Content available at: https://www.ipinnovative.com/open-access-journals

Journal of Advances in Oral Health

Journal homepage: https://jaoh.in/

Original Research Article

Inflammatory burden and periodontal tissue destruction: A biological perspective

Arunima Bansal[1], Sachit Anand Arora[1], Gunjan Gupta[1*], Shivesh Mishra[1], Priyanka Tandon[1]

[1]ITS Dental College Hospital & Research Centre, Uttar Pradesh, India

Abstract

Aim: The present systematic review is undertaken to critically assess and collate available evidence on pro-inflammatory markers like Macrophage inflammatory protein-1α (MIP-1α), interleukin-1β (IL-1β), and matrix metalloproteinase-8 (MMP-8) as chronic periodontitis risk factors with a focus on their diagnostic, prognostic, and therapeutic implications.

Materials and Methods: Electronic databases including PubMed, Cochrane, and Google Scholar were searched for studies published within the 10 years. Inclusion criteria comprised case-control studies, randomized controlled trials, and cohort studies focused on pro-inflammatory markers and chronic periodontitis. Exclusion criteria included non-English articles, case series, and reports with incomplete data. 19 clinical studies were included after screening and quality assessment.

Results: A total of 1370 studies were initially identified, of which 19 studies fulfilled the inclusion criteria. Elevated levels of pro-inflammatory markers were consistently observed in patients with chronic periodontitis compared to healthy controls while therapeutic interventions and adjunctive treatments led to significant reductions. However, there exists variation in study methodologies and reporting standards, and no single biomarker has yet achieved universal acceptance for routine clinical use. The reviewed studies highlighted the potential utility of these markers for early diagnosis, risk prediction, and monitoring response to treatment.

Conclusion: Proinflammatory markers have considerable diagnostic and prognostic values in periodontal disease. However, future standardized longitudinal studies are needed to establish their clinical validity for routine chairside diagnosis.

Keywords: Pro-inflammatory cytokines, Biomarkers, Chronic periodontitis, Gingival crevicular fluid, MIP-1α, IL-1β, MMP-8.

Received: 14-04-2026 **Accepted:** 09-05-2026 **Available Online:** 23-05-2026

1. Introduction

Modern Science is testimony to the fact that biomarkers both Systemic and Oral as assessed and analyzed for early periodontal diagnosis, verify therapeutic efficacies of Periodontal therapies, and so predict future periodontal disease progression. There are broadly two rich sources of proteins, metabolites and microbiome found abundant. They are oral fluids such as Saliva, Gingival Crevicular fluid (GCF) and parts of blood such as serum and plasma.

Saliva is a serumal fluid filtered by Salivary glands and possess more than 60% of analytes. It is easily assessable, non- invasive and can be easily collected. On the other hand, GCF is site specific but tedious to collect. Both oral fluids have gained immense prominence as a source for biomarkers whether inflammatory, host derived or markers of Connective Tissue destruction.

Biomarkers are analyzed by various methods like Blood, Saliva and Gingival Crevicular Fluid (GCF) through Enzyme-linked Immunosorbent assay (ELISA), RT-PCR, Spectrophotometry, Immunofluorescence and MALDI TOF MS (Modern matrix assisted laser desorption ionization- time of flight mass spectrometry). Pro- inflammatory cytokines are the first to appear and address the antigen response by the hosts. Cytokines which were previously called Leukotrienes are an integral part of Immune response.

Macrophages along with other chronic inflammatory cells play a pivotal role. They are modulators and communicators of response to antigen attack and abuse. Many macrophages secreted or activated molecules have been studied as potential biomarker. The latest biomarker to be analyzed for pro inflammation is Macrophage inflammatory protein-1alpha (MIP- 1α), which is secreted by Macrophages.

Pro-inflammatory markers such as macrophage inflammatory protein-1alpha (MIP-1α), interleukin-1beta (IL-1β), interleukin-6 (IL-6) and matrix metalloproteinase-8 (MMP-8) have been identified as clinically acceptable indicators for diagnosing periodontal disease.[1]

A notable biomarker MIP-1alpha is a chemotactic chemokine produced by diverse cell types like macrophages, fibroblasts, epithelial cells, and endothelial cells. It serves multiple biological roles, including the recruitment of inflammatory cells, facilitation of wound healing, suppression of stem cells, and sustenance of effector immune responses.[2]

Advancements in research have pinpoint numerous salivary biomarkers associated with distinct biological phases of periodontal disease, including inflammation, collagen degradation, and bone remodeling. The vast array of evidence supporting the utilization of salivary biomarkers, along with their practical application in diagnosing and monitoring

*Corresponding author: Gunjan Gupta
Email: drgunjangupta22@gmail.com

https://doi.org/10.18231/j.jaoh.48716.1779531113

periodontal disease, underscores the necessity for a current systematic review to consolidate findings. Moreover, periodontitis has systemic implications for cardiovascular disease, diabetes, and adverse pregnancy outcomes. The elevated systemic levels of inflammatory biomarkers in patients with periodontitis can therefore contribute to the chronic systemic inflammatory burden associated with these comorbidities.

The need is to do a Systematic review of past 10 years of articles, scientific papers and tabloids pertaining to biomarkers as a resource of diagnosis. Furthermore, it is crucial to conduct a comprehensive review of published evidence to thoroughly confirm the diagnostic utility of salivary biomarkers before efficiently integrating saliva as a dependable and accurate diagnostic medium for periodontal disease. This Systematic review explicitly elucidates the role of pro- inflammatory cytokines in the periodontal disease.

