Original Article

Association of Salivary Janus Kinase 1 and Secretory Leukocyte Protease Inhibitor with Dental Caries and Periodontal Status in Different Stages of Type II Diabetes Mellitus: A comparative cross-sectional study

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Abstract

Objective: This research was formulated to investigate the relationship between salivary biomarkers which include Janus Kinase 1 (JAK1) and Secretory Leukocyte Protease Inhibitor (SLPI), and glycemic status in individuals with normal, prediabetic, controlled diabetic and uncontrolled diabetic conditions, and to assess their potential role in oral health.

Methods: Unstimulated saliva was obtained from 80 individuals aged 30-60 years who participated in this study: 20 healthy individuals and 60 with type II diabetes mellitus. Participants were assigned into four groups (20 in each group) according to their HbA1c level: normal, prediabetic, controlled diabetic and uncontrolled diabetic. Salivary pH was measured using Merck pH paper. All saliva samples were stored at -80 ℃, and salivary JAK1 and SLPI levels were measured using ELISA. Each participant was examined at the time of sample collection for dental caries and periodontal health using the decayed, missing, and filled teeth (DMFT) index and clinical attachment loss (CAL), respectively.

Results: Salivary JAK1 and SLPI showed no significant differences among the groups ($p = 0.423$ and $p = 0.940$, respectively). In contrast, DMFT scores ($p = 0.031$) and CAL ($p = 0.006$) were significantly higher in the diabetic groups than in controls. HbA1c was positively correlated with CAL ($r = 0.420$, $p < 0.001$) and DMFT ($r = 0.248$, $p = 0.027$). Regression analysis revealed that age and HbA1c were significant predictors of periodontal status, while salivary biomarkers were not associated with clinical outcomes.

Conclusions: Poor glycemic control was associated with increased periodontal attachment loss and higher caries experience, while salivary JAK1 and SLPI showed no significant diagnostic value. Age and HbA1c emerged as key predictors of oral health outcomes in diabetic patients.

Keywords: *Diabetes mellitus, Dental caries, Periodontitis, Saliva, Biomarkers, ELISA.*

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Introduction

The global prevalence of diabetes is estimated to be around 285 million, with a projected 50% increase by 2030[1]. Diabetes mellitus is a general term that refers to a group of metabolic disorders characterized by long-term hyperglycemia, which results in damage to and failure of various organs, including the heart, blood vessels, kidneys, eyes, and nerves[2,3]. An evidence-based correlation has developed between oral health and systemic conditions such as diabetes in the last few decades[4]. Diabetes has been identified as a significant risk factor for periodontitis in epidemiological studies, with a risk that is approximately three times higher than that of an individual without diabetes[5]. The most notable modifications in uncontrolled diabetes are the heightened susceptibility to infection and the reduction in defense mechanisms, which ultimately result in destructive periodontal disease. Periodontal abscesses, accelerated bone loss, deep periodontal pockets, and severe gingival inflammation are frequently observed in diabetic patients who have poor oral hygiene[6]. The transition from periodontally healthy states to disease conditions is promoted by dysbiosis between oral bacteria and host immune response[7].

Salivary composition and functions are altered in diabetes mellitus. Pathogenic bacteria are initiated by changes in the oral environment. Saliva normally has a protective effect; however, when salivary function is significantly reduced, dental caries may develop. An acidogenic environment is created by the low pH of the saliva that promotes the development of aciduric bacteria, causing dental caries[8].

The pathway through which numerous cytokines that are implicated in inflammatory pathologies communicate is called the Janus kinase-signal transducer and activator of transcription pathway. Janus Kinase 1 is involved in signaling by pro-inflammatory cytokines, such as IL-6 and IFN, which are soluble factors produced and secreted by both immune and non-immune cells. Several immune-mediated inflammatory diseases are characterized by the loss of immune homeostasis, which is the result of abnormal cytokine production or responsiveness[9].

Secretory leukocyte protease inhibitor (SLPI) is an anti-protease that protects mucosal tissue integrity through its antimicrobial and immunomodulatory properties. It has the capacity to allow scarless wound healing and keep epithelial integrity of junctional epithelium[10].

