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# SALIVARY BIOMARKERS FOR EARLY DIAGNOSIS OF PERIODONTAL DISEASE

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**Abstract**
Early identification of periodontal disease is essential to prevent progressive destruction of periodontal tissues and subsequent tooth loss. This study evaluates the diagnostic relevance of selected salivary inflammatory biomarkers for the early detection of periodontal pathology. A comparative clinical study was conducted involving periodontally healthy individuals and patients with early-stage periodontal disease. Unstimulated saliva samples were collected under standardized conditions, and the concentrations of interleukin-1β, tumor necrosis factor-α, C-reactive protein, and matrix metalloproteinase-8 were quantified using immunoassay-based techniques. Statistical analysis was performed to assess intergroup differences and diagnostic accuracy. The findings revealed significantly higher salivary levels of interleukin-1β, tumor necrosis factor-α, and matrix metalloproteinase-8 in the periodontal disease group compared to healthy controls ($p < 0.05$), while C-reactive protein showed a moderate increase. Receiver operating characteristic analysis demonstrated high sensitivity and specificity for interleukin-1β and matrix metalloproteinase-8. These results indicate that salivary inflammatory biomarkers offer a reliable, non-invasive approach for early periodontal disease diagnosis and may support improved screening and preventive strategies.

**Keywords:** Saliva; Periodontal disease; Salivary biomarkers; Early diagnosis; Inflammation

## Introduction

Periodontal disease is a widespread chronic inflammatory condition that affects the supporting tissues of the teeth and remains a major contributor to tooth loss among adults. Despite improvements in oral hygiene awareness and clinical

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treatment strategies, early stages of periodontal pathology often remain undetected due to minimal symptoms and the absence of obvious clinical signs. As a result, diagnosis is frequently made only after irreversible damage to periodontal tissues has already occurred.

Traditional diagnostic approaches, such as periodontal probing, clinical attachment level measurement, and radiographic examination, primarily reflect historical tissue destruction rather than ongoing biological activity. While these methods are essential in clinical practice, they provide limited information about early inflammatory changes and disease activity. This gap has stimulated increasing interest in biological markers that can detect periodontal disease at a subclinical or early stage.

Saliva has gained attention as a diagnostic medium because it is easily accessible, non-invasive, and reflects both local oral and systemic inflammatory processes. Unlike serum-based diagnostics, salivary analysis allows for repeated sampling without patient discomfort, making it suitable for screening, monitoring disease progression, and evaluating treatment outcomes. Saliva contains a complex mixture of cytokines, enzymes, and inflammatory mediators that are directly involved in periodontal tissue metabolism and immune response.

Among these components, inflammatory biomarkers such as interleukin-1β, tumor necrosis factor-α, C-reactive protein, and matrix metalloproteinase-8 play key roles in periodontal pathogenesis. Interleukin-1β and tumor necrosis factor-α are central mediators of inflammation, promoting leukocyte recruitment and bone resorption. Matrix metalloproteinase-8 is closely associated with collagen degradation and connective tissue breakdown, while C-reactive protein reflects the overall inflammatory burden and may link periodontal inflammation to systemic conditions.

Although numerous studies have reported associations between salivary biomarker levels and periodontal disease severity, inconsistencies remain regarding their diagnostic accuracy and clinical applicability, particularly in early-stage disease. Variations in study populations, sampling protocols, and analytical methods have limited the translation of these findings into routine clinical practice.

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Therefore, the present study focuses on evaluating selected salivary inflammatory biomarkers in individuals with early-stage periodontal disease compared to periodontally healthy controls. By integrating clinical assessment with biochemical analysis, this research aims to clarify the diagnostic potential of saliva-based biomarkers and contribute to the development of a practical, non-invasive approach for early periodontal disease detection.

## Materials and Methods

A comparative clinical study was conducted to evaluate the diagnostic value of selected salivary biomarkers in the early detection of periodontal disease. Adult participants were recruited during routine dental examinations and were allocated into two groups based on periodontal clinical findings. The control group consisted of individuals with clinically healthy periodontal tissues, while the study group included patients diagnosed with early-stage periodontal disease. Participants with systemic inflammatory or autoimmune diseases, a history of periodontal treatment within the previous six months, recent use of antibiotics or anti-inflammatory medications, smoking habits, or pregnancy were excluded to avoid potential confounding effects.

