 0.43 | 1.77 ± 0.29 | <0.001* |
| Gingival Bleeding Index | 19.49 ± 14.16 | 86.23 ± 12.75 | <0.001* |
| Probing Pocket Depth (mm) | 2.09 ± 0.13 | 4.22 ± 0.97 | <0.001* |
| Clinical Attachment Level (mm) | 0.00 ± 0.00 | 4.67 ± 0.86 | <0.001* |
| PISA ($mm^2$) | 345.74 ± 210.27 | 1638.66 ± 569.46 | <0.001* |
| Salivary MIP-1α (pg/mL) | 5.59 ± 1.41 | 9.30 ± 6.73 | 0.009* |

The clinical parameters, PISA value and saliva MIP-1α concentration of the study groups are presented in Table 2. Chronic periodontitis group patients showed significant increase for all clinical symptoms and signs when compared with healthy controls at baseline for plaque index, gingival bleeding index, probing pocket depth, clinical attachment level, PISA and salivary MIP-1α score. There was a significant improvement at 3 months post-therapy in all clinical periodontal parameters. Similarly, periodontal therapy (specifically non-surgical periodontal therapy) resulted in a significant decrease in both PISA as well as salivary MIP-1α levels following therapy ($p<0.001$), indicating a periodontal health status improvement and reduction in periodontal inflammation after therapy.

**Table 2. Comparison of Clinical Periodontal Parameters, PISA and Salivary MIP-1α among Study Groups**

| Parameter | Group 1 Healthy n = 20 | Group 2 Baseline CP n = 20 | Group 3 Post-SRP n = 20 | p-value |
|---|---|---|---|---|
| Plaque Index | 0.83 ± 0.33 | 1.60 ± 0.35 | 0.37 ± 0.22 | <0.001* |
| Gingival Index | 0.81 ± 0.43 | 1.77 ± 0.29 | 0.44 ± 0.24 | <0.001* |
| Gingival Bleeding Index | 19.49 ± 14.16 | 86.23 ± 12.75 | 16.00 ± 9.03 | <0.001* |
| Probing Pocket Depth (mm) | 2.09 ± 0.13 | 4.22 ± 0.97 | 3.36 ± 0.53 | <0.001* |
| Clinical Attachment Level (mm) | 0.00 ± 0.00 | 4.67 ± 0.86 | 3.46 ± 0.68 | <0.001* |
| PISA ($mm^2$) | 345.74 ± 210.27 | 1638.66 ± 569.46 | 330.43 ± 220.42 | <0.001* |
| Salivary MIP-1α (pg/mL) | 5.59 ± 1.41 | 9.30 ± 6.73 | 5.60 ± 1.59 | <0.001* |

A correlation study has been performed between clinical periodontal parameters and PISA and salivary MIP-1α levels in the various groups of patients (Table 3). In healthy subjects, the indices of positive correlation between PISA were high and statistically significant with both the gingival index and gingival bleeding index. Results indicated that,

at baseline, MIP-1α level in saliva of chronic periodontitis patients was positively correlated with PISA, probing pocket depth and CAL, and PISA was strongly positively correlated with gingival bleeding index, probing pocket depth and CAL. The post treatment evaluation revealed a high correlation of PISA and MIP-1α with gingival index, gingival bleeding index, probing pocket depth and clinical attachment level. These findings showed that there appears to be a high correlation between the amount of MIP-1α and PISA in the saliva and the severity of periodontal disease and inflammatory burden.

**Table 3. Correlation Analysis Between Clinical Parameters, PISA and Salivary MIP-1α**

| Group | Variable | Correlated Parameter | Spearman's rho | p-value |
|---|---|---|---|---|
| Group 1 | PISA | Gingival Index | 0.63 | 0.003* |
| | | Gingival Bleeding Index | 0.6 | 0.005* |
| Group 2 | Salivary MIP-1α | PISA | 0.67 | 0.001* |
| | | Probing Pocket Depth | 0.65 | 0.002* |
| | | Clinical Attachment Level | 0.67 | 0.001* |
| | PISA | Gingival Bleeding Index | 0.57 | 0.008* |
| | | Probing Pocket Depth | 0.81 | <0.001* |
| | | Clinical Attachment Level | 0.79 | <0.001* |
| Group 3 | Salivary MIP-1α | Probing Pocket Depth | 0.46 | 0.04* |
| | PISA | Gingival Bleeding Index | 0.75 | <0.001* |
| | | Probing Pocket Depth | 0.5 | 0.03* |
| | | Clinical Attachment Level | 0.51 | 0.02* |