SLPI has several important biological functions. It protects tissues against inflammatory products by downregulating the macrophage response to bacterial lipopolysaccharide (LPS). In addition, SLPI safeguards local tissues from the harmful effects of inflammation by inhibiting the activity of various proteases, including cathepsin G, elastase, trypsin, polymorphonuclear neutrophil (PMN) chymotrypsin, acinar cell trypsin, and mast cell chymase. It reduces C5a-related chemotactic activity, promotes cutaneous wound healing, and exhibits antimicrobial activity against bacteria, fungi, and viruses[11].

Periodontitis and diabetes adversely affect each other in a chronic, vicious cycle. Diabetes can also lead to dry mouth and an increased risk of dental caries. On the other hand, HbA1c is increased by periodontitis, causing or worsening diabetes and its complications[12]. Therefore, this study aims to evaluate salivary biomarkers (JAK1 and SLPI) alongside clinical oral examination in patients with different stages of type II diabetes mellitus, compared to people without diabetes, and to assess the association between biochemical and clinical parameters. However, the diagnostic value of salivary JAK1 and SLPI across different glycemic stages remains unclear.

Patients and Methods

Study Design

The eighty individuals who participated in the study were divided into four groups: 20 healthy individuals and 60 with type II diabetes mellitus diagnosed for at least two years. The diabetic patients were divided into three groups (20 in each group) according to their HbA1c levels into prediabetic, controlled, and uncontrolled diabetes according to the American Diabetes Association (ADA)[13]. G Power software version 3.1.9.7 was utilized to determine the sample size depending on data from a previous study using DMFT as primary outcome[14]. An effect size of 0.4 was assumed, with the significance level (α) set at 0.05 and statistical power of 80%. Group 1: healthy individuals with HbA1c (less than 5.7%; 39 mmol/mol). Group 2: prediabetes with HbA1c (between 5.7% and 6.4%; between 39 mmol/mol and 48 mmol/mol). Group 3: controlled type 2 diabetes with HbA1c (between 6.5% and 7.0%; between 48 mmol/mol and 53 mmol/mol). Group 4: uncontrolled type 2 diabetes with HbA1c (More than 7.0%; 53 mmol/mol). Inclusion criteria were male and female patients aged 30-60 years diagnosed with type II diabetes for at least 2 years. Exclusion criteria included those with systemic disease other than diabetes, smokers, pregnant women, and edentulous individuals.

Sample collection

Unstimulated whole saliva was collected from 80 participants aged 30-60 years in the morning, between 9 a.m. and 11 a.m. The individuals were requested to refrain from eating, drinking, and brushing for at least 90 minutes prior to saliva collection. The participants were asked to sit upright in a chair in a cool environment, with their heads slightly bent forward, while collecting saliva. The participants expectorated all secreted saliva directly into

sterilized plastic cups every minute for 5 minutes[15]. Salivary pH was measured directly using Merck pH paper (Merck, Germany); the paper strips were dipped into the saliva samples for 1-3 seconds, and the color was compared to the reference chart[8]. The samples were transferred into sterile Eppendorf tubes, placed in a cold box at 4℃, and then stored at -80℃ for long-term storage. The saliva samples were placed at room temperature and centrifuged for 20 minutes at 2000 revolutions per minute to get clear supernatant ready for the ELISA test[16]. Salivary concentrations of JAK1 and SLPI were measured by ELISA according to the manufacturer's instructions. The JAK1 ELISA kit had a sensitivity of 0.14 ng/mL with a standard curve range of 0.25-16 ng/mL. The SLPI ELISA kit demonstrated a sensitivity of 10.23 ng/L, and a standard curve range of 20-4500 ng/L. Ethical approval was obtained before conducting the experiment.

Salivary JAK1 and SLPI measurement

ELISA (sandwich technique) was used to measure JAK1 and SLPI levels in saliva samples, using JAK1 and SLPI ELISA kits from (BT LAB/China). The saliva samples were transferred into sterile Eppendorf tubes, placed in a cold box at 4℃, and then stored at -80℃ for long-term storage. The saliva samples were placed at room temperature and centrifuged for 20 minutes at 2000 revolutions per minute according to the manufacturer's instructions to get clear supernatant ready for the ELISA test, as shown in Figure 3.