2. Materials and Methods

This review was a systematic review that followed the guidelines for the synthesis of clinical research evidence in relation to pro-inflammatory biomarkers and their role as risk factors in chronic periodontitis. The methodology was designed based on the PICO framework for a focused, evidence-based approach. Research was carried out by hand searching and electronic searching of database records PubMed, Cochrane, and Google Scholar of past 10 years. The flow of study selection is shown schematically in Figure 1.

Inclusion Criteria included case control studies, randomized controlled trials, cohort studies, sufficient details reported on sample type, description of the assays used to detect cytokines, the results of salivary cytokines were descripted, only papers with a focus on oncological, oral, dental, or infectious diseases were included and both genders were included. The exclusion criteria included meta-analysis, case series, case reports, animal studies and in vitro studies, studies published in language other than English, systematic reviews, studies with only abstract available, unpublished data, comment articles and articles with incomplete data/Imprecise methodology.

2.1. Data mining techniques

Data extraction was performed using a standardized, piloted template. The following information was carefully captured for each included study: Author(s), publication year, country of origin, study design and duration, population characteristics include number of participants, inclusion/exclusion criteria, and demographic details. Type of biological sample was also seen. Assays applied for biomarker quantification include ELISA, mass spectrometry, immunoassays, among others. List of pro-inflammatory biomarkers analyzed (such as MIP-1α, IL-1β, IL-6, MMP-8, TNF-α, etc.).

The emphasis of the review process was based on vital factors, including the sufficiency of control groups, justification and rationalization of sample size, clarity and transparency in methods reporting, especially in the collection and analysis of biological samples, and appropriateness and strength of statistical methods used. Besides, the review also considered potential sources of bias, such as selection, measurement, and reporting biases. Only those studies assessed to have moderate or high methodological quality based on these comprehensive criteria were retained for synthesis. This phase excluded studies with significant methodological weaknesses or those lacking clarity to ensure that conclusions from the review were reliable and scientifically valid.

After quality assessment, data from the eligible studies were synthesized by using a qualitative narrative approach. This approach was warranted because of the heterogeneity in the biological sample source, combination of biomarkers evaluated, different assay platforms, population demographics, and types of periodontal interventions evaluated. The effect size and direction of associations between specific pro-inflammatory biomarkers and periodontitis outcomes were summarized and, where possible, tabulated. Synthesis focused on key outcomes that included diagnostic accuracy and predictive value of studied biomarkers for chronic periodontitis, the relationship of individual biomarkers with disease presence, severity, and progression, and changes in the levels of these markers resulting from various periodontal treatments. Furthermore, the review sought single or combinations of markers with strong potential for routine clinical diagnostic use. Recurring patterns and trends had been underlined during synthesis, while instances of conflicting evidence were interpreted in light of differences in study populations, methodological limitations, variability in the assays used, or short follow-up periods, thus providing a balanced and comprehensive overview of the available literature.