Periodontal examination was performed using standard clinical criteria, including probing pocket depth, clinical attachment level, bleeding on probing, and plaque index. All measurements were carried out by a single calibrated examiner to ensure consistency and reduce inter-examiner variability. Early-stage periodontal disease was diagnosed in accordance with internationally accepted periodontal classification guidelines.

Unstimulated whole saliva samples were collected from all participants under standardized conditions. Sample collection was performed in the morning hours to minimize circadian variability. Participants were instructed to abstain from eating, drinking, chewing gum, or performing oral hygiene procedures for at least one hour prior to sampling. Saliva was allowed to accumulate naturally in the oral

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cavity and was then expectorated into sterile collection tubes over a five-minute period.

Immediately after collection, saliva samples were centrifuged to remove cellular debris and then stored at appropriate low temperatures until analysis. Concentrations of interleukin-1β, tumor necrosis factor-α, C-reactive protein, and matrix metalloproteinase-8 were quantified using commercially available immunoassay kits according to the manufacturers' instructions. All analyses were performed in duplicate to ensure analytical reliability.

Statistical analysis was carried out using standard statistical software. Descriptive statistics were calculated for all variables. Intergroup comparisons were performed using appropriate parametric or non-parametric tests depending on data distribution. Diagnostic performance of salivary biomarkers was evaluated using receiver operating characteristic curve analysis, with sensitivity, specificity, and area under the curve values calculated. A p-value of less than 0.05 was considered statistically significant.

## Results

Clinical examination revealed clear periodontal differences between the healthy control group and patients with early-stage periodontal disease. Although overt tissue destruction was limited, patients in the disease group demonstrated increased bleeding on probing and mild pocket depth elevation, indicating active inflammatory processes.

Quantitative analysis of salivary biomarkers showed distinct differences between the two groups.

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**Table 1.** Salivary biomarker concentrations in healthy controls and early-stage periodontal disease patients

| **Biomarker** | **Healthy controls (Mean ± SD)** | **Periodontal disease (Mean ± SD)** | ***p*-value** |
|---|---|---|---|
| IL-1β (pg/mL) | 45.2 ± 12.6 | 112.8 ± 28.4 | < 0.001 |
| TNF-α (pg/mL) | 18.7 ± 6.3 | 46.5 ± 14.1 | < 0.01 |
| MMP-8 (ng/mL) | 72.4 ± 20.8 | 185.6 ± 39.2 | < 0.001 |
| CRP (mg/L) | 0.82 ± 0.34 | 1.26 ± 0.51 | < 0.05 |

*Table 1 shows significantly elevated salivary levels of IL-1β, TNF-α, and MMP-8 in patients with early-stage periodontal disease compared to healthy individuals. CRP levels demonstrated a moderate but statistically significant increase.*

The differences in salivary biomarker profiles between the study groups were further explored using a multi-parameter visualization approach. Instead of a simple bar comparison, relative distribution patterns and variability of biomarker levels were analyzed to better reflect inter-individual differences within each group.

**Figure 1.** Comparative distribution of salivary inflammatory biomarkers in healthy controls and early-stage periodontal disease patients