Intra-oral examination

This included examining all 80 participants in the study and recording their clinical attachment loss and DMFT index. To determine if a tooth was decayed, missing, or filled (DMFT /dmft), the WHO modification (World Health Organization, 2013) [17] was followed, in which D/d represents the number of decayed teeth, M/m represents the number of missing teeth due to caries, and F/f represents the number of filled teeth. A systematic approach to examination of tooth condition was conducted, beginning from the upper right side to the upper left side in an orderly manner, followed by the lower teeth in the same manner. Full mouth CAL examination was performed for all participants using William's periodontal probe, and the measurements were recorded, as shown in Figure 3-A. CAL was determined by adding the extent of gingival recession to the probing depth measurement. However, when the recession was not visible, the height of the marginal gingiva coronal to the cementoenamel junction (CEJ) was assessed, and that measurement was subtracted from the probing depth to determine the level of clinical attachment loss[18].

The severity of periodontitis based on the CAL is classified according to the new classification of periodontal diseases by the American Academy of Periodontology into 4 stages[19]: Stage I periodontitis: Interdental CAL of 1-2 mm at ≥ 2 non-adjacent teeth.

- Stage II periodontitis: Interdental CAL of 3-4 mm at ≥ 2 non-adjacent teeth.
- Stage III and IV periodontitis: Interdental CAL of ≥ 5 mm at ≥ 2 non-adjacent teeth.

Reliability was assessed to assess the consistency of the clinical measurements. A strong positive correlation was observed between repeated measurements, with an inter-item correlation coefficient r = 0.931. The interclass correlation coefficient (ICC) was calculated using a two-way mixed effects model with a consistency definition. The analysis demonstrated an ICC value of 0.952 (95% CI: 0.536–0.995; p = 0.006), indicating excellent reliability of the DMFT index measurement. Calibration between examiners for CAL measurements was performed following the same standardized protocol used for DMFT scoring.

Statistical Analysis

To test the normality of data, the Shapiro-Wilk test was used. For data analysis, IBM SPSS version 22 was used. The mean with standard deviation and the median with interquartile range were used for quantitative variables, with the latter used for non-normally distributed data, while for qualitative data, frequencies and percentages were used. ANOVA and the Kruskal-Wallis tests were used to compare the means and medians of normally distributed and non-normally distributed data, respectively. Chi-square test was used for qualitative variables. Spearman's Correlation was used to determine the correlation between quantitative variables, and Multiple linear regression analysis was performed to identify independent predictors of the dental health outcome, DMFT, which was considered the dependent variable, while age, HbA1c, CAL, JAK1, and SLPI were included as independent variables.

Results

Descriptive statistics

A total of 80 participants were included in the study, comprising 35 males (43.8%) and 45 females (56.3%). The median age of the participants was 48.0 years with an interquartile range (IQR) of 41.5 to 54.0 years. The median HbA1c level was 6.5% (IQR: 5.6–8.1), indicating a range of glycemic control among the participants. Salivary JAK1 levels had a median of 0.51 ng/mL (IQR: 0.43–0.60), and SLPI had a median of 0.76 ng/mL (IQR: 0.61–0.91). The mean DMFT score was 10.83 ± 4.89, reflecting the participants' dental caries experience. The median clinical attachment loss (CAL) was 2.83 mm (IQR: 0.0–4.0), and

the median salivary pH was 6.0 (IQR: 6.0–7.0), indicating slightly acidic to neutral salivary conditions, as shown in Table 1.

Demographic and Clinical Characteristics

Gender distribution was relatively balanced across all groups, with no significant difference observed ($p = 0.681$). The percentage of males ranged from 55% in the controlled-diabetic group to 35% in the uncontrolled-diabetic group. Age appeared higher in the diabetic groups than in the normal group, but the difference was not statistically significant ($p = 0.073$). As expected, HbA1c levels differed significantly among the groups ($p < 0.001$), with median values increasing progressively from 5.05% in the normal group to 10.7% in the uncontrolled diabetic group. Salivary pH showed a median value of 6.0 across all diabetic groups and 6.5 in the normal group. However, this difference was not statistically significant ($p = 0.614$), as shown in Table 2.

Comparison of Biomarker Levels, Dental Caries, and Periodontal Status Across Glycemic Groups.

There was no statistically significant difference in the levels of salivary JAK1 among the groups ($p = 0.423$). The median JAK1 concentration was 0.58 ng/mL in the controlled diabetic group and it was 0.48 ng/mL in the prediabetic group. Similarly, SLPI levels did not differ significantly between groups ($p = 0.940$), with median value was 0.77 ng/mL in both the prediabetic and controlled diabetic groups and 0.70 ng/mL in the normal group. In contrast, the DMFT scores differed significantly across the groups ($p = 0.031$). The highest scores were observed in the diabetic groups, particularly the controlled diabetic group (12.0 ± 5.9), while the normal group had the lowest mean DMFT score (8.1 ± 4.3). In clinical attachment loss (CAL) between the groups, the normal group had a median CAL of 0.0 mm, which progressively increased with the severity of diabetes, reaching 4.0 mm (IQR: 2.0-5.8) in the uncontrolled diabetic group, which is a statistically significant result ($p = 0.006$), as shown in Table 3.

