Review Article

Salivary and Serum Inflammatory Biomarkers During Periodontitis Progression and After Treatment

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Abstract

Periodontitis is a chronic, multifactorial inflammatory disease characterized by progressive destruction of the tooth-supporting structures, including the gingiva, periodontal ligament, cementum, and alveolar bone. It represents a major public health concern due to its high prevalence and its role as a leading cause of tooth loss in adults. The disease is initiated by a dysbiotic microbial biofilm but is primarily driven by an exaggerated and dysregulated host immune-inflammatory response. In recent years, considerable research interest has been directed towards the identification of biological markers that can reflect disease activity, progression, and response to therapy. Among the various biological fluids, saliva and serum have emerged as promising diagnostic media due to their ability to reflect local and systemic inflammatory processes, respectively. This review of literature elaborates on the pathophysiology of periodontitis, the role of inflammatory mediators, and the current evidence supporting the use of salivary and serum biomarkers in predicting disease progression and monitoring therapeutic outcomes.

Keywords: Alveolar bone resorption; Cytokines; Inflammatory mediators; Salivary biomarkers; Serum biomarkers

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INTRODUCTION

Periodontitis is one of the most prevalent chronic inflammatory diseases affecting humans and constitutes a major global oral health burden. Epidemiological studies suggest that more than half of the adult population is affected by some form of periodontal disease, with severe periodontitis ranking among the most common non-communicable diseases worldwide.[1] The condition is characterized by a progressive inflammatory destruction of periodontal tissues, ultimately resulting in tooth mobility and tooth loss if left untreated. The pathogenesis of periodontitis involves a complex interaction between pathogenic microorganisms within the dental biofilm and the host immune system. While the presence of bacterial plaque is essential for disease initiation, tissue destruction is largely mediated by the host's immune-inflammatory response rather than direct bacterial damage.[2] This host response leads to the release of a wide range of inflammatory mediators, proteolytic enzymes, and oxidative molecules that contribute to connective tissue degradation and alveolar bone resorption.[3] Traditional diagnostic approaches rely on clinical and radiographic parameters such as probing depth, clinical attachment loss, bleeding on probing, and radiographic bone loss.

However, these parameters provide information primarily on historical tissue destruction and do not adequately reflect current disease activity or predict future progression. Consequently, there is an increasing need for objective biological markers that can identify individuals at risk of disease progression and evaluate treatment response in real time.[4]

Pathogenesis of periodontitis and systemic inflammation

Current concepts describe periodontitis as a polymicrobial inflammatory disease rather than a classical infectious condition. The transition from a symbiotic to a dysbiotic microbial community results in the dominance of inflammophilic bacteria that thrive in an inflammatory environment.[5] Keystone pathogens such as *Porphyromonas gingivalis* play a critical role in subverting host immune mechanisms, promoting immune evasion, and sustaining chronic inflammation.[6] The inflammatory cascade in periodontitis is characterized by increased production of pro-inflammatory cytokines including IL-1β, IL-6, IL-8, TNF-α, and IFN-γ, along with matrix metalloproteinases such as MMP-8 and MMP-9, which are responsible for collagen breakdown and extracellular matrix degradation.[7] Additionally, growth factors such as VEGF and regulatory molecules such as osteoprotegerin (OPG) influence angiogenesis and bone metabolism within periodontal tissues. Importantly, periodontal inflammation is not confined to the oral cavity. Inflammatory mediators and microbial products may enter the systemic circulation, contributing to a low-grade systemic inflammatory state.[8] This systemic dissemination provides a biological basis for the observed associations between periodontitis and systemic conditions such as diabetes mellitus, cardiovascular disease, rheumatoid arthritis, and adverse pregnancy outcomes.