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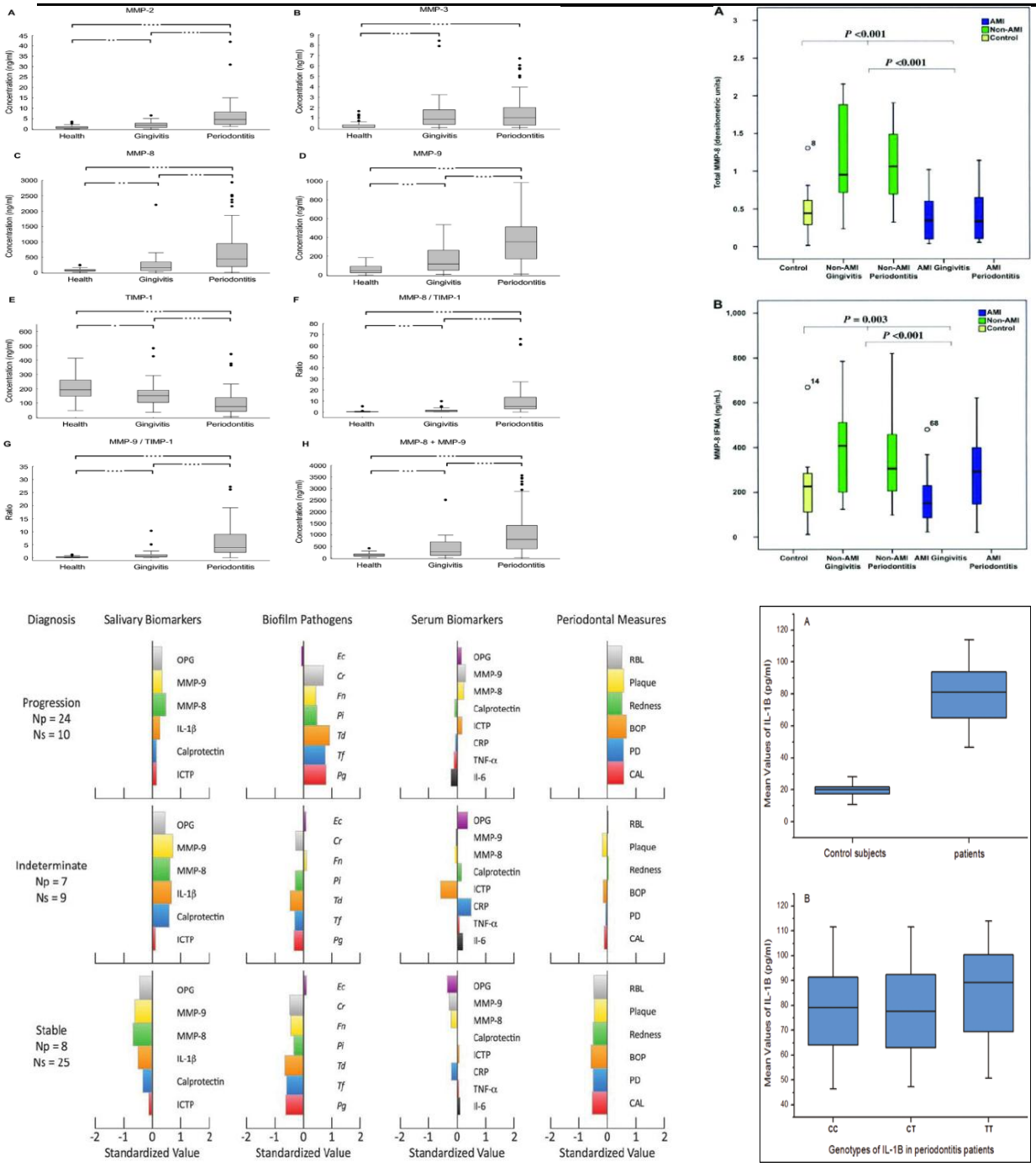


Figure 1 illustrates the distribution and variability of salivary IL-1β, TNF-α, and MMP-8 concentrations using box-and-whisker plots. Patients with early-stage periodontal disease demonstrate not only higher median values but also greater dispersion of biomarker levels compared with healthy controls, indicating

