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Impact of Salivary Biomarkers on Early Detection of Periodontitis in Geriatric Patients

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Abstract

The study aimed to assess the accuracy of salivary matrix metalloproteinases (MMPs)-8 and -9, as well as tissue inhibition of MMP (TIMP)-1, in the diagnosis of periodontal disease and in discriminating between stages S1 to S3 of the condition. This research was a case-control study, including those with healthy periodontia and those with stages S1 through S3. Saliva was collected; next was the clinical data collection, including medical attachment degree, probe pocket dimension, and plaque measure. Radiograph evaluation of the alveolar bone levels confirmed the medical diagnosis. An enzyme-linked immunosorbent assay was used to evaluate salivary indicators. Enrolled as a comparison were 45 persons total—15 from each phase—and 18 healthy people. All salivary and medical marker concentrations were significantly higher in those with periodontitis than in the control group. With an accuracy range of 0.98 to 1.000, these markers also showed high diagnostic precision in differentiating S1 periodontal from the controls. Including S1 gingivitis, this study found that salivary markers showed notable diagnostic accuracy in separating periodontally healthy from periodontally diseased. TIMP1 differentiates S1 from S3.

Keywords: Salivary, Biomarkers, Periodontitis, Geriatric Patients.

1 INTRODUCTION

Pathogenic bacteria produce the chronic inflammatory condition known as periodontal disease, which breaks away connective tissue and alveolar bones Di Stefano et al. (2022). Traditionally, gum disease diagnosis has depended on medical and radiographic evaluations showing a history of the disease, but they are inadequate for spotting present activity of the illness. Early diagnosis of periodontal tissue breakdown helps track the illness's evolution and prevents further harm. Beneficial for assessment, saliva collection is a simple, noninvasive test of bodily fluids because saliva contains omics components that might reflect the current physiological status of oral tissue Liao, Chen, and Fu (2023).

Over the past few decades, many salivary indicators have been examined as potential indicators to distinguish between periodontitis sufferers and healthy individuals. Prior research has shown conflicting or even contradictory findings. During periodontal illness, individuals in the gingivitis phase have inflammation of the gingival area without damage to connective tissue or bone Heitz-Mayfield (2024). In the first phase of gingivitis, individuals exhibit gingival swelling accompanied by connective tissue degradation, which then advances to alveolar bone deterioration in the later phases of the illness.

The research asserts that the alteration of biomarkers transpires sequentially throughout various stages of gingivitis, and therefore, a composite of biomarkers is utilized more successfully for identifying the disease state. The present research aims to assess the diagnostic efficacy of these markers (indicative of inflammatory disorders, tissue deterioration, and dental infectious agents) in healthy individuals, those with gingivitis, and patients with periodontitis, and to integrate them to develop a successful predictive panel for identifying periodontal illness Cafiero et al. (2021).

2 MATERIALS AND METHODS

2.1. Study

This research used a case-control design, whereby patients with periodontitis constituted the cases, while those with normal periodontia served as the controls. All methods were executed in compliance with the Helsinki Statement and its subsequent revisions regarding human studies. Before inclusion in the trial, every individual was provided complete details about the nature and objectives of the research and completed a written consent form. The College of Medicine's Ethics Board approved the approach. For research and result reporting, this clinical trial followed the Strengthened Reporting of Observational Studies in Epidemiology (STROBE) recommendations Rubin et al. (2024).

2.2. Study Cohort

Participants in this study were those referred either for or seeking periodontal therapy. After demographic data were recorded, each participant's salivary glands were collected; medical and radiological evaluations came next. First recognized medically for the first staging, the gingivitis patients then had confirmation of the disease by radiographic assessment of the damage to the most affected tooth Al-Harthi et al. (2022).

2.3. The eligibility criteria

In the last 12 weeks, participants in this study had not used any medications; they were physically fit, had at least 20 teeth, Attending the Dental Centre for regular exams, individuals in the controlling group had BOP < 12%, Probing Pocket Depth (PPD) ≤ 4 mm Werner et al. (2024) and intact periodontium. The case description of periodontist adhered to the 2018 categorization of periodontal diseases and disorders, whereby interdental Clinical Attachment Loss (CAL) Adam et al. (2024) was identified at two or more non-adjacent teeth, or facial CAL of 3 mm or more was linked with PPD exceeding 3 mm at two or more teeth. Individuals with periodontitis were categorized into three categories: S1 (12-14% bone reduction), S2 (bone reduction impacting one-third of the roots), and S3 (bone reduction impacting the middle one-third of the roots). All participants with periodontal disease had a widespread extent and severity, including more than 30% of teeth, classified as class B or C, and presented an unstable condition characterized by PPD of 6 mm or greater, or PPD exceeding 4 mm accompanied by Bleeding on Probing (BOP).

2.4. Criteria for Exclusion

The list of participants encompassed people who had dental implants; those afflicted by systemic illnesses such as kidneys or renal failure, bowel inflammation (e.g., Crohn's disease); people with previous experience of organ transplantation or tumour treatment; those with any coronary or renovascular diseases; or those who smoke. Further exclusion criteria were any prior dental care during the past three years or ongoing active treatment for periodontal disease. In addition to pregnant or lactating women, individuals who had antibiotic therapy or immunosuppressant medicine in the past three months were eliminated.

2.5. Periodontal Metrics

The test excluded the wisdom teeth. Clinical variables were assessed for the whole mouth, such as full mouth (FM) plaque indicator (PI), which was documented as either present (1) or missing (0). The revealing agent was used to ascertain PI's presence or lack of dental plaques. PPD was assessed from the gingival edges to the bottom of the pockets. At the same time, CAL was defined as the length from the cemento-enamel junctions (CEJ) to the bottom of the pockets or succusses. A comprehensive dental checkup was conducted with a periodontal instrument at six locations per tooth. Radiographic images of the teeth most impacted by gum effect, namely the tooth exhibiting the most interdental CAL, were used to validate the clinical picture.

