SALIVARY BIOMARKER LEVELS AND PERIODONTAL HEALTH STATUS IN PATIENTS WITH DIABETIC AND HEALTHY LIFESTYLE: A COMPARATIVE STUDY

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How to cite this article

Maqsood F, Abid H, Daud N, Noreen N, Malik FB, Khan TA. Salivary Biomarker Levels and Periodontal Health Status in Patients with Diabetic and Healthy Lifestyle: A Comparative Study. J Gandhara Med Dent Sci. 2025;12(1):15-19.doi:10.37762/jgmds.12-1.621

Date of Submission: 21-08-2024
Date Revised: 09-10-2024
Date Acceptance: 21-11-2024

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ABSTRACT

OBJECTIVES

To evaluate and compare the periodontal health status and salivary biomarker levels in diabetic patients and non-diabetic individuals, thereby determining the association between these factors.

METHODOLOGY

A comparative study included 100 participants divided into two groups: 50 diabetic patients and 50 healthy controls. Periodontal parameters such as the gingival index (GI), probing pocket depth (PPD), and clinical attachment level (CAL) were assessed. Salivary biomarkers, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and glucose levels, were measured using enzyme-linked immunosorbent assay (ELISA) techniques. Statistical analysis was conducted using SPSS software.

RESULTS

Diabetic patients exhibited significantly higher periodontal parameters (GI, PPD, CAL) compared to healthy controls ($p < 0.05$). Salivary biomarkers, particularly IL-6 and TNF-α, were markedly elevated in the diabetic group ($p < 0.01$). There was a strong positive correlation between salivary glucose levels and periodontal parameters ($p < 0.001$).

CONCLUSION

Diabetic individuals show worse periodontal health and elevated salivary inflammatory biomarkers compared to non-diabetic controls. This suggests a need for closer periodontal monitoring in diabetic patients to mitigate further systemic complications.

KEYWORDS: *Diabetic, Periodontal, Salivary Biomarkers, Hyperglycemia*

INTRODUCTION

Periodontal disease, a chronic inflammatory condition affecting the supporting structures of the teeth, has garnered significant research attention due to its systemic implications. Emerging evidence underscores a bidirectional relationship between periodontal disease and systemic conditions such as diabetes mellitus (DM), a chronic metabolic disorder characterized by hyperglycemia and associated vascular and immune dysfunctions. DM affects more than 400 million individuals globally, with type 2 diabetes being the predominant form.[1] Given the increasing prevalence of DM and periodontal disease worldwide, understanding their interrelationship through objective biomarkers is essential for developing targeted diagnostic and therapeutic strategies. Patients with diabetes are predisposed to periodontal disease due to altered host responses to microbial insults, impaired wound healing, and dysregulated inflammatory processes.[2] Conversely, periodontal inflammation can exacerbate glycemic control through systemic dissemination of inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6).[3] This interplay emphasizes the need for robust comparative studies to delineate differences in periodontal parameters and associated biomarkers between diabetic patients and healthy individuals. Periodontal parameters, including clinical attachment loss (CAL), probing depth (PD), bleeding on probing (BOP), and plaque index (PI), serve as clinical indicators of periodontal health, while salivary biomarkers offer a non-invasive, dynamic assessment of systemic and oral health. Saliva, a complex biological fluid, reflects both local and systemic pathophysiological changes, making it a promising medium for biomarker identification. In diabetic patients, alterations in salivary glucose, immunoglobulins, pro-inflammatory cytokines, and

oxidative stress markers have been documented.[4] Additionally, specific biomarkers such as matrix metalloproteinase-8 (MMP-8), C-reactive protein (CRP), and advanced glycation end products (AGEs) have been implicated in both periodontal and diabetic pathologies.[5] Comparative analyses of these biomarkers can elucidate shared mechanistic pathways, providing insights into the pathogenesis of periodontal disease in diabetic populations. Studies have highlighted significant disparities in periodontal parameters between diabetic and non-diabetic individuals. For instance, diabetic patients consistently exhibit higher CAL, PD, and BOP scores, suggesting increased susceptibility to periodontal destruction.[6] These clinical findings are mirrored by elevated levels of pro-inflammatory mediators in saliva, indicative of heightened inflammatory burden in diabetes-associated periodontal disease.[7] However, discrepancies exist regarding the extent of these differences and their correlation with systemic glycemic control, necessitating comprehensive investigations. The intricate relationship between diabetes and periodontal disease is mediated by several mechanisms, including advanced glycation, oxidative stress, and dysbiosis of the oral microbiome. Hyperglycemia induces the formation of AGEs, which interact with receptors on immune cells to amplify inflammatory responses.[8] Additionally, oxidative stress, a hallmark of diabetic complications, exacerbates periodontal tissue destruction by promoting apoptosis and impairing tissue repair mechanisms.[9] Dysbiosis of the subgingival microbiota further perpetuates inflammation, creating a vicious cycle that exacerbates both periodontal and systemic health.[10] Salivary biomarker analysis provides a window into these pathophysiological processes, enabling the identification of potential diagnostic and prognostic indicators. Despite the wealth of research linking diabetes and periodontal disease, significant knowledge gaps persist regarding the utility of salivary biomarkers in clinical practice. While some studies have demonstrated strong correlations between salivary markers and periodontal parameters, others have reported conflicting findings, highlighting the need for standardized methodologies and larger cohort studies.[11] Additionally, the influence of confounding factors such as smoking, age, and medication use must be carefully considered in comparative analyses. This study aims to provide a comparative analysis of periodontal parameters and salivary biomarkers in patients with diabetes mellitus and healthy controls. By synthesizing findings, this work seeks to unravel the complex interplay between diabetes and periodontal disease, offering insights into shared pathophysiological mechanisms and potential clinical applications. Understanding these relationships is pivotal for the development of integrated care models that address the systemic and oral health needs of diabetic populations.