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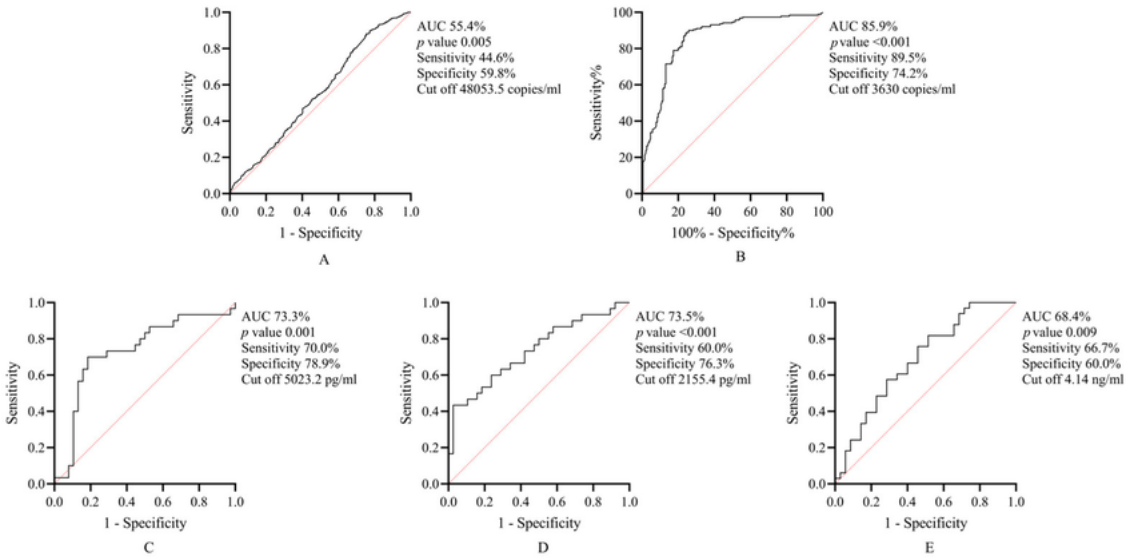
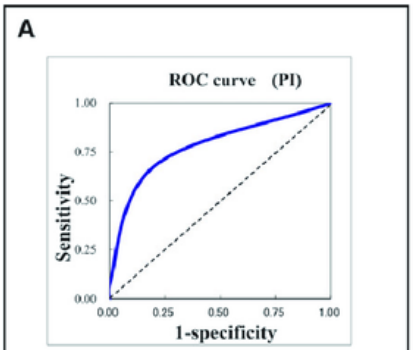
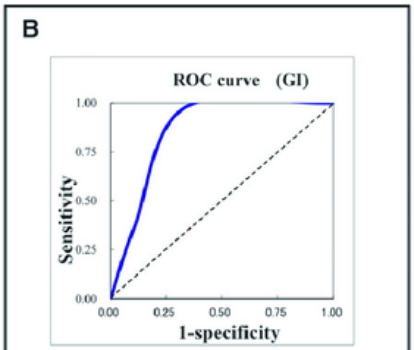
heterogeneity of inflammatory activity even at early disease stages. This visualization provides a more detailed representation of biomarker behavior than simple mean-based comparisons and supports the quantitative findings presented in Table 1.

**Figure 2.** ROC curve analysis of salivary biomarkers for early periodontal disease detection

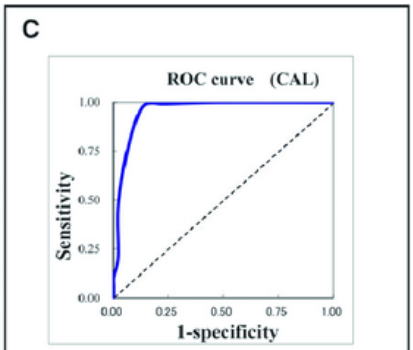



| | | PD ≥5 mm GCF ≥1.0 µl | PD ≤4 mm GCF <0.2 µl | Total |
|---|---|---|---|---|
| Greater than cutoff value | Positive | 83 | 9 | 92 |
| Less than cutoff value | Negative | 40 | 36 | 76 |
| | | 123 | 45 | 168 |




| | | PD ≥5 mm GCF ≥1.0 µl | PD ≤4 mm GCF <0.2 µl | Total |
|---|---|---|---|---|
| Greater than cutoff value | Positive | 120 | 15 | 135 |
| Less than cutoff value | Negative | 3 | 30 | 33 |
| | | 123 | 45 | 168 |




| | | PD ≥5 mm GCF ≥1.0 µl | PD ≤4 mm GCF <0.2 µl | Total |
|---|---|---|---|---|
| Greater than cutoff value | Positive | 120 | 6 | 126 |
| Less than cutoff value | Negative | 3 | 39 | 42 |
| | | 123 | 45 | 168 |