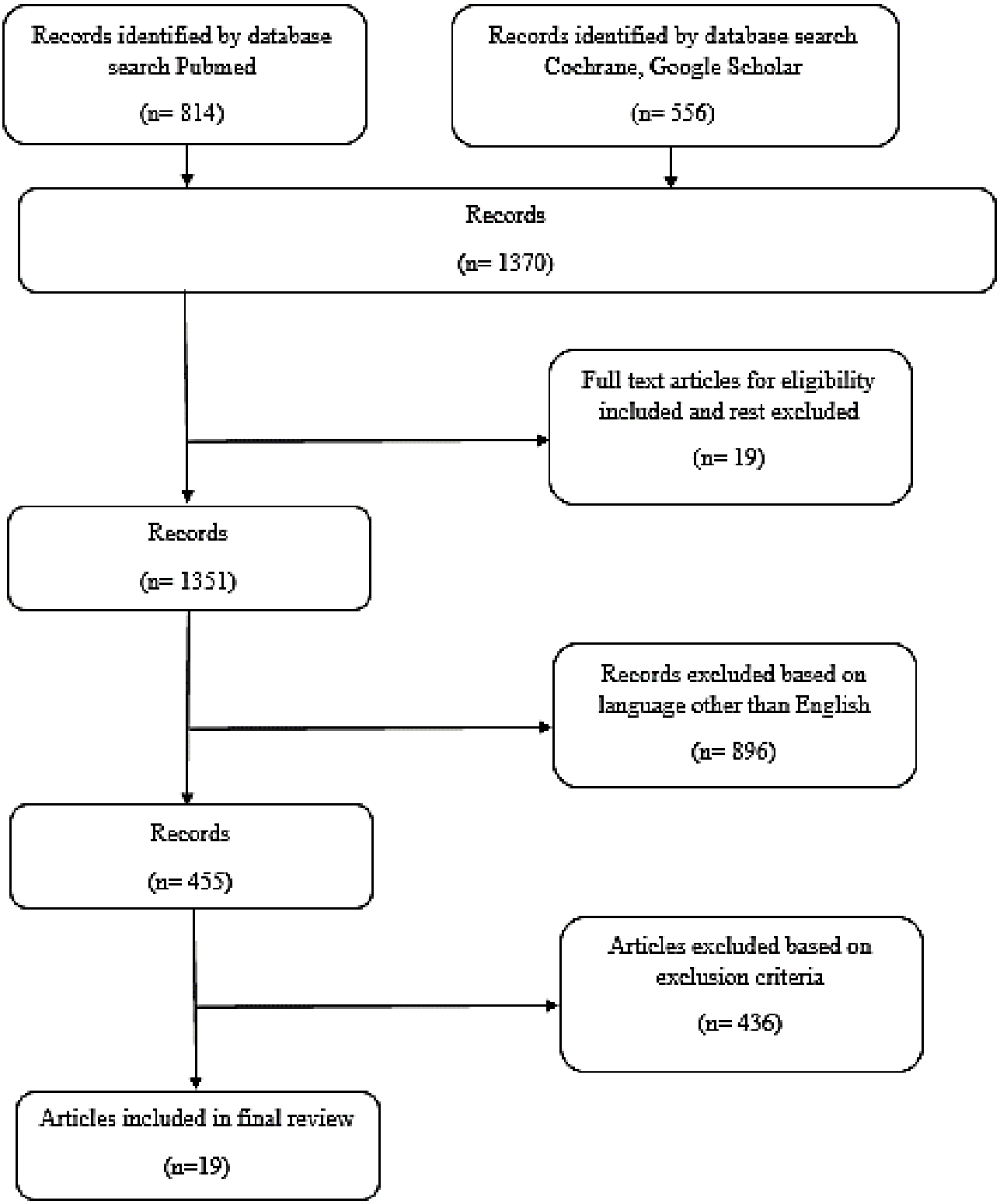

Figure 1: *Methodology*

Table 1. *Result*

S No.	Author and publication year	Number of subjects	Study design	Study duration	Biochemical parameters	Results	Country
1.	Eldessouky et al 2024[1]	20	Twenty elderly women with chronic periodontitis were split evenly into two groups by random assignment. Patients in group II (the research group) were given soft gelatin capsules containing PUFAs to be consumed directly once daily for 12 months, as opposed to group I (the control group), who received soft gelatin capsules containing some olive oil (placebo).	12 months	AST and osteocalcin	Significant improvements in clinical indicators and a notable decrease in AST levels within the GCF were observed.	Saudi Arabia
2.	Keskin et al 2023	44	Baseline periapical exudate samples were obtained, and the patients were assigned to either control or intracanal cryotherapy group according to the final irrigation with distilled water either at room temperature or 2.5°C.	6 months	IL-8, TNF-α, PGE2 and MMP-8 levels	There was a significant decrease in IL-8, TNF-α, PGE2 and MMP-8 levels.	Turkey
3.	Moore et al 2023	76	76 patients with Stages III-IV, Grade B periodontitis were assigned to three groups: interproximal brush (IB), IB with tracking device (TD), or oral irrigator (OI).	6 weeks	IL-1β	Results showed improvements in periodontal parameters and reduction in inflammatory markers across all groups.	USA
4.	Pilloni et al 2023	8	Eight patients 24 h post-surgery after HA application (HA group) and compared with those obtained from the same patients without HA application (no treatment; NT group).		MMP-1 protein, and TIMP1 gene expression	MMP-1 protein, and TIMP1 gene expression were significantly upregulated in the HA compared to the NT group.	Italy
5.	Aimetti et al 2023	44	Sites were randomly treated with subgingival instrumentation with or without topic DOX application.	2 weeks	(IL)-1β, matrix-metalloproteinases (MMP)-8 and MMP-9.	The total amount of interleukin (IL)-1β, matrix-metalloproteinases (MMP)-8 and MMP-9 in the GCF significantly decreased in the test group at T1, with relevant differences compared to controls.	Italy
6.	Persson et al 2023	30	Participating individuals with T2D were randomly assigned to a test (OBND) (n=14), or control group (n=16).	4 weeks	of IFNγ, Eotaxin IL-9, IP10, IL17a, MCP-1	Results showed reduction of serum levels of IFNγ, Eotaxin IL-9, IP10, IL17a and MCP-1, compared to the control diet.	USA
7.	Elsadek et al 2022	60	Participants were randomized in two groups: Group A – SRP + PDT (test group) and Group B – SRP alone.	6 months	(IL)-1β and IL-6	Reduction in the IL-6 was maintained until 6 months of re-evaluation.	Saudi Arabia
8.	Alkimavičienė et al 2022	46	Forty-six patients diagnosed with periodontitis were randomised into 2 groups: 23 patients in the MINST group and 23 patients in the MINST + PACNs group received the intended treatment.	8 weeks	MMP-3	Additional use of PACNs improved MMP-3 concentration in saliva more than MINST alone.	Lithuania

