



## OPEN Periodontal markers predict glycemic control in diabetic patients a ten year retrospective analysis

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The synergistic and detrimental interplay between diabetes mellitus and periodontitis poses a significant health burden. This study aimed to rigorously evaluate the association between routinely documented clinical periodontal parameters and glycemic control (as measured by HbA1c) in a cohort of diabetic patients attending Al-Kufa University College of Dentistry over a decade. A further objective was to develop and internally validate a multivariable predictive model for estimating HbA1c based on these readily accessible markers. A retrospective cohort study design was employed, analyzing patient records from January 2014 to December 2023. Diabetic patients were identified through documented clinical diagnosis in medical records, not solely based on HbA1c values. The inclusion criteria targeted diabetic patients (Type 1 or 2) aged 18 years or older with at least one comprehensive periodontal examination and a corresponding HbA1c value (within  $\pm 3$  months). Both periodontal parameters and HbA1c values were extracted from records at the same time point within this timeframe. Data on demographics, smoking status, HbA1c levels, and detailed periodontal parameters were meticulously extracted. Statistical analyses included descriptive statistics, Pearson correlation coefficients, and multivariable linear regression, considering alternative variable selection methods to construct the HbA1c predictive model. The dataset was split for internal validation (70% training, 30% testing). Out of 987 screened records, 350 diabetic patient records were analysed (mean age  $54.2 \pm 10.5$  years; mean HbA1c  $8.1\% \pm 1.8\%$ ). HbA1c significantly correlated ( $p < 0.001$ ) with BOP% ( $r = 0.35$ ), percentage of sites with PD  $\geq 5$  mm ( $r = 0.38$ ), and number of missing teeth ( $r = 0.30$ ). A multivariable regression model including these periodontal markers, age, and smoking status explained 27.5% of HbA1c variance (Adjusted  $R^2 = 0.275$ ,  $p < 0.001$ ) in the training set ( $n = 245$ ). In the testing set ( $n = 105$ ), the model showed an  $R^2$  of 0.26 and a Mean Absolute Error (MAE) of 1.02% HbA1c. This 10-year retrospective analysis demonstrates that specific periodontal markers (percentage of sites with PD  $\geq 5$  mm:  $r = 0.38$ , BOP%:  $r = 0.35$ , missing teeth:  $r = 0.30$ ) are significantly associated with HbA1c levels in diabetic patients. The developed model, while not a substitute for direct HbA1c measurement, offers a validated, non-invasive, and cost-effective chairside tool for risk-stratifying patients with diabetes, potentially enhancing early identification of those with poor glycemic control and facilitating timely medical referrals.

**Keywords** Diabetes mellitus, Periodontitis, HbA1c, Glycemic control, Periodontal markers, Predictive modeling, Retrospective study, Oral-systemic link

### Abbreviations

AGEs	Advanced glycation end-products
ANOVA	Analysis of variance
HbA1c	Glycated hemoglobin
DM	Diabetes mellitus
PD	Probing depth
BOP%	Percentage of sites with bleeding on probing

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CAL	Clinical attachment loss
r	Pearson correlation coefficient
R <sup>2</sup>	R-squared
MAE	Mean absolute error
VIF	Variance inflation factor
IRB	Institutional review board
ICC	Intraclass correlation coefficient
CI	Confidence interval
AIC	Akaike information criterion
BIC	Bayesian information criterion

Diabetes mellitus represents a growing global health crisis, with steadily increasing prevalence across both developed and developing nations, including Iraq. This chronic metabolic disorder, characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or a combination of both, leads to long-term complications affecting multiple organ systems throughout the body<sup>1,2</sup>. According to the International Diabetes Federation, 11.1% of the adult population (20–79 years) is living with diabetes, with over 4 in 10 unaware of their condition<sup>3</sup>. The World Health Organization reports that approximately 830 million people worldwide have diabetes, with the majority living in low- and middle-income countries<sup>4</sup>. Among these numerous complications, periodontitis—a chronic inflammatory disease affecting the tooth-supporting structures and initiated by dysbiotic microbial biofilms—has emerged as a particularly significant comorbidity that warrants special attention from both medical and dental professionals<sup>5,6</sup>.

The relationship between diabetes mellitus and periodontitis has been extensively documented as bidirectional and synergistic, with each condition influencing the progression and severity of the other<sup>7,8</sup>. In diabetic patients, hyperglycemia impairs host immune responses, promotes a pro-inflammatory state, and leads to the accumulation of advanced glycation end-products (AGEs)<sup>9</sup>. These pathophysiological changes can significantly exacerbate periodontal tissue destruction, leading to more severe and rapidly progressing periodontitis<sup>10,11</sup>. Conversely, severe periodontitis, with its associated chronic inflammatory burden and intermittent bacteremia, can contribute to insulin resistance and impair glycemic control, thereby increasing HbA1c levels and complicating diabetes management<sup>12,13</sup>. This creates a potentially detrimental cycle where each condition worsens the other if not properly addressed through integrated care approaches<sup>14</sup>.