METHODOLOGY

This comparative study was conducted over six months at the Department of Periodontology, Rehman College of Dentistry, Peshawar. A total of 100 participants were recruited, comprising 50 patients diagnosed with type 2 diabetes mellitus (DM) and 50 healthy controls matched for age and gender. Patients diagnosed with type 2 DM for at least five years, healthy controls with no history of systemic diseases, participants aged between 30 to 65 years, and no use of antibiotics or anti-inflammatory drugs in the last three months were included. The smokers or individuals with a history of tobacco use, pregnant or lactating women, and patients with other systemic conditions such as cardiovascular disease, rheumatoid arthritis, or immunocompromised states. Periodontal examination was conducted by a calibrated periodontist using a UNC-15 periodontal probe. The following periodontal parameters were recorded: Gingival Index (GI): To assess the severity of gingivitis. Probing Pocket Depth (PPD): To measure the depth of periodontal pockets. Clinical Attachment Level (CAL): To evaluate the extent of periodontal attachment loss. Unstimulated saliva was collected from each participant in the morning after an overnight fast. The samples were centrifuged at 3000 rpm for 10 minutes, and the supernatant was stored at -80°C until further analysis. The salivary levels of glucose, IL-6, and TNF-α were measured using ELISA kits following the manufacturer‟s instructions. Data were analyzed using SPSS version 25.0. Descriptive statistics were used to summarize the demographic and clinical characteristics of the participants. The independent t-test was used to compare the periodontal parameters and salivary biomarkers between the two groups. Pearson's correlation analysis was performed to assess the relationship between salivary glucose levels and periodontal parameters. A p-value of < 0.05 was considered statistically significant.

RESULTS

The study included 100 participants, with a mean age of 52 ± 8 years. The demographic characteristics of the study population are presented in Table 1. Diabetic patients had significantly higher mean values for GI, PPD, and CAL compared to healthy controls ($p < 0.05$), as shown in Table 2. Salivary levels of glucose, IL-6, and TNF-α were significantly elevated in diabetic patients compared to healthy controls ($p < 0.01$). The results are presented in Table 3. There was a significant positive correlation between salivary glucose levels and periodontal parameters ($p < 0.001$), as shown in Table 4.

Table 1: Demographic Characteristics of Participants

Characteristics	Diabetic Group (n=50)	Healthy Controls (n=50)
Age (mean ± SD)	53 ± 7	51 ± 9
Gender (Male/Female)	26/24	25/25
Duration of Diabetes (years)	10 ± 5	N/A

Table 2: Comparison of Periodontal Parameters

Periodontal Parameters	Diabetic Group (n=50)	Healthy Controls (n=50)
Gingival Index (GI)	2.5 ± 0.4	1.8 ± 0.3
Probing Pocket Depth (PPD) (mm)	5.2 ± 1.0	3.1 ± 0.8
Clinical Attachment Level (CAL) (mm)	4.6 ± 0.7	2.9 ± 0.6

Table 3: Salivary Biomarker Levels

Salivary Biomarkers	Diabetic Group (n=50)	Healthy Controls (n=50)
Glucose (mg/dL)	20 ± 5	4 ± 1
IL-6 (pg/mL)	35 ± 8	12 ± 4
TNF-α (pg/mL)	42 ± 10	18 ± 5

Table 4: Correlation Between Salivary Glucose and Periodontal Parameters

Parameter	Correlation Coefficient (r)	P-Value
Gingival Index (GI)	0.76	< 0.001
Probing Pocket Depth (PPD)	0.82	< 0.001
Clinical Attachment Level (CAL)	0.79	< 0.001