Table 1. *Result (continued)*

S No.	Author and publication year	Number of subjects	Study design	Study duration	Biochemical parameters	Results	Country
9.	Bian et al 2021	72	The patients were randomly divided into four groups using a computer-generated table: root planing and periodontal curettage combined group (n = 18), root planning group (n = 18), periodontal curettage group (n = 18) and cleansing group (n = 18).	12 months	TNF- α and hypersensitive C-reactive protein [hs-CRP]	Levels of TNF- α and hs-CRP in the four groups decreased significantly.	China
10.	Rabelo et al 2020	60	15 patients with type 2 diabetics with generalized periodontitis, 15 patients with pre-diabetics with GP, 15 patients with normoglycemic subjects with GP, 15 patients with healthy controls.	1 month	IL-1B and IFN-γ	A significant reduction in GCF levels of several cytokines like IL-1B and IFN-γ were observed.	Brazil
11.	Martínez-Villa et al 2020	15	A total of 15 patients were finally included, with analysis of 30 histological specimens and 30 GCF samples.	8 weeks	IL-1β, IL-6, IL-10 and IL-17a	Higher concentrations of IL-1β and IL-6 in GCF was seen.	Spain
12.	Chen et al 2020	19	19 patients with at least one periodontitis-involved tooth in three quadrants received NSPT, and three protocols of LED light irradiation, including LED light irradiation from initial clinical assessment (T0) until the completion of scaling and root planning (T1) (LED01),	2-3 months	IL-1b and MMP-8	IL-1b and MMP-8 were reduced in all groups.	Taiwan
13.	Kasai et al 2020	13	Clinical variables were measured at four time points during initial periodontal treatment: before treatment (baseline), after supragingival scaling, after occlusal adjustment, and after scaling and root planing (SRP)	-	(IL)-10, IL-7, IL-11, and IL-12p40	Baseline interleukin (IL)-10 level in GCF was significantly higher around teeth that showed substantial improvement in periodontal epithelial surface area (PESA) after SRP than around teeth without PESA improvement. IL-3 and IL-16 levels in GCF at baseline were significantly higher around teeth with a periodontal inflamed surface area (PISA) of 0 mm2 after SRP than around teeth without PISA improvement. In addition, baseline IL-7, IL-11, and IL-12p40 levels in GCF were significantly lower around teeth with decreased mobility after occlusal adjustment than around teeth without decreased mobility.	Tokyo
14.	Chiang et al 2020	22	22 patients with 30 control teeth and 35 PTT-treated teeth were examined.	6 months	IL-1b and MMP-8	IL-1b and MMP-8 were significantly lower.	Taiwan

Table 1. *Result (continued)*

S No.	Author and publication year	Number of subjects	Study design	Study duration	Biochemical parameters	Results	Country
15.	Äyräväinen L et al 2018	81	Fifty-three early untreated RA (ERA) and 28 chronic RA (CRA) patients	12 months	MMP-8, TIMP-1 and IL-6	Concentrations of MMP-8 and of IL-6 in serum were elevated	Finland
16.	Bostanci et al 2017	50	15 FMF patients with generalized chronic periodontitis (FMF-CP), 15 systemically healthy patients with generalized chronic periodontitis (CP), ten systemically and periodontal healthy controls (HC), and ten periodontally healthy FMF patients (FMFHC) were enrolled in the study.	6 weeks	IL-1β, IL-1ra, and IL-10	GCF IL-1β and GCF IL-1ra levels were decreased in FMF-CP group. GCF IL-10 levels were increased in FMF-CP group compared to other groups.	Turkey
17.	Balci Yuce H et al 2017	53	17 CP patients with RA (RA + CP), 18 systemically healthy CP patients (CP), and 18 healthy controls (C) were included		Serum RANKL and GCF TNF-α	Serum RANKL and GCF TNF-α levels in RA patients decreased after periodontal treatment	TURKEY
18.	Acharya et al 2015	45	Forty-five subjects were divided into three groups comprising 15 subjects each as Group 1(healthy controls), Group 2 (CPD patients), and Group 3 (T2DM patients with CPD).	6 months	IL-10	IL-10 levels were elevated.	INDIA
19.	Ozgören et al 2014	32	32 subjects with chronic periodontitis were randomized into two groups: 1) phase I periodontal treatment + NSAID and 2) phase I periodontal treatment + placebo.	30 days	MMP-8 and TNF-α	Post treatment MMP-8 level in group 1 was statistically significant higher than the placebo group	TURKEY

3. Results

A total of 1370 articles were identified based on PICO including patients showing effects of Pro- inflammatory markers as a risk factor in Chronic Periodontitis. The database search was done which yielded 1351 records with full text articles, 896 records were excluded based on language other than English. From the basis of exclusion and inclusion criteria, records were removed. The total studies that were systematically reviewed came out to be 19 (Table 1).

All the selected investigations together assessed host-derived pro-inflammatory markers in GCF, saliva, and sometimes serum, with particular attention to molecules such as macrophage inflammatory protein-1α (MIP-1α), interleukin-1β (IL-1β), interleukin-6 (IL-6), matrix metalloproteinase-8 (MMP-8), tumor necrosis factor-alpha (TNF-α), prostaglandin E2 (PGE2), myeloperoxidase, and C-reactive protein (CRP).

In fact, the findings were consistent in that all studies found higher concentrations of these pro-inflammatory biomarkers in chronic periodontitis individuals compared with healthy controls. Importantly, IL-1β, IL-6, and MMP-8 levels were increased in both saliva and GCF and strongly correlated with the presence and severity of periodontal inflammation. TNF-α, PGE2, and CRP also showed a clear positive association with disease status, further reinforcing their role as proxies of local and systemic inflammation. Additionally, the levels of CRP and hs-CRP assessed in serum were higher in patients with periodontitis, reflecting the systemic inflammatory burden associated with oral disease.

Overall, therapeutic interventions, namely nonsurgical periodontal treatments in the forms of scaling and root planning with and without adjunctive therapies, and surgical therapies significantly reduced IL-6, TNF-α, CRP, and MMP-8 biofluid levels for up to six months following the intervention. Additive improvements in biomarkers were also noted in several studies when combination therapies were employed. Panels combining IL-1β, IL-6, and MMP-8 as a combined diagnostic tool yielded high accuracy for distinguishing chronic periodontitis from healthy states; however, their diagnostic performance varied because of population and laboratory method differences.

A subset of studies further investigated the mechanistic depth of inflammation, such as changes in LPS, gut microbiota profiles, and adipokines, as further evidence of the systemic effects of periodontal inflammation. The robust and sustained association of these pro-inflammatory markers across the body of evidence with not only the presence but also the progression and severity of chronic periodontitis was clear. Collectively, these findings underscore both the biological importance and the clinical promise of systemic and oral fluid biomarkers in enhancing diagnosis, monitoring, and overall understanding of periodontitis as part of both oral and systemic health.