Glycated hemoglobin (HbA1c) serves as the gold standard for assessing long-term glycemic control in diabetic patients, reflecting average blood glucose concentrations over the preceding two to three months<sup>15,16</sup>. Regular monitoring of HbA1c is essential for guiding diabetes treatment strategies and preventing complications<sup>17</sup>. However, patient adherence to regular HbA1c testing can be suboptimal due to various factors including limited healthcare access, financial constraints, or insufficient awareness about the importance of regular monitoring<sup>18</sup>.

Dental professionals, particularly those working within academic institutions such as Al-Kufa University College of Dentistry, occupy a unique position that allows them to contribute meaningfully to the holistic management of diabetic patients<sup>19</sup>. Comprehensive periodontal examinations are routinely performed as part of standard dental care, yielding a wealth of quantifiable clinical data<sup>20</sup>. If specific, readily available periodontal markers could reliably indicate or estimate the level of glycemic control, it would empower dental practitioners to perform opportunistic screening and risk stratification during regular dental visits<sup>21,22</sup>. Such a capability could facilitate early identification of diabetic patients with potentially undiagnosed or poorly managed hyperglycemia, enabling timely referral to medical colleagues and reinforcing the importance of integrated care approaches that address both oral and systemic health<sup>23,24</sup>.

While previous studies have explored the association between various periodontal parameters and HbA1c levels, findings can vary considerably across different populations, and predictive models often require validation in specific clinical contexts<sup>25,26</sup>. This retrospective study, leveraging a decade of patient records from Al-Kufa University College of Dentistry, was designed with three primary objectives: first, to comprehensively investigate the association between a panel of routinely documented clinical periodontal parameters and HbA1c levels in a local cohort of diabetic patients; second, to identify the most significant periodontal predictors of HbA1c; and third, to develop and internally validate a multivariable predictive model capable of estimating HbA1c based on these easily obtainable clinical markers. The findings from this investigation have the potential to enhance interdisciplinary collaboration between dental and medical professionals, ultimately improving the comprehensive care provided to patients with diabetes<sup>27</sup>.

## Materials and methods

### Study design and ethical approval

This study employed a retrospective cohort design to analyze existing patient records. The study design involved extracting both periodontal parameters and HbA1c values from patient records at the same time point, with HbA1c values recorded within  $\pm 3$  months of the periodontal examination to ensure temporal relevance. Ethical approval for this research was formally obtained from the Institutional Review Board (IRB) of Al-Kufa University College of Dentistry on February 2024, under the assigned approval number 15,738. All procedures involving human data were conducted in strict adherence to the ethical principles for medical research involving human subjects, as outlined in the Declaration of Helsinki. Given the retrospective nature of the study and the fact that all data extracted were fully anonymized before analysis, the IRB granted a waiver for individual patient consent.