Spearman's correlation was used to evaluate the relationship between salivary biomarkers (JAK1, SLPI), glycemic control (HbA1c) and clinical dental parameters (CAL, DMFT). A statistically significant positive correlation was observed between HbA1c and CAL ($\rho = 0.420$, $p < 0.001$), indicating that greater periodontal attachment loss was associated with higher HbA1c levels. Additionally, HbA1c was also positively correlated with DMFT ($\rho = 0.248$, $p = 0.027$), suggesting a link between increased dental caries experience and poor glycemic control. JAK1 showed a moderate positive correlation with SLPI ($\rho = 0.532$, $p < 0.001$), whereas no significant correlations were observed between the other clinical parameters and JAK1. SLPI was not significantly correlated with HbA1c, DMFT, or CAL. No significant correlations were detected between CAL and either salivary biomarker (JAK1 or SLPI), nor between DMFT and the salivary biomarkers, as shown in Table 4.

Multiple Linear Regression

To recognize factors associated with DMFT scores, Multiple linear regression analysis was used. The model included age, salivary JAK1, SLPI, HbA1c and clinical attachment loss (CAL) as independent variables. None of the predictors showed a statistically significant association with DMFT scores. Age demonstrated a marginal positive association with DMFT ($B = 0.136$, $p = 0.092$), but this did not reach statistical significance. HbA1c ($B = 0.225$, $p = 0.353$), JAK1 ($B = 3.311$, $p = 0.260$), SLPI ($B = -1.128$, $p = 0.559$), and CAL ($B = 0.069$, $p = 0.795$) were also not significantly associated with DMFT scores. These findings suggest that within the studied sample, none of the included variables were significant predictors of dental caries experience as measured by DMFT, as shown in Figure 1.

Multiple linear regression analysis was utilized to assess the association between age, salivary JAK1, SLPI, HbA1c, and DMFT scores with the dependent variable (CAL). The model revealed that both HbA1c and age were statistically significant predictors. Specifically, age demonstrated a significant positive association ($B = 0.152$, $SE = 0.031$, standardized $\beta = 0.486$, 95% CI: 0.090–0.214, $p < 0.001$), indicating that the dependent variable increased with increasing age. Similarly, HbA1c showed a significant positive effect ($B = 0.331$, $SE = 0.099$, standardized $\beta = 0.315$, 95% CI: 0.134–0.529, $p = 0.001$), indicating that higher glycemic levels were associated with higher outcome measure values. In contrast, DMFT as well as the salivary biomarkers JAK1 and SLPI scores were not significantly associated with the outcome. Salivary JAK1 ($B = 0.597$, $SE = 1.291$, standardized $\beta = 0.050$, 95% CI: –1.975 to 3.168, $p = 0.645$). Similarly, SLPI was not significantly associated with the outcome ($B = –0.639$, $SE = 0.844$, standardized $\beta = –0.081$, 95% CI: –2.321 to 1.043, $p = 0.452$). DMFT also did not exhibit a statistically significant effect within the regression model ($B = 0.013$, $SE = 0.051$, standardized $\beta = 0.025$, 95% CI: –0.088 to 0.115, $p = 0.795$). These findings suggest that among the studied variables, only age and glycemic control (HbA1c) had a meaningful influence on the dependent outcome, whereas salivary biomarkers and dental caries index (DMFT) did not show significant associations in this analysis, as shown in Figure 2.

Table 1: Descriptive statistics for the number or percentage of the demographic characteristics, clinical parameters, and salivary biomarkers.

	Variables	Frequency (%)
Gender **Male** **Female**		 35 (43.8%) 45 (56.3%)
Age (Year)	Median (IQR)	48.0 (41.5-54.0)
HbA1c (%)	Median (IQR)	6.5 (5.6-8.1)
JAK1 (ng/mL)	Median (IQR)	0.51 (0.43-0.60)
SLPI (ng/mL)	Median (IQR)	0.76 (0.61-0.91)
DMFT	Mean ± SD	10.83 ± 4.89
CAL (mm)	Median (IQR)	2.83 (0.0-4.0)
Salivary pH	Median (IQR)	6.0 (6.0-7.0)

Table 2: Demographic and Clinical Characteristics Across Glycemic Status Groups.