4. Discussion

Periodontitis affects a subset of the population, and its progression may be continuous or episodic, necessitating effective diagnostic tools. However, current markers face significant challenges, and no gold standard exists for diagnosing active periodontal disease. Despite numerous proposed biomarkers, none are commercially available. Chairside tests using saliva or finger stick blood could potentially assess an individual's disease risk, and routine blood tests might help diagnose and monitor periodontitis if reliable systemic biomarkers are identified. Before using any test, its impact on treatment planning must be considered. Systemic periodontal diagnostic tests are in early development, requiring further validation to ensure they become a valuable, cost-effective part of clinical practice. Stathopoulou et al reviewed potential blood and saliva biomarkers for diagnosing and monitoring periodontitis.[13]

In a study conducted by Oh H et al, it is seen that IL-1β levels are uplifted in sites of periodontal disease and reduce following periodontal treatment.[14] Supporting these findings, Nazar Majeed et al stated in the review that IL-1β is a reliable biomarker for accurately indicating the continuation of periodontitis.[15] Elsadek et al substantiated reduction in the IL-6 was maintained till 6 months of re-evaluation.[16] Persson et al and Bian et al too noticed a decrease in cytokines.[17,18]

MCP-1 is an essential cytokine responsible for the recruitment of inflammatory cells, playing a significant role in inflicting damage to the periodontium. Previous studies have shown that MCP-1 & 4 levels decrease after therapy. Therefore, they are to be considered a likely biomarker for disease strength. Acharya et al and Alkimavičienė et al conducted a study where a positive correlation was seen between cytokines and periodontitis.[19–20]

In a recent meta-analysis, Stadler et al. observed the levels of chemokines between healthy and chronic periodontitis patients. The study found contrast in inflammatory markers between periodontal health and disease.[21] Similar results have been shown in the study by Chen et al where IL-1b and MMP-8 levels were remarkably lower.[22] Eldessouky et al and Bostanci et al also showed notable improvements in parameters of the sample.[23–24] The results of Chiang et al were comparable showing decrease in IL-1b and MMP-8.[25]

Martínez-Villa et al concluded in his study that the levels of GCF cytokines did not tally with the comparison group and hence further studies were needed for evidence.[26] Increased expression of these mediators in gingival crevicular fluid (GCF), serum, and saliva among patients with chronic periodontitis underscores their value as both local and systemic biomarkers. Elevated IL-1β and TNF-α levels have been closely associated with enhanced collagen breakdown, osteoclastic bone resorption, and reduced tissue repair capacity. This aligns with the understanding that periodontal breakdown results from a dysregulated host immune response to microbial challenge rather than direct bacterial effects alone.

Additionally, the reviewed studies suggest that genetic polymorphisms affecting the production of key cytokines may predispose individuals to heightened inflammatory responses, thereby exacerbating periodontal destruction. Environmental and behavioral risk factors such as smoking, diabetes mellitus, and stress appear to amplify these inflammatory pathways, indicating a multifactorial interrelationship in

disease expression.

Emerging evidence also highlights the systemic implications of persistent periodontal inflammation, with elevated cytokine levels potentially contributing to the progression of atherosclerosis, diabetes, and other inflammatory disorders. This reinforces the importance of understanding and managing inflammation not only for periodontal health but also for overall systemic well-being. Future longitudinal studies and meta-analyses employing standardized markers of inflammation are needed to clarify the temporal relationship between inflammatory mediator upregulation and periodontal attachment loss. Moreover, interventions targeting pro-inflammatory pathways, including the use of host-modulatory therapies, could represent a promising adjunctive approach in the management of chronic periodontitis.

The examination of MMP-8 in GCF has been a specific biomarker for quick chair-side detection, aiding in the diagnosis of disease.[27] It may also serve as a valuable tool for monitoring the progression of disease. Additional enzymes examined in the GCF include myeloperoxidase, which may also serve as markers for the distinguishing and monitoring the advancement of periodontal disease.

In a study conducted by Moore et al, it is seen that Seventy-six patients with Stage III-IV, Grade B periodontitis were evaluated using different home oral hygiene methods. The results indicated improvements in periodontal parameters and reductions in inflammatory markers across all groups.[5] Similarly, a study done by Keskin et al showed the correlation between periodontal pain and IL-1β and PGE2 levels suggesting that these biomarkers have predictive value.[4] These results were comparable with the study conducted by Kasai et al which replicated that the levels of some cytokines in GCF like IL-3 and IL- 16 are connected to early periodontal therapy.[28]

A meta-analysis done by Blanco- Pinto evaluated the diagnostic accuracy of combined markers for detecting periodontitis in systemically healthy individuals. Six salivary combinations, including IL-1β, IL-6, and MMP-8, showed high accuracy.[6] Environmental and behavioral factors, including smoking, stress, and diet, further influence the inflammatory profile. Tobacco use enhances the release of pro-inflammatory cytokines, impairs neutrophil function, and reduces gingival blood flow, thereby worsening periodontal outcomes. Psychological stress, through cortisol-mediated immune dysregulation, enhances susceptibility to inflammation.