Multiple linear regression analysis for the prediction of the clinical periodontal parameters and salivary MIP-1α and PISA levels are shown in Table 4. Both baseline and post-treatment chronic periodontitis groups showed clinical attachment level as a significant predictor of MIP-1α level of saliva. Gingival bleeding index and clinical attachment level were significant predictors for both groups in PISA. Both regression models showed good predictive values especially for PISA, which suggests that destruction of periodontal tissue and gingival inflammation have a significant impact on periodontal inflammatory burden and on the levels of salivary biomarkers.

**Table 4. Multiple Linear Regression Analysis for Prediction of Salivary MIP-1α and PISA**

| Dependent Variable | Group | Predictor Variable | β Coefficient | p-value | $R^2$ |
|---|---|---|---|---|---|
| Salivary MIP-1α | Group 2 | Clinical Attachment Level | 4.31 | 0.01* | 0.31 |
| Salivary MIP-1α | Group 3 | Clinical Attachment Level | 1.27 | 0.008* | 0.34 |
| PISA | Group 2 | Gingival Bleeding Index | 21.94 | <0.001* | 0.81 |
| | | Clinical Attachment Level | 411.58 | <0.001* | |
| PISA | Group 3 | Gingival Bleeding Index | 21.14 | 0.02* | 0.75 |
| | | Clinical Attachment Level | 18.39 | <0.001* | |

**Discussion**

Chronic Periodontitis is defined by chronic host inflammatory response to the effects of pathogenic biofilm, resulting in the destruction of the alveolar bone and connective tissue [15]. Chemokines are now known as important regulators of migration, activation and accumulation of leukocytes within the periodontal tissues [3,16] and are thus central to this inflammatory cascade. Of these mediators, Macrophage Inflammatory Protein-1 Alpha (MIP-1 alpha) has been determined to be one of the most important inflammatory biomarkers, owing to its strong chemotactic and osteoclast-activating effect [17-18].

A number of inflammatory cells, such as macrophages, lymphocytes, neutrophils, epithelial cells, and fibroblasts, release MIP-1α in response to bacterial lipopolysaccharides and pro-inflammatory cytokines [19]. It induces recruitment of monocytes, T lymphocytes, dendritic cells and osteoclast precursors via CCR1 and CCR5 receptors, which results in a further increase in periodontal inflammation and bone resorption [20]. In regard to the biologic function, the importance of studying salivary MIP-1α as a marker of periodontal inflammation was established in the current study.

In the present study, clinically these parameters were significantly more elevated in patients of chronic periodontitis than in the healthy ones showing higher inflammatory burden and

periodontal destruction in chronic periodontitis patient subjects. All plaque index, gingival index, gingival bleeding index, probing pocket depth and clinical attachment level were significantly high in chronic periodontitis patients at baseline ($p<0.001$). Emingil et al. (2005), Al-Sabbagh et al. (2011), Nisha et al. (2018), and Subramanyam et al. (2019) similarly showed significantly high periodontal inflammatory parameters levels in the patients with periodontitis when compared to the healthy patients [9,11.21-22].

Three months after the scaling and root planing (SRP) therapy all the clinical periodontal parameters showed significantly decreased values. Plaque index reduced from 1.60 ± 0.35 to 0.37 ± 0.22, while gingival index decreased from 1.77 ± 0.29 to 0.44 ± 0.24 following therapy. There is a good disruption of subgingival biofilm and inflammation reduction following non-surgical periodontal treatment (NSPT) that is reflected in this improvement. A similar decrease after SRP was reported by Syndergaard et al [13]. The beneficial effects of SRP are mainly due to reduction of microbial load and the creation of a root surface with biological factors which enhance periodontal healing [24].