Variable		Normal (n=20)	Prediabetic (n=20)	Controlled DM (n=20)	Uncontrolled DM (n=20)
Age	Median (IQR)	39.5 (34.0-49.5)	50.0 (46.0-54.5)	50.5 (45.0-54.0)	45.5 (44.5-51.5)
Sex					
Male	n (%)	9 (45.0%)	8 (40.0%)	11 (55.0%)	7 (35.0%)
Female		11 (55.0%)	12 (40.0%)	9 (45.0%)	133 (65.0%)
HbA1c (%)	Median (IQR)	5.05 (4.9-5.3)	6.25 (6.0-6.4)	6.95 (6.8-7.0)	10.7 (9.8-12.4)
Salivary pH	Median (IQR)	6.5 (6.0-7.0)	6.0 (6.0-7.0)	6.0 (6.0-7.0)	6.0 (6.0-7.0)

*Determined by Kruskal-Wallis Test, **Determined by Chi-square Test

Table 3: Comparison of Biomarker Levels, Dental Caries, and Periodontal Status Across Glycemic Groups.

Variable		**Normal (n=20)**	**Prediabetic (n=20)**	**Controlled DM (n=20)**	**Uncontrolled DM (n=20)**	***p-value***
JAK1(ng/mL)	Median (IQR)	0.51 (0.41-0.60)	0.48 (0.41-0.58)	0.58 (0.45-0.63)	0.52 (0.42-0.59)	0.423**
SLPI (ng/mL)	Median (IQR)	0.70 (0.52-0.83)	0.77 (0.62-0.97)	0.77 (0.66-0.91)	0.76 (0.60-0.96)	0.940**
DMFT	Mean± SD	8.1 ± 4.3	11.95 ± 4.2	12.0 ± 5.9	11.3 ± 4.2	0.031*
CAL (mm)	Median (IQR)	0.0 (0.0-1.6)	2.0 (1.0-3.9)	3.7 (1.8-4.6)	4.0 (2.0-5.8)	0.006**

*Determined by one-way ANOVA Test, **Determined by Kruskal-Wallis Test

Table 4: Spearman's Correlation Coefficients between HbA1c, salivary biomarkers (JAK1, SLPI) and clinical parameters (CAL, DMFT).

Parameters	**HbA1c (ρ)**	***P-value***	**JAK1 (ρ)**	***P-value***	**SLPI (ρ)**	***P-value***	**CAL (ρ)**	***P-value***	**DMFT (ρ)**	***P-value***
HbA1c	1.0	-	0.071	0.533	0.144	0.204	0.420	<0.001	0.248	0.027
JAK1	0.071	0.533	1	-	0.532	<0.001	-0.113	0.319	0.103	0.364
SLPI	0.144	0.204	0.532	<0.001	1	-	0.038	0.736	0.150	0.183
CAL	0.420	<0.001	-0.113	0.319	0.038	0.736	1	-	0.137	0.226
DMFT	0.248	0.027	0.103	0.364	0.150	0.183	0.137	0.226	1	-

Spearman's Correlation (ρ)

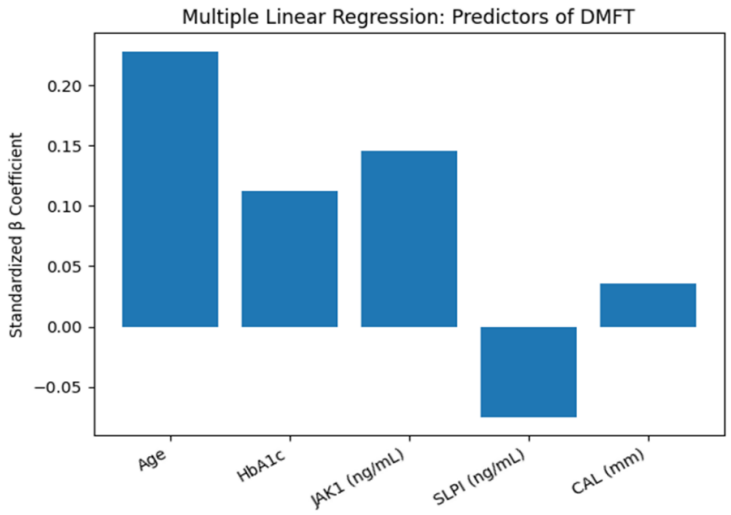

Figure 1: Multiple Linear Regression Analysis of the Association Between Age, HbA1c, Salivary Biomarkers (JAK1 and SLPI), Clinical Attachment Loss (CAL), and DMFT Scores.