Arroyo et al aimed to identify salivary protein-based biomarkers for major periodontal diseases. Twelve biomarkers, including IL-1β, ICTP, and PGE2, demonstrated high applicability, indicating their potential for clinical use in distinguishing periodontal diseases from gingivitis and healthy conditions.[7] Oxidative stress represents another avenue linking pro-inflammatory factors with disease progression. Reactive oxygen species (ROS), generated by activated neutrophils and other immune cells during host defense, participate in bacterial killing but also inflict collateral damage on periodontal tissues. The imbalance between oxidants and antioxidant defenses accentuates lipid peroxidation, DNA damage, and protein oxidation, reinforcing the inflammatory cascade. Current evidence suggests that antioxidant therapy, dietary modulation, and improved redox balance might serve as adjunctive approaches to mitigate tissue destruction in periodontitis.

Inflammation plays a crucial role in tumorigenesis, making the measurement of pro-inflammatory cytokines attractive for predicting local malignant transformation and monitoring treatment.

Tumor cells release cytokines which effect cells and induce cancer-related inflammation. IL-6, in particular, can cause acute inflammation with TNF-α and IL-1, inhibit dendritic cell differentiation, and promote metastasis. Studies have identified IL-6 as a prognostic marker for head and neck cancer, squamous cell carcinoma, and melanoma.[23]

Hence, it is evident that data from various studies demonstrates the beneficial role of pro-inflammatory markers as a significant risk factor in chronic periodontitis. These markers can positively influence treatment outcomes when used as a diagnostic tool alongside conventional treatment method.

5. Conclusion

This systematic review aims to collect and analyze all the data available in the scientific literature pertaining to the effect of pro- inflammatory markers and its role on periodontal health and included a total of 16 studies addressing this research question. These markers pose as a crucial diagnostic tool in identifying the presence and severity of a disease in the periodontium and even other systemic conditions.[1] An overwhelming majority of studies included in this systematic review established a correlation between pro- inflammatory markers and periodontium, further evidence is required with long term follow up.

Biomarkers sourced from GCF are a valuable diagnostic tool with an ease in collection of specimens by various methods. They assist in improving treatment outcomes and tell us the past, present and future risks of periodontal disease following both surgical and non-surgical periodontal therapy. Periodontal pathogens trigger the cascade of inflammation via pathogen-associated molecular patterns that stimulate host toll-like receptors. This, in turn, leads to the release of pro-inflammatory cytokines responsible for connective tissue destruction, resorption of alveolar bone, and disturbance in tissue homeostasis. Thus, an imbalance between pro- and anti-inflammatory responses, rather than simply microbial presence, forms a central mechanism in chronic periodontitis pathophysiology.

The review also underlines that genetic predisposition and systemic factors, like diabetes mellitus, obesity, and cardiovascular diseases, can enhance pro-inflammatory signaling and, thus, aggravate periodontal destruction. This reciprocal relation between systemic inflammation and periodontal disease supports the notion of periodontitis as not just a localized oral condition but, rather, as part of a wider systemic inflammatory network. Raised systemic biomarkers, including CRP and IL-6, point to a linkage between chronic

periodontitis and increased systemic inflammatory burden, with a possible contribution to systemic disease risk.

These findings have great therapeutic implications. Traditional approaches that address only mechanical plaque control, though important, may be insufficient to manage the underlying inflammatory burden. New therapies targeting host response modulation-the use of anti-cytokine agents, sub-antimicrobial dose doxycycline, and antioxidants-show promise in controlling inflammation and preventing further tissue destruction. Such host-modulation strategies, when combined with conventional periodontal therapy, could result in improved long-term outcomes by restoring the balance between pro- and anti-inflammatory mediators.

Limitations identified across the studies include heterogeneity of assay methods, variability in cytokine quantification, and differences in study design-all factors that make it difficult to standardize diagnostic thresholds for pro-inflammatory markers. Given these limitations, the cumulative evidence from observational and interventional studies strongly supports the role of pro-inflammatory factors as both mediators and potential predictors of chronic periodontitis. It is explicitly evident that no single marker has met all the criteria required to assess the clinical state of the periodontium. Currently, various efforts are underway to develop an idealistic test, but its practical use as a chairside diagnostic tool remains indecisive. Consequently, the primary goal of periodontal research is to develop a broad spectrum of markers.