The gingival bleeding index was significantly higher in the patients with chronic periodontitis (86.23 ± 12.75) than in the healthy subjects (19.49 ± 14.16) which indicated that chronic periodontitis (CP) patients had active gingival inflammatory state and vascular alterations related to periodontal disease. The presence of bleeding on probing is regarded as one of the best indicators of the presence of periodontal inflammation as bleeding is the result of infiltration of inflammatory cells through ulcerated sulcular epithelium and engorgement of vessels [25]. The gingival bleeding index (GBI) was significantly reduced to 16.00 ± 9.03 following SRP, indicating good resolution of gingival inflammation. The same conclusions were drawn by Subramanyam et al. [22].

The probing depths and clinical attachment levels are thought to be the most accurate assessments of periodontal destruction [26]. Chronic periodontitis patients had significantly higher probing pocket depth (4.22 ± 0.97 mm) and clinical attachment loss (4.67 ± 0.86 mm) than the healthy controls. This has been further reported by Nisha et al. [21]. Both parameters showed significant improvement after therapy and post-healing improvement in periodontal inflammation and gain in periodontal attachment. Nevertheless there were also some residual pockets after treatment, possibly because of irreversible periodontal attachment loss [15].

Considering the fact that it is an important issue of the present study, the evaluation of Periodontal Inflamed Surface Area as quantitative indicator of periodontal inflammatory burden is a key finding of the present study. The PISA was found to be higher in the chronic periodontitis patients (1638.66 ± 569.46 $mm^2$) when compared to healthy subjects (345.74 ± 210.27 $mm^2$), suggesting higher amount of inflamed periodontal surface area in the chronic periodontitis patients. Nesse et al. proposed PISA as an index with accuracy concerning the total amount of inflamed periodontal epithelial surface that is in contact with the systemic circulation [14]. The same significantly raised PISA scores were also found in other studies conducted by Park et al. [27].

After SRP, PISA was dramatically decreased to 330.43 ± 220.42 $mm^2$, which indicates a significant reduction in the periodontal inflammatory burden after healing. This decrease is indicative of improvements in inflamed pocket epithelium and post-periodontal-therapy bleeding tendencies. The probing depth, bleeding on probing and attachment loss score are all combined in one single numerical value in this form of PISA, thus giving a more representative indication of the inflammatory burden than when using each parameter individually [27].

Increased levels of salivary MIP-1α were the most important observation of the present study, with the chronic periodontitis patients (9.30±6.73 pg/mL) having higher levels than the healthy controls (5.59± 1.41 pg/mL) with a p value of 0.009. The findings of this study were very significant in support of the role of MIP-1α in periodontal inflammation and periodontal tissue destruction. Increase of salivary MIP-1α was also found by Al-Sabbagh M et al. and Nisha et al. in patients with periodontitis [11,21].

Increased production of chemokines in response to bacterial stimulation can explain this mechanism of elevated MIP-1α production in periodontitis by macrophages, epithelial cells, fibroblasts and osteoclasts [28]. Recruitment of the inflammatory cells is not the only action that brings about alveolar bone resorption in CCR1 mediated pathways; in this process, MIP-1α stimulates osteoclast differentiation as well [29]. This dual inflammatory and osteoclastogenic effect is associated to increase salivary MIP-1 α, which is strongly linked to the degree of periodontal destruction.

The present study also showed a significant decrease in salivary MIP-1α levels following non-surgical periodontal therapy and levels were close to that of healthy controls (5.60 ± 1.59 pg/mL). This decrease is associated with elimination of periodontal pathogens further ensuing reduction of inflammation and the inhibition of inflammation pathways mediated by chemokines. Subramanyam et al. [22] also noted similar decreases post SRP.

The present study also revealed that the levels of MIP-1α in saliva had significant positive correlations with probing pocket depth (PPD), clinical attachment level (CAL) and PISA scores in

chronic periodontitis patients. The results showed that MIP-1α level is a significant marker that is associated with the severity of periodontal destruction and inflammatory burden. The same correlations were found by Park et al. [27].

One interesting finding of the present study was that the Clinical attachemnet loss proved to be a significant factor in predicting the level of MIP-1α in saliva in regression analyses. The observation indicates that irreversible periodontitis had a significant effect on chemokine levels in saliva. Gingival bleeding index and clinical attachment level were also identified predictors of PISA and indicated the direct link between inflammation and periodontal tissue damage.