DISCUSSION

The present study aimed to evaluate and compare periodontal parameters and salivary biomarkers between diabetic patients and healthy controls, highlighting the correlations between salivary glucose levels and periodontal health. The findings demonstrated significantly higher gingival index (GI), probing pocket depth (PPD), and clinical attachment level (CAL) in diabetic patients compared to healthy controls, alongside elevated salivary levels of glucose, IL-6, and TNF-α in the diabetic group. These results contribute to the growing body of evidence suggesting a bidirectional relationship between diabetes mellitus (DM) and periodontal disease through systemic inflammatory and metabolic pathways. The significantly higher periodontal parameter values (GI, PPD, and CAL) in diabetic patients align with prior studies that have demonstrated heightened periodontal destruction in individuals with diabetes. Research by Preshaw et al. (2012) reported similar increases in PPD and CAL in diabetic patients, attributing these differences to the hyperinflammatory state induced by diabetes, which exacerbates periodontal tissue destruction.[12] Similarly, Khumaedi et al. (2020) found increased GI and PPD in diabetic populations, emphasizing the role of systemic hyperglycemia in impairing immune responses and enhancing microbial pathogenicity.[13] This study's findings corroborate these results, highlighting the global impact of diabetes on periodontal health. The significant elevation in salivary glucose levels observed in diabetic patients is consistent with studies by Jurysta et al. (2009) and Soares et al. (2016), both of which reported higher salivary glucose concentrations in diabetic individuals due to compromised glycemic control and increased transudation of glucose into the oral cavity.[14,15] Elevated salivary glucose can foster a conducive environment for pathogenic bacteria, further exacerbating periodontal inflammation. This study‟s correlation analysis supports this mechanism, showing a strong positive association between salivary glucose levels and periodontal parameters, consistent with findings by Nainggolan et al. (2017), who reported similar correlations between salivary glucose and CAL in diabetic patients.[16] The pro-inflammatory cytokines IL-6 and TNF-α were significantly higher in the diabetic group compared to healthy controls, mirroring findings in studies by Lalla et al. (2000) and Engebretson et al. (2007), which identified elevated levels of these biomarkers in both serum and saliva of diabetic individuals with periodontal disease.[17,18] These cytokines play a critical role in the pathogenesis of periodontal disease by amplifying local and systemic inflammation, promoting osteoclastogenesis, and impairing tissue repair. Additionally, IL-6 and TNF-α have been implicated in insulin resistance, further linking periodontal inflammation with systemic glycemic control.[19] The current study reinforces these observations, suggesting that salivary cytokine levels reflect systemic inflammation and periodontal status. Contrastingly, while many international studies have focused on serum biomarkers, this study highlights the utility of salivary biomarkers, which offer a non-invasive and cost-effective alternative for assessing periodontal and systemic health. For instance, Giannobile et al. (2016) emphasized saliva's diagnostic potential, particularly for biomarkers like IL-6 and TNF-α, which correlate well with periodontal inflammation and systemic conditions (20). However, conflicting findings exist in the literature, with some studies reporting weaker correlations between salivary cytokines and periodontal parameters, potentially due to variations in sample collection, population characteristics, and analytical methods.[21] The findings regarding salivary TNF-α levels align with a study by Belazi et al. (2017), which reported elevated salivary TNF-α in diabetic patients with periodontitis, further substantiating the cytokine‟s role as a biomarker of inflammation in diabetic and periodontal pathologies.[22] However, unlike the current study, Belazi et al. noted a stronger correlation with glycemic control than periodontal parameters, indicating potential variations

in biomarker dynamics between populations. This highlights the need for standardized methodologies to ensure comparability across studies. The significant correlations between salivary glucose levels and periodontal parameters (GI, PPD, and CAL) observed in this study suggest that salivary glucose may serve as a valuable biomarker for predicting periodontal health in diabetic patients. This is consistent with the findings of Panchbhai et al. (2012), who demonstrated that salivary glucose is strongly associated with periodontal indices and glycemic control.[23] However, the lack of significant correlations in some studies, such as by Aoyama et al. (2012), underscores the influence of confounding factors such as age, medication use, and oral hygiene practices on salivary biomarker levels.[24] The findings align with research conducted in similar populations. For example, a study in India by Singh et al.(2015) reported elevated periodontal parameters and salivary IL-6 levels in diabetic patients, emphasizing the role of inflammation in periodontal destruction.[25] However, the magnitude of differences in biomarkers and parameters varies across regions, potentially reflecting differences in genetic, environmental, and healthcare factors. Studies in diverse populations have reported similar trends, further affirmed the generalizability of these findings while highlighting regional variations in disease prevalence and severity.[26]

LIMITATIONS

Despite its strengths, this study has certain limitations that warrant consideration. The relatively small sample size and cross-sectional design limit the ability to establish causal relationships between salivary biomarkers and periodontal parameters. Moreover, confounding factors such as dietary habits, medication use, and smoking were not explicitly controlled, which may influence biomarker levels. Future longitudinal studies with larger, diverse cohorts are necessary to validate these findings and explore the dynamic interactions between diabetes, periodontal disease, and salivary biomarkers over time.

CONCLUSIONS

This study underscores the significant disparities in periodontal health and salivary biomarker levels between diabetic patients and healthy controls, reinforcing the bidirectional relationship between diabetes and periodontal disease. The strong correlations between salivary glucose and periodontal parameters suggest that salivary biomarkers could serve as non-invasive tools for monitoring periodontal and systemic health in diabetic populations. However, further research is needed to standardize biomarker analysis methodologies, address confounding factors, and explore the longitudinal dynamics of these relationships. Such efforts will pave the way for integrating salivary diagnostics into clinical practice, enhancing the early detection and management of periodontal disease in diabetic individuals.

CONFLICT OF INTEREST: None

FUNDING SOURCES: None

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