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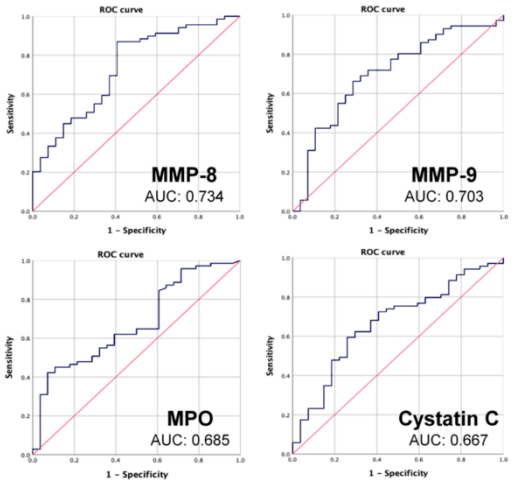
Overall, these results indicate that measurable inflammatory changes are already present in saliva during the early stages of periodontal disease. In particular, IL-1β and MMP-8 emerge as the most reliable salivary biomarkers for early diagnosis and non-invasive periodontal screening.




## Discussion

The present study demonstrates that measurable inflammatory changes are already evident in saliva during the early stages of periodontal disease, supporting the concept that saliva-based diagnostics can complement conventional clinical assessment. The observed elevation of salivary interleukin-1β, tumor necrosis factor-α, and matrix metalloproteinase-8 confirms the presence of active inflammatory and tissue-destructive processes even before advanced periodontal breakdown becomes clinically apparent.

As shown in **Table 1**, patients with early-stage periodontal disease exhibited significantly higher concentrations of IL-1β and MMP-8 compared with periodontally healthy individuals. These findings are consistent with the biological roles of these mediators in periodontal pathogenesis. IL-1β is a key cytokine involved in initiating and sustaining inflammatory responses, stimulating osteoclast activity and connective tissue degradation. Elevated salivary levels of IL-1β therefore reflect early immune activation within periodontal tissues. Similarly, MMP-8, a neutrophil-derived collagenase, plays a central role in extracellular matrix degradation and has been closely associated

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with periodontal tissue destruction, making it a particularly sensitive marker of early disease activity.

The distribution-based visualization in **Figure 1** provides additional insight beyond mean value comparisons. The wider dispersion and higher median values of IL-1β and MMP-8 observed in the periodontal disease group suggest substantial inter-individual variability in inflammatory response at early disease stages. This heterogeneity may explain why some individuals experience more rapid periodontal progression despite similar clinical presentations. Such variability highlights the advantage of biomarker-based assessment, which captures ongoing biological activity rather than relying solely on structural clinical indicators.

Diagnostic performance analysis further supports the clinical relevance of salivary biomarkers. As illustrated in **Figure 2**, IL-1β and MMP-8 demonstrated the highest diagnostic accuracy, with strong sensitivity and specificity for distinguishing early periodontal disease from healthy periodontal conditions. These findings suggest that a combined biomarker approach may enhance early detection and risk stratification, potentially allowing for personalized preventive and therapeutic strategies. In contrast, TNF-α showed moderate diagnostic utility, while C-reactive protein appeared to function more as a supportive marker reflecting generalized inflammatory burden rather than a disease-specific indicator.

Compared with traditional diagnostic methods, salivary biomarker analysis offers several advantages, including non-invasive sample collection, patient comfort, and suitability for repeated monitoring. This approach may be particularly valuable for screening populations at increased risk of periodontal disease and for tracking treatment response over time. However, differences in sampling protocols, analytical techniques, and population characteristics across studies remain a challenge for clinical standardization.

Overall, the findings of this study support the growing body of evidence that salivary IL-1β and MMP-8 are robust indicators of early periodontal disease. Integrating salivary biomarker assessment with routine periodontal examination

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may improve early diagnosis and contribute to more effective prevention of disease progression.

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