For the present study, diagnostic fluid of choice was saliva, due to its non-invasive, economical and easily reproducible nature to perform a periodontal biomarker assessment [10]. As the saliva represents pooled inflammatory changes throughout the oral cavity, it provides a better representation of overall periodontal disease activity than does gingival crevicular fluid [18].

De Lima et al. conducted a systematic review and meta-analysis to assess "the diagnostic accuracy of the various salivary biomarkers studied for differentiating periodontal health from disease" which found that MIP-1α had one of the highest accuracy in differentiating periodontal health from disease [12]. The present study provides another brick in the wall supporting this evidence by showing that not only are there higher levels of salivary MIP-1α in chronic periodontitis, but that there are significant decreases after periodontal therapy.

Based on the results of the present study, salivary MIP-1α levels are well related to periodontal inflammation, tissue loss, and periodontal therapy outcome. With a substantial decrease in MIP-1α concentration after scaling and root planing, it could be used as a valid non-invasive tool for assessing the activity of periodontal disease and therapeutic efficacy.

**Conclusion**

Macrophage Inflammatory Protein-1 Alpha plays a significant role in periodontal inflammation and tissue destruction. The high levels observed in saliva during chronic periodontitis and the decrease after non-surgical periodontal treatment suggest its excellent potential as a non-invasive periodontal disease activity indicator and an indicator of treatment responsiveness.

Salivary MIP-1α could then be used as a useful additional marker for screening for early diagnosis, for monitoring the progression of inflammation, and assessing the outcome of periodontal therapy.

**References:**


1. How KY, Song KP, Chan KG. Porphyromonas gingivalis: An Overview of Periodontopathic Pathogen below the Gum Line. Front Microbiol. 2016;7:53. doi: 10.3389/fmicb.2016.00053. PMID: 26903954; PMCID: PMC4746253.
2. Cekici A, Kantarci A, Hasturk H, Van Dyke TE. Inflammatory and immune pathways in the pathogenesis of periodontal disease. Periodontol 2000. 2014 Feb;64(1):57-80. doi: 10.1111/prd.12002. PMID: 24320956; PMCID: PMC4500791.
3. Moser B, Wolf M, Walz A, Loetscher P. Chemokines: multiple levels of leukocyte migration control☆. Trends in immunology. 2004;25(2):75-84.
4. Moser B, Loetscher P. Lymphocyte traffic control by chemokines. Nature immunology. 2001;2(2):123.
5. Olson TS, Ley K. Chemokines and chemokine receptors in leukocyte trafficking. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2002;283(1):R7-28.
6. Ryu OH, Choi SJ, Linares AM, Song IS, Kim YJ, Jang KT, Hart TC. Gingival epithelial cell expression of macrophage inflammatory protein-1α induced by interleukin-1β and lipopolysaccharide. Journal of periodontology. 2007;78(8):1627-34.
7. Gemmell E, Carter CL, Seymour GJ. Chemokines in human periodontal disease tissues. Clinical & Experimental Immunology. 2001;125(1):134-41.
8. Kabashima H, Yoneda M, Nagata K, Hirofuji T, Maeda K. The presence of chemokine (MCP-1, MIP-1α, MIP-1β, IP-10, RANTES)-positive cells and REFERENCES 114 chemokine receptor (CCR5, CXCR3)-positive cells in inflamed human gingival tissues. Cytokine. 2002;20(2):70-7.
9. Emingil G, Atilla G, Başkesen A, Berdeli A. Gingival crevicular fluid EMAP-II, MIP-1α and MIP-1β levels of patients with periodontal disease. Journal of clinical periodontology. 2005;32(8):880-5.
10. Jaedicke KM, Preshaw PM, Taylor JJ. Salivary cytokines as biomarkers of periodontal diseases. Periodontology 2000. 2016;70(1):164-83.
11. Al-Sabbagh M, Alladah A, Lin Y, Kryscio RJ, Thomas MV, Ebersole JL, Miller CS. Bone remodeling-associated salivary biomarker MIP-1α distinguishes periodontal disease from health. Journal of periodontal research. 2012;47(3):389-95.
12. de Lima CL, Acevedo AC, Grisi DC, Taba Jr M, Guerra E, De Luca Canto G. Host-derived salivary biomarkers in