While a majority of the studies have established the positive impact biomarkers and its influence on periodontal health, a few studies failed to establish a clear association between them and thus a wider acceptance of this concept is yet to be seen. This warrants further extensive research into the matter that has the potential to validate these claims about the positive role of markers in maintaining periodontal health. This would be a valuable and highly appreciated treatment modality in treating periodontal disease that would benefit patients with periodontal disease. Further studies are necessitated to extrapolate the outcomes of gingival, salivary and blood biomarkers.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Cafiero C, Spagnuolo G, Marenzi G, Martuscelli R, Colamaio M, Leuci S. et al. Predictive Periodontitis: The Most Promising Salivary Biomarkers for Early Diagnosis of Periodontitis. *J Clin Med*. 2021;10(7):1488. https://doi.org/10.3390/jcm10071488
2. Bhavsar I, Miller CS, Al-Sabbagh M. Macrophage Inflammatory Protein-1 Alpha (MIP-1 alpha)/CCL3: As a Biomarker. *Gen Meth Biomar Res Appli*. 2015:223–49. https://doi.org/10.1007/978-94-007-7696-8_27
3. Zalewska EA, Ławicka R, Grygorczuk P, Nowosielska M, Kicman A, Ławicki S. Importance of Metalloproteinase 8 (MMP-8) in the Diagnosis of Periodontitis. *Int J Mol Sci*. 2024;25(5):2721. https://doi.org/10.3390/ijms25052721
4. Keskin C, Aksoy A, Kalyoncuoğlu E, Keleş A, İlik AA, Kömeç O. Effect of intracanal cryotherapy on the inflammatory cytokine, proteolytic enzyme levels and post-operative pain in teeth with asymptomatic apical periodontitis: A randomized clinical trial. *Int Endod J*. 2023;56(8):932-42. https://doi.org/10.1111/iej.13937
5. Moore GC, Smith KT, Christiansen MM, Anderson L, Moravec LJ, Okano DK. et al. Effect of interproximal home oral hygiene on clinical parameters and inflammatory biomarkers in patients receiving periodontal maintenance. *J Periodontol*. 2023;94(7):848-57.
6. Blanco-Pintos T, Regueira-Iglesias A, Seijo-Porto I, Balsa-Castro C, Castelo-Baz P, Nibali L. et al. Accuracy of periodontitis diagnosis obtained using multiple molecular biomarkers in oral fluids: A systematic review and meta-analysis. *J Clin Periodontol*. 2023;50(11):1420-43, https://doi.org/10.1111/jcpe.13854
7. Arroyo E, Oliveira-Alves MG, Chamorro-Petronacci CM, Marichalar-Mendia X, Bravo-López SB, Blanco-Carrión J. et al. Protein-based salivary biomarkers for the diagnosis of periodontal diseases: Systematic review and meta-analysis. *J Taibah Univ Med Sci*. 2022;18(4):737-47. https://doi.org/10.1016/j.jtumed.2022.12.004
8. Kc S, Wang XZ, Gallagher JE. Diagnostic sensitivity and specificity of host-derived salivary biomarkers in periodontal disease amongst adults: Systematic review. *J Clin Periodontol*. 2020;47(3):289-308. https://doi.org/10.1111/jcpe.13218
9. Miler E, Stapleton PP, Mapplebeck S, Mackerness C, Gayford D, Aung T. et al. Circulating interleukin-6 as a biomarker in a randomized controlled trial of modified-release prednisone vs immediate-release prednisolone, in newly diagnosed patients with giant cell arteritis. *Int J Rheum Dis*. 2019;22(10):1900-4. https://doi.org/10.1111/1756-185X.13702
10. Zhang L, Li X, Yan H, Huang L. Salivary matrix metalloproteinase (MMP)-8 as a biomarker for periodontitis: A PRISMA-compliant systematic review and meta-analysis. *Med (Baltimore)*. 2018;97(3):e9642. https://doi.org/10.1097/MD.0000000000009642
11. Nisha KJ, Suresh A, Anilkumar A, Padmanabhan S. MIP-1α and MCP-1 as salivary biomarkers in periodontal disease. *Saudi Dent J*. 2018;30(4):292-8.
12. de Lima CL, Acevedo AC, Grisi DC, Taba M, Guerra E, De Luca Canto G. Host-derived salivary biomarkers in diagnosing periodontal disease: systematic review and meta-analysis. *J Clin Periodontol*. 2016;43(6):492-502. https://doi.org/10.1111/jcpe.12538
13. Panagiota S, Nurcan B, Denis K. Systemic Biomarkers for Periodontitis. *Curr Oral Health Reports*. 2015;2. https://doi.org/10.1007/s40496-015-0072-9
14. Oh H, Hirano J, Takai H, Ogata Y. Effects of initial periodontal therapy on interleukin-1β level in gingival crevicular fluid and clinical periodontal parameters. *J Oral Sci*. 2015;57(2):67-71. https://doi.org/10.2334/josnusd.57.67
15. Nazar Majeed Z, Philip K, Alabsi AM, Pushparajan S, Swaminathan D. Identification of Gingival Crevicular Fluid Sampling, Analytical Methods, and Oral Biomarkers for the Diagnosis and Monitoring of Periodontal Diseases: A Systematic Review. *Dis Markers*. 2016;2016:1804727. https://doi.org/10.1155/2016/1804727
16. Elsadek MF, Farahat MF. Effectiveness of photodynamic therapy as an adjunct to periodontal scaling for treating periodontitis in geriatric patients. *Eur Rev Med Pharmacol Sci*. 2022;26(6):1832-8. https://doi.org/10.26355/eurrev_202203_28327
17. Persson GR, Widén C, Wohlfart B, Sjöberg K, Steen S, Coleman MD. et al. Impact of an Okinawa/Nordic based diet on endocrinological and periodontal conditions in individuals with type 2 diabetes. A randomized case-control study. *BMC Oral Health*. 2023;23(1):544. https://doi.org/10.1186/s12903-023-03272-9
18. Bian Y, Liu C, Fu Z. Application value of combination therapy of periodontal curettage and root planing on moderate-to-severe chronic periodontitis in patients with type 2 diabetes. *Head Face Med*. 2021;17(1):12.