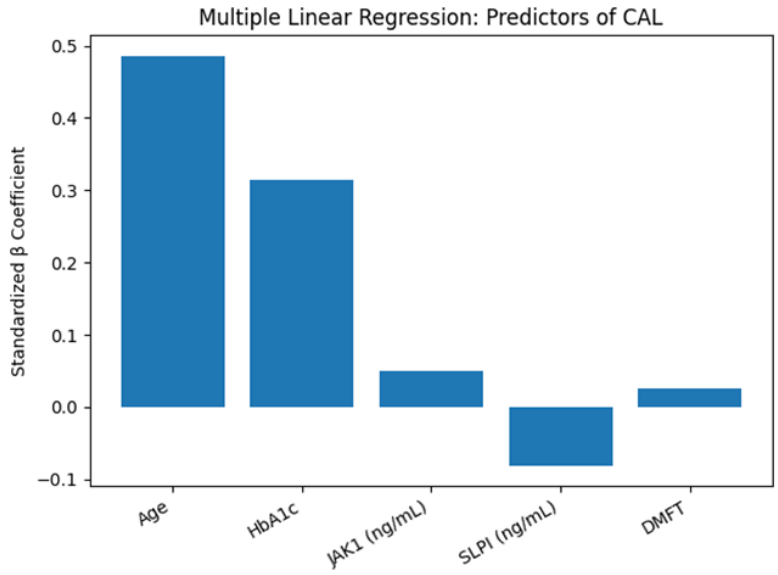

Figure 2: Multiple Linear Regression Analysis of the Association Between Age, HbA1c, Salivary Biomarkers (JAK1 and SLPI), DMFT scores, and Clinical Attachment Loss (CAL).