2.6. Validation and Result Metrics

Calibration meetings for periodontal variables were performed on four periodontitis participants excluded from the study, yielding coefficients of parameters correlation for ongoing information exceeding 0.92 and kappa factors for contradictory data surpassing 85%, deemed acceptable as earlier outlined. The clinical measures were the main results of the research, whereas salivary indicator quantities were regarded as secondary results.

2.7. Collection and Analysis of Salivary Samples

Participants were instructed to execute their standard oral hygiene practices. Salivary specimens were obtained from the research participants between 08:00 and 10:00 before the oral assessment. The passive salivary dripping technique gathered all of the saliva. A micropipette was employed for aspirating a precise amount of 600 μL of saliva into an inflatable Eppendorf tube containing 60 μL of protease-inhibiting solutions. After collection, samples were spun at 4500 g for 3 minutes and preserved at -32 °C. The protein content of every biomarker was quantified using enzyme-linked immunosorbent assay (ELISA).

2.8. Statistical Examination

Descriptive information was presented as percentages, means, standard deviations, frequencies, and medians. Before inferential examination, the Gaussian shape of the information was assessed using the

Shapiro-Wilk analysis, which revealed that the information collected from ELISA was not dispersed. Comparisons across several groups were conducted utilizing the Kruskal-Wallis analysis, and in instances of findings, further intergroup analyses were executed with the Bonferroni post hoc analysis. The periodontal variables exhibited standard patterns; thus, a multigroup analysis was performed using an Analysis of Variance (ANOVA) method, followed by the Tukey post-hoc analysis when findings were substantial. After correction, the significance threshold was established at $p < 0.04$ for multigroup analyses. Every statistical evaluation was performed with the GraphPad Prism program.

3 DISCUSSIONS

This research included a total of 85 individuals. The gender demography and tooth loss condition were equivalent between the three subgroups. Twenty-five patients were assigned to the healthy category (H), twenty-four individuals to the gingivitis category (G), and thirty-one individuals to the periodontitis category (P). As expected, no significant variations were seen in the salivary flow rates across the three classes. Compared to the normal cohort, the diseased subgroups (gingivitis and periodontitis) had elevated PI and BOP levels. The periodontitis group exhibited greater age, probing depth (PD), and CAL than the healthy and gingivitis categories.

The salivary concentrations of IL1ß, MMP8, ICTP, and Pg were quantified and are shown. An ANOVA analysis was conducted to examine the differences among the three categories. The periodontitis category had markedly elevated levels compared to the healthy category and increased levels of IL1ß, ICTP, and Pg relative to the gingivitis group. The gingivitis cohort had elevated IL1ß, MMP8, and Pg levels compared to the healthy cohort. No substantial change in MMP8 was seen between the gum disease and periodontitis cohorts; no significant difference was detected between the gingivitis and healthy cohorts.

The research assessed the relationship between all indicators and clinical indicators (Age, PD, and BOP) with a model using linear regression. The findings indicated that IL1ß and ICTP moderately correlated with Periodontal Disease (PD) and BOP. None of the four indicators showed a significant connection with age, and the result revealed no gender-specific variations in the levels of these indicators ($p > 0.05$).

3.1. Comparison between the periodontitis category and the healthy category

All four indicators evaluated in this research demonstrated a substantial disparity between the periodontal and normal cohorts. IL1ß produced an AUC value of 0.85, whereas the other three markers exhibited 0.72 and 0.82. Logistic regression was used to assess different pairings of the four indicators. IL1ß and ICTP yielded an AUC value of 0.89, indicating 82% selectivity and 85% sensitivity. Combining IL1ß, ICTP, and MMP8 generated an AUC value of 0.91, indicating 92% selectivity and 85% recall. Combining IL1ß, ICTP, and Pg yielded an AUC value of 0.90, with 96% sensitivity and

85% specificity. With the hybrid of all four biomarkers, the AUC value turned out to be 0.92, which is ideal.

3.2 Comparison of the Gingivitis Group with the Healthy Group IL1ß, MMP8, and Pg levels greatly varied between the gingivitis control and the afflicted group.

While Pg resulted in a lower AUC value, IL1ß and MMP8 generated similar results. Variations across these biomarker combinations were found using logistic regression analysis. IL1ß and MMP8 taken together had an AUC value of 0.81, indicating 65% selectivity and 90% recall. Combining IL1ß, MMP8, and Pg gave an improved AUC value of 0.82 with 82% specificity and 81% sensitivity.

3.3 Comparison of the Periodontitis Group with the Gingivitis Group IL1ß, ICPT, and Pg concentrations showed significant variations among the gingivitis and periodontitis groups, creating corresponding AUC values.

Many combinations of two indicators were investigated after logistic regression analysis. Combining IL1ß with ICTP generated an AUC of 0.72 with 80% sensitivity and 72% specificity. For the combination usage of IL1ß and Pg, a similar AUC value was seen. With 84% responsiveness and 72% specificity, IL1ß, Pg, and ICTP had the best AUC value of 0.73.

4 CONCLUSION

Salivary markers (MMP8, MMP9, and TIMP1) showed significant diagnostic accuracy in separating among gingival medical and periodontitis, including S1 gingivitis. Using a combination of MMPs and TIMP1 improved the accuracy yet further. These markers can lack the same diagnostic value in differentiating periodontal stages S1 through S3.

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