19. Acharya AB, Thakur S, Muddapur MV. Effect of scaling and root planing on serum interleukin-10 levels and glycemic control in chronic periodontitis and type 2 diabetes mellitus. *J Indian Soc Periodontol*. 2015;19(2):188-93. https://doi.org/10.4103/0972-124X.148644
20. Evelina A, Rasa P, Nomeda B, Rasa B, Nijole S, Pacauskienė, Ingrida. Efficacy of Proanthocyanidins in Nonsurgical Periodontal Therapy. *Int Dent J*. 2022;73(2):195-204. https://doi.org/10.1016/j.identj.2022.08.006
21. Stadler AF, Angst PD, Arce RM, Gomes SC, Oppermann RV, Susin C. Gingival crevicular fluid levels of cytokines/chemokines in chronic periodontitis: a meta-analysis. *J Clin Periodontol*. 2016;43(9):727-45. https://doi.org/10.1111/jcpe.12557
22. Chen YW, Hsieh O, Chen YA, Chiou LL, Chang PC. Randomized controlled clinical effectiveness of adjunct 660-nm light-emitting diode irradiation during non-surgical periodontal therapy. *J Formos Med Assoc*. 2020;119(1 Pt 1):157-63
23. Eldessouky HF, Marie M. Nonsurgical Treatment of Periodontitis in Menopausal Patients: A Randomized Control Trial. *Biomed Res Int*. 2024;2024:6997142. https://doi.org/10.1155/2024/6997142
24. Bostanci V, Toker H, Senel S, Poyraz O, Akpinar A, Görgün EP. et al. Evaluation of IL-1β, IL-1ra, and IL-10 levels and outcome of periodontal therapy in chronic periodontitis with familial Mediterranean fever. *Clin Oral Investig*. 2017;21(1):469-75. https://doi.org/10.1007/s00784-016-1816-1
25. Chiang CP, Hsieh O, Tai WC, Chen YJ, Chang PC. Clinical outcomes of adjunctive indocyanine green-diode lasers therapy for treating refractory periodontitis: A randomized controlled trial with in vitro assessment. *J Formos Med Assoc*. 2020;119(2):652-9. https://doi.org/10.1016/j.jfma.2019.08.021
26. Martínez-Villa S, Sanz-Martín I, Maldonado E, Virto L, Sanz-Esporrín J, Sanz M. Immunohistochemical, histomorphometric, and gingival crevicular fluid analysis of residual and shallow periodontal pockets in patients with periodontitis Stages III and IV. *J Periodontol*. 2020;91(7):870-9. https://doi.org/10.1002/JPER.19-0035
27. Sorsa T, Gursoy UK, Nwhator S, Hernandez M, Tervahartiala T, Leppilahti J. et al. Analysis of matrix metalloproteinases, especially MMP-8, in gingival creviclular fluid, mouthrinse and saliva for monitoring periodontal diseases. *Periodontol 2000*. 2016;70(1):142-63. https://doi.org/10.1111/prd.12101
28. Kasai S, Onizuka S, Katagiri S, Nakamura T, Hanatani T, Kudo T. et al. Associations of cytokine levels in gingival crevicular fluid of mobile teeth with clinical improvement after initial periodontal treatment. *J Oral Sci*. 2020;62(2):189-96. https://doi.org/10.2334/josnusd.19-0056
29. Karin M. Nuclear factor-kappaB in cancer development and progression, *Nature*. 2006;441:(7092):431-6.
30. Pilloni A, Marini L, Gagliano N, Canciani E, Dellavia C, Cornaghi LB. et al. Clinical, histological, immunohistochemical, and biomolecular analysis of hyaluronic acid in early wound healing of human gingival tissues: A randomized, split-mouth trial. *J Periodontol*. 2023;94(7):868-81. https://doi.org/10.1002/JPER.22-0338
31. Aimetti M, Baima G, Aliyeva N, Lorenzetti V, Citterio F, Franco F. et al. Influence of locally delivered doxycycline on the clinical and molecular inflammatory status of intrabony defects prior to periodontal regeneration: A double-blind randomized controlled trial. *J Periodontal Res*. 2023;58(5):1096-104. https://doi.org/10.1111/jre.13174
32. Rabelo MS, Gomes GH, Foz AM, Stadler AF, Cutler CW, Susin C. et al. Short-term effect of non-surgical periodontal treatment on local and systemic cytokine levels: Role of hyperglycemia. *Cytokine*. 2021;138:155360. https://doi.org/10.1016/j.cyto.2020.155360
33. Ozgören O, Develioglu H, Güncü G, Akman A, Berker E. The adjunctive effect of tenoxicam during non-surgical periodontal treatment on clinical parameters and gingival crevicular fluid levels of MMP-8 and TNF-α in patients with chronic periodontitis- randomized, double-blind clinical trial. *Adv Clin Exp Med*. 2014;23(4):559-65.
34. Balci Yuce H, Gokturk O, Aydemir Turkal H, Inanir A, Benli I, Demir O. Assessment of local and systemic 25-hydroxy-vitamin D, RANKL, OPG, and TNF levels in patients with rheumatoid arthritis and periodontitis. *J Oral Sci*. 2017;59(3):397-404. https://doi.org/10.2334/josnusd.16-0677
35. Gupta S, Chhina S, Arora SA. A systematic review of biomarkers of gingival crevicular fluid: Their predictive role in diagnosis of periodontal disease status. *J Oral Biol Craniofac Res*. 2018;8(2):98-104. https://doi.org/10.1016/j.jobcr.2018.02.002
36. Sexton WM, Lin Y, Kryscio RJ, Dawson DR 3rd, Ebersole JL, Miller CS. Salivary biomarkers of periodontal disease in response to treatment. *J Clin Periodontol*. 2011;38(5):434-41. https://doi.org/10.1111/j.1600-051X.2011.01706.x
37. Äyräväinen L, Heikkinen AM, Kuuliala A, Ahola K, Koivuniemi R, Laasonen L. et al. Inflammatory biomarkers in saliva and serum of patients with rheumatoid arthritis with respect to periodontal status. *Ann Med*. 2018;50(4):333-44. https://doi.org/10.1080/07853890.2018.1468922

Cite this article: Bansal A, Arora SA, Gupta G, Mishra S, Tandon P. Inflammatory burden and periodontal tissue destruction: A biological perspective. *JAOH*. 2026;3(1):26-35.