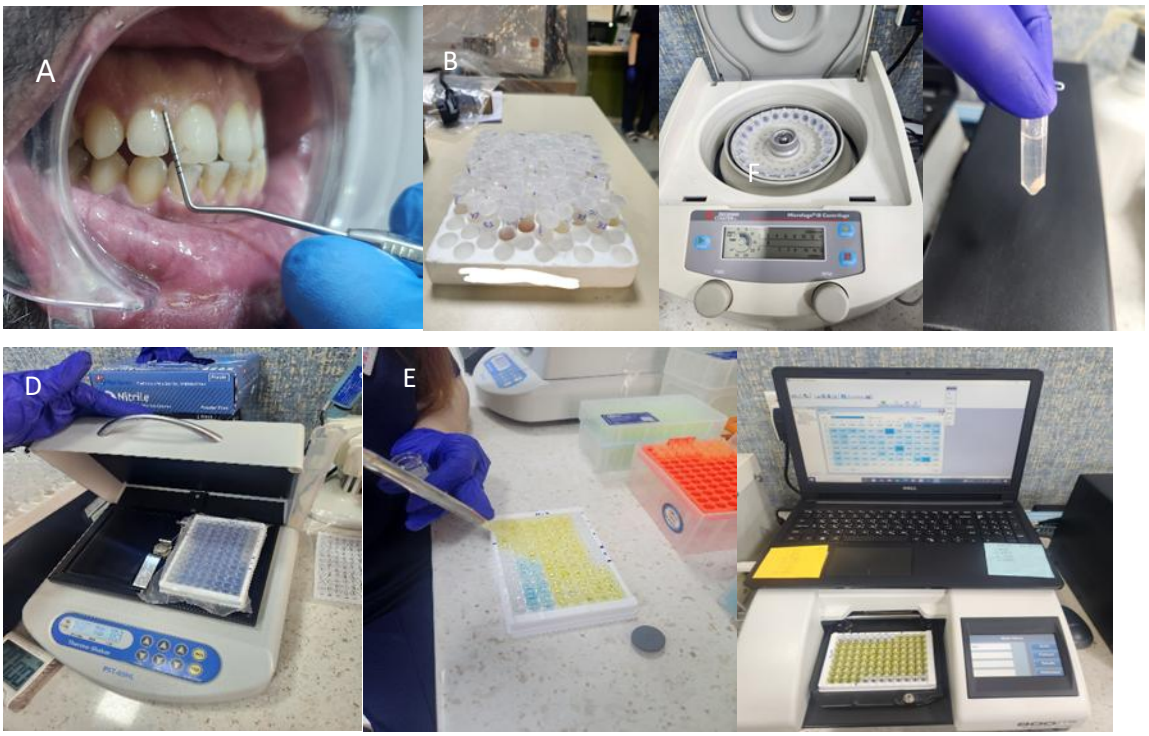

Figure 3: **A:** Full mouth clinical data collection. **B:** Saliva collection from participants. **C:** Saliva samples centrifugation. **D:** Obtaining supernatant. **E:** Saliva samples in incubator. **F:** Color changing of saliva samples after adding Stop Solution to each well. **G:** Determining the optical density of each well using a microplate reader.

Discussion

Type II diabetes mellitus is a substantial worldwide health issue. At present, the diagnosis of diabetes mellitus is determined through the invasive assessment of serological parameters, which may be discomforting for the patient. It is intriguing that novel diagnostic methods, such as the use of non-invasive methods to obtain specimens such as saliva, are currently being implemented[20].

New and recurrent dental lesions are more likely to develop in diabetic patients, and a decrease in the salivary purifying and buffering capacity can increase the incidence of tooth decay. Inadequate glycemic control can be linked to the outbreak and progression of gingivitis, periodontitis, and alveolar bone loss. The prevalence of severe periodontitis in nondiabetic patients is 39%, while in diabetic patients it is 59.6%[21].

Saliva is an appropriate biomaterial that offers a modern and readily accessible physiological fluid that can be obtained in a non-invasive manner and evaluated using a variety of analytical methods[22]. The Enzyme-Linked Immunosorbent Assay (ELISA) is a widely used method for the detection and quantification of specific proteins, such as salivary biomarkers, in biological samples[23].

The mean age of participants demonstrated a progressive increase from the normal to uncontrolled diabetic group, which is consistent with the well-established trend that impaired glucose tolerance and type 2 diabetes become more prevalent as age increases. This finding is consistent with the findings of Ahmed et al. (2017) and Al-Maweri et al. (2021), who attributed this pattern to the accumulation of metabolic risk factors over time [16,24]. The sex distribution in our sample was relatively balanced, with no statistically significant differences between the categories. This parity minimizes the likelihood of sex-related confounding effects in biomarker and oral health outcomes, as hormonal and behavioral factors have been demonstrated to affect salivary composition and periodontal status[25].

Although previous research has established a correlation between systemic inflammation in diabetes and JAK-STAT signaling pathways, the salivary levels observed in this study did not adequately reflect these associations[26]. The glycemic groups did not show any statistically significant differences in the salivary concentrations of JAK1 and SLPI. Similarly, SLPI displayed constant levels across all groups, suggesting that its expression may be controlled by processes other than glucose management, such as systemic immunological responses or local oral inflammation[10]. The salivary levels found in this investigation would reflect localized rather than systemic inflammatory activity.

Our results differ from a study conducted by Sun et al, 2024 in which blood SLPI levels were observed to fluctuate greatly across healthy controls, individuals with diabetes, and patients with varied stages of diabetic kidney disease (DKD). The concentrations were progressively higher at more advanced stages of illness. The different regulation mechanisms and compartmentalization of these biomarkers in systemic circulation vs oral fluids may be indicative of the considerable disparities in serum—but not salivary—SLPI levels[27].

Although there were no significant differences in salivary JAK1 levels across glycemic groups or clinical parameters in the current investigation, there was a positive association between JAK1 and SLPI ($r = 0.532$, $p < 0.001$), suggesting a potential role in regulating the oral immune system. In contrast, Yang et al. (2023) demonstrated that Inhibiting JAK1 in human periodontal ligament stem cells reduced inflammatory damage and enhanced osteogenic differentiation. The current study investigated total salivary JAK1, which may not reflect its intracellular activity, while Yang et al. focused on activated JAK1 (phosphorylated form) under inflammatory conditions. The discrepancy in observed outcomes is likely related to differences in study models—in vitro cellular stress versus in vivo salivary biomarker analysis[28].