diagnosing periodontal disease: systematic review and meta-analysis. Journal of clinical periodontology. 2016;43(6):492-502
13. Fokkema SJ, Loos BG, Van Der Velden U. Monocyte-derived RANTES is intrinsically elevated in periodontal disease while MCP-1 levels are related to inflammation and are inversely correlated with IL-12 levels. Clinical & Experimental Immunology. 2003;131(3):477-83.
14. Nesse W, Abbas F, Van Der Ploeg I, Spijkervet FK, Dijkstra PU, Vissink A. Periodontal inflamed surface area: quantifying inflammatory burden. Journal of clinical periodontology. 2008 Aug;35(8):668-73
15. Newmann MG, Takei HH, Klokkevold PR, Carranza FA. Carranza's Clinical Periodontology. 11th ed. South Asia edition. Saunders Elsevier; 2012; pg: 265
16. Zlotnik A, Yoshie O. Chemokines: a new classification system and their role in immunity. Immunity 2000;12:121–7.
17. Cook DN, Beck MA, Coffman TM, Kirby SL, Sheridan JF, Pragnell IB, et al. Requirement of MIP-1 α for an inflammatory response to viral infection. Science 1995;269:1583–5
18. Bhavsar I, Miller CS, Al-Sabbagh M. Macrophage inflammatory protein-1 Alpha (MIP-1 alpha)/CCL3: as a biomarker. General Methods in Biomarker Research and their Applications. 2014:1-22.
19. HJ, Lim SS. Production of macrophage inflammatory protein (MIP)-1α and MIP1β by human polymorphonuclear neutrophils stimulated with porphyromonas endodontalis lipopolysaccharide. Journal of endodontics. 2002;28(11):754-7.
20. Kaufmann A, Salentin R, Gemsa D, Sprenger H. Increase of CCR1 and CCR5 expression and enhanced functional response to MIP-1α during differentiation of human monocytes to macrophages. Journal of leukocyte biology. 2001;69(2):248-52.
21. Nisha KJ, Suresh A, Anilkumar A, Padmanabhan S. MIP-1α and MCP-1 as salivary biomarkers in periodontal disease. The Saudi dental journal. 2018 Oct 1;30(4):292-8
22. Subramanyam MB, Cheppali SR, Anumla D, Sighinam B, Prasuna E, Reddy RN. Estimation of macrophage inflammatory protein-1α (MIP-1 α) levels in serum and gingival crevicular fluid in periodontal health, disease, and after treatment A clinic-biochemical study. J NTR Univ Health Sci 2019;8:107-13
23. Syndergaard B. Salivary biomarkers associated with gingivitis and response to therapy. Journal of periodontology. August 2014;85(8): e295-e303.
24. Ishikawa I, Baehni P. Nonsurgical periodontal therapy–where do we stand now?. Periodontology 2000. 2004 Oct;36(1):9-13
25. Newbrun, E. Indices to Measure Gingival Bleeding. Journal of Periodontology. 1996; 67(6): 555–561. doi:10.1902/jop.1996.67.6.555.
26. Hefti A F. Periodontal Probing.Crit Rev Oral Biol Med. 1997; 8(3):336-356.
27. Park SY, Ahn S, Lee JT, Yun PY, Lee YJ, Lee JY, Song YW, Chang YS, Lee HJ. Periodontal inflamed surface area as a novel numerical variable describing periodontal conditions. Journal of periodontal & implant science. 2017;47(5):328-38.
28. Morandini AC, Sipert CR, Gasparoto TH, Greghi SL, Passanezi E, Rezende ML, Sant'ana AP, Campanelli AP, Garlet GP, Santos CF. Differential Production of Macrophage Inflammatory Protein-1α, Stromal-Derived Factor-1, and IL-6 by Human Cultured Periodontal Ligament and Gingival Fibroblasts Challenged With Lipopolysaccharide From P. gingivalis. Journal of periodontology. 2010;81(2):310-7
29. Choi SJ, Cruz JC, Craig F, Chung H, Devlin RD, Roodman GD, et al. Macrophage inflammatory protein 1-alpha is a potential osteoclast stimulatory factor in multiple myeloma. Blood 2000;96:671–5.