Saliva as a diagnostic medium

Saliva has gained significant attention as a diagnostic fluid in periodontal research due to its non-invasive, cost-effective, and easily repeatable collection. Saliva contains a complex mixture of locally produced inflammatory mediators, host-derived enzymes, antibodies, microbial components, and systemic biomarkers that collectively reflect periodontal health status.[9] Numerous studies have demonstrated elevated salivary levels of cytokines such as IL-1β, IL-6, IL-8, IFN-γ, as well as proteolytic enzymes like MMP-8 in individuals with active periodontitis compared to healthy controls. These biomarkers are directly involved in the inflammatory and tissue destructive processes and therefore represent biologically plausible indicators of disease activity. Kinney et al. identified specific salivary biomarker signatures that could distinguish between stable and progressing periodontal sites, highlighting the potential of saliva in early disease detection and risk assessment. Furthermore, salivary biomarkers provide a dynamic reflection of disease status, allowing repeated monitoring over time without patient discomfort.[10]

Serum biomarkers and periodontal disease

Serum biomarkers provide insight into the systemic inflammatory burden associated with periodontal disease. Elevated serum levels of acute-phase proteins such as CRP and inflammatory enzymes including MMP-8, MMP-9, and MPO have been consistently reported in patients with moderate to severe periodontitis. Unlike saliva, serum biomarkers reflect generalized inflammation rather than site-specific periodontal activity. Although serum markers may not be sufficiently sensitive to detect subtle periodontal changes, they are valuable in understanding the systemic implications of periodontitis and its role as a contributor to systemic inflammatory load. The presence of elevated systemic biomarkers supports the concept that periodontitis may act as a chronic inflammatory stimulus, potentially influencing the pathophysiology of various systemic diseases through immune modulation and endothelial dysfunction.[11]

Biomarkers and periodontitis progression

Longitudinal investigations into periodontal biomarkers are essential for understanding disease dynamics. Most earlier studies employed cross-sectional designs, limiting their ability to assess disease progression. Nagarajan et al. emphasized that biomarker fluctuations over time are more informative than single measurements and reflect true disease trajectory. In the landmark study by Teles et al., patients with progressing periodontitis demonstrated persistently elevated salivary levels of IFN-γ, IL-6, VEGF, IL-1β, MMP-8, IL-10, and OPG over a one-year observation period. These findings suggest that a sustained pro-inflammatory salivary profile is a hallmark of disease progression, whereas serum biomarkers showed weaker associations due to limited localized progression per patient.[12]

Effect of periodontal therapy on biomarkers

Non-surgical periodontal therapy remains the gold

standard initial approach for the management of periodontitis. Mechanical disruption of the biofilm through scaling and root planing leads to a significant reduction in microbial load and subsequent resolution of inflammation. Several studies have demonstrated a marked decrease in salivary inflammatory mediators following therapy, including IL-1β, IL-6, IL-8, MMP-8, OPG, and IFN-γ. These reductions correlate strongly with clinical improvements such as decreased probing depth and gain in clinical attachment, supporting the use of salivary biomarkers as objective indicators of treatment success.[13]

Clinical implications of biomarker research

The clinical application of biomarker research represents a paradigm shift in periodontal diagnostics. Biomarkers have the potential to facilitate early diagnosis, identify high-risk individuals, predict disease progression, and enable personalized treatment strategies. Chairside diagnostic kits based on salivary biomarkers could revolutionize periodontal screening, particularly in community and preventive dentistry settings. However, challenges remain, including biological variability among individuals, lack of standardized cutoff values, and the need for large-scale longitudinal validation before routine clinical implementation.[14]

CONCLUSION

An increasing body of evidence supports the role of salivary and serum inflammatory biomarkers as valuable tools in understanding the pathogenesis, progression, and treatment response of periodontitis. Salivary biomarkers, in particular, demonstrate strong potential for real-time monitoring of disease activity and therapeutic outcomes due to their close association with local periodontal inflammation. Serum biomarkers provide complementary information regarding systemic inflammatory status. Future research should focus on developing validated biomarker panels and translating laboratory findings into clinically applicable diagnostic tools, thereby advancing personalized periodontal care and improving long-term patient outcomes.

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