Our findings did not show a statistically significant association between the presence or severity of dental caries and JAK1 concentrations. The study suggests that salivary JAK1 may not be a sensitive or specific biomarker for caries-related processes in the oral environment, despite its well-known role in inflammatory signaling through the JAK-STAT pathway, consistent with the results of a study by Paqué et al. (2023). Although participants with poor oral health exhibited a decline in SLPI, the glycemic groups did not show significant differences in salivary SLPI levels, and these levels were not strongly associated with caries or periodontal status. This is consistent with the findings of a study by Ahmed and Al-Jubouri (2017). The combined findings of both studies indicate that SLPI levels may not be a dependable diagnostic indicator for periodontal disease or caries, even if it may have a protective effect on oral health[16,29].

The results of the current study indicate that clinical oral health parameters, including periodontal status (CAL) and dental caries experience (DMFT), varied significantly among various glycemic control groups. In comparison to the healthy participants, members of the diabetic groups, particularly those with controlled and uncontrolled diabetes, exhibited significantly greater clinical attachment loss and higher DMFT, which is similar to

several other studies[30-33]. Although diabetes mellitus has been associated with an elevated risk of dental caries due to changes in pH, salivary composition, and the host immune response, this association is not inevitable. There is evidence to suggest that individuals who adhere to well-regulated oral hygiene practices, including interdental cleansing, regular toothbrushing and routine professional dental care, can keep caries rates that are comparable to those of non-diabetic individuals[34,35].

In this study, the uncontrolled diabetic group exhibited a substantially higher level of Clinical Attachment Loss (CAL) than the controlled diabetics and healthy individuals. This result is consistent with other studies, who reported that higher CAL values were found in patients with inadequately controlled type 2 diabetes than both well-controlled diabetics and non-diabetic controls[36-38]. Compared with the study by Luong et al. (2021), notable differences in methodology are evident. Although our research was based on clinical measurements of CAL and periodontal status in diabetic patients, Luong et al. conducted a thorough examination of the molecular mechanisms linking periodontitis and diabetes. Their analysis underscores common inflammatory pathways, including elevated pro-inflammatory cytokines (e.g., TNF-α, IL-6), oxidative stress, and altered immune responses. These pathways contribute to both periodontal tissue disintegration and impaired glycemic regulation. Although the two studies differ in their methodologies, they both acknowledge that diabetes has a substantial impact on periodontal health[39].

The uncontrolled diabetic participants in the current study exhibited a lower salivary pH, with the lowest values compared to the normal healthy group. This acidic shift in the salivary environment may increase susceptibility to dental caries and periodontal destruction, emphasizing the adverse effects of poor glycemic control on oral homeostasis. Prathibha et al. also reported a reduction in salivary pH among type 2 diabetes mellitus (T2DM) patients when compared to non-diabetics[40].

The present study has several limitations. First, the relatively small sample size and single-center recruitment may restrict the generalizability of the findings to the broader population. Additionally, potential confounding factors such as oral hygiene practices, dietary habits, and medication used were not fully controlled and may have influenced the results. Another limitation of this study is its cross-sectional design, which limits the ability to establish causal relationships among the variables studied. Also, salivary biomarker levels can be affected by physiological and environmental factors such as saliva flow rate. The absence of longitudinal follow-up limits the ability to assess changes in biomarker levels and periodontal status over time. Finally, the study lacks a comparison of inflammatory markers.

Conclusion

This study reveals that salivary JAK1 and SLPI levels do not significantly differ across those individuals with varying glycemic control, suggesting limited diagnostic value of these biomarkers for diabetes detection or oral disease evaluation. Nonetheless, their positive correlation shows a possible interaction in local immune regulation within the oral cavity. Clinically, diabetic patients- particularly those with poor glycemic control- exhibited greater clinical attachment loss, higher DMFT scores, and lower salivary pH, emphasizing the detrimental impact of hyperglycemia on oral health. These findings reinforce the importance of maintaining optimal glycemic control and strict oral hygiene practices to prevent caries progression and periodontal deterioration in patients with diabetes.

Declarations

Ethics Approval and Informed Consent (Institutional Review Board) Statement: This research was approved by the Ethics Committee of the College of Dentistry, University of Sulaimani, Iraq, under application No. (COD-EC-24-0033), Issued on 16/12/2024. Informed consent statement: Written informed consent was obtained from all participants prior to their inclusion in the study.

Author Contributions: RAS; Conceptualization, Writing the manuscript, software and validation, data collection and curation, and project administration. FAK: Writing and Supervision. All authors have read and agreed to the published version of the manuscript.

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