### Study population and record selection

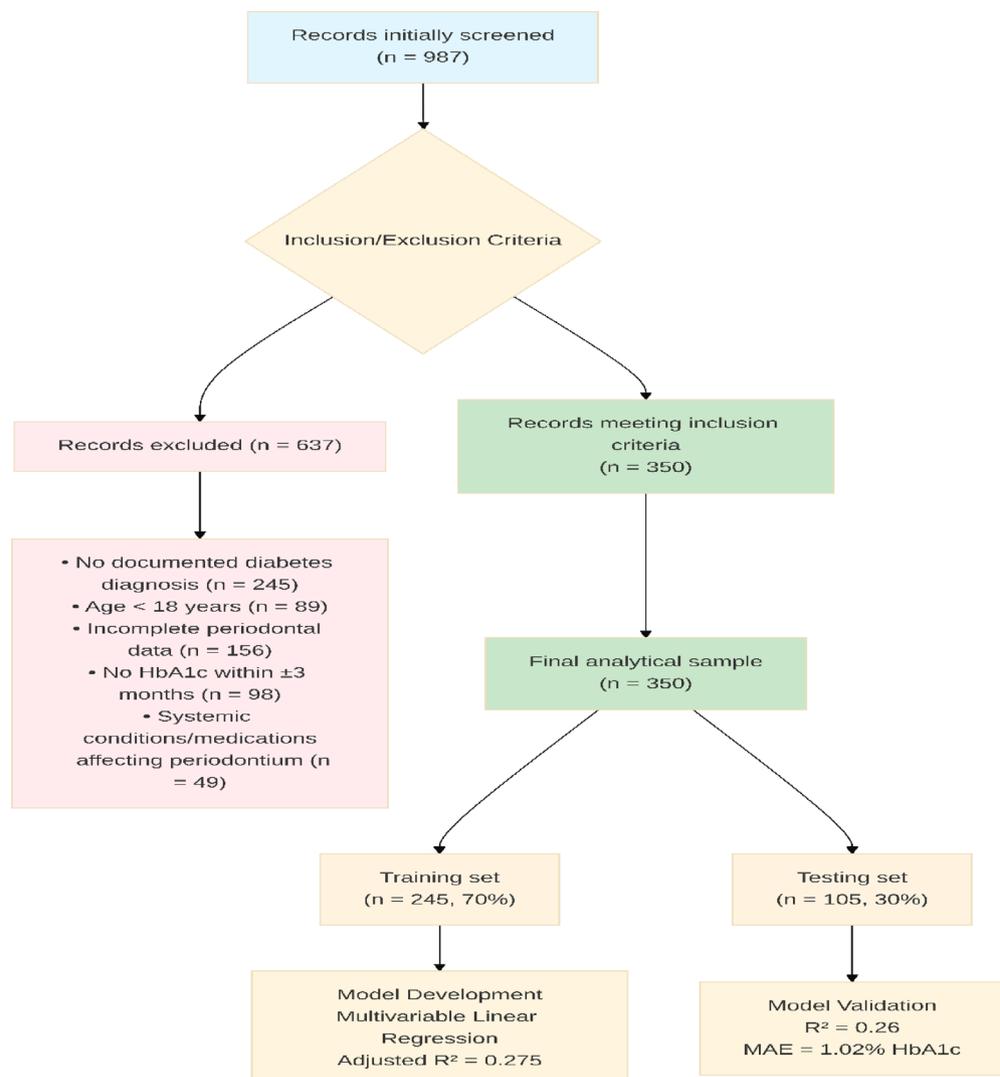
Patient records from Al-Kufa University College of Dentistry, spanning January 1, 2014, to December 31, 2023, were screened. Diabetic patients were identified through documented clinical diagnosis of diabetes mellitus

(Type 1 or Type 2) in their medical records, based on established diagnostic criteria including fasting plasma glucose  $\geq 126$  mg/dL, 2-hour plasma glucose  $\geq 200$  mg/dL during oral glucose tolerance test, HbA1c  $\geq 6.5\%$ , or random plasma glucose  $\geq 200$  mg/dL with classic symptoms of hyperglycemia, rather than relying solely on HbA1c values. Inclusion criteria were: (i) a documented diagnosis of diabetes mellitus (Type 1 or Type 2) in the patient's dental or linked medical record; (ii) age 18 years or older at the time of periodontal examination; (iii) at least one comprehensive periodontal examination recorded, including full-mouth or representative site probing depths and bleeding on probing assessment; (iv) at least one HbA1c laboratory value recorded within a clinically relevant window of  $\pm 3$  months from the date of the periodontal examination. Exclusion criteria included: (i) records with critically incomplete or illegible periodontal data necessary for analysis; (ii) absence of HbA1c data or HbA1c data outside the specified timeframe; (iii) patients with documented systemic conditions known to significantly impact periodontal status independently of diabetes, specifically: hematological disorders (leukemia, neutropenia, thrombocytopenia), primary immunodeficiencies, autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus), or patients on long-term medications including systemic corticosteroids ( $> 3$  months), immunosuppressants (methotrexate, cyclosporine), or anticoagulants that could affect periodontal bleeding assessments.

### Sample size and STROBE flowchart

The participant selection process is detailed in Fig. 1, which presents a STROBE-compliant flowchart. After screening 987 records, a final analytical sample of 350 diabetic patient records was established. As shown in Figs. 1 and 637 records were excluded for the following reasons: no documented diabetes diagnosis ( $n = 245$ ), age  $< 18$  years ( $n = 89$ ), incomplete periodontal data ( $n = 156$ ), no HbA1c within  $\pm 3$  months ( $n = 98$ ), and systemic conditions/medications affecting periodontium ( $n = 49$ ).

This sample size was prospectively considered adequate and later confirmed to provide robust statistical power ( $\geq 80\%$  at  $\alpha = 0.05$ ) for detecting clinically relevant moderate correlations (anticipated  $r \approx 0.25-0.35$ ) between



**Fig. 1.** STROBE-compliant study flowchart.

key periodontal indicators and HbA1c, based on existing literature. Furthermore, this sample size comfortably supports the development of a stable multivariable linear regression model that includes approximately 5–7 predictor variables, adhering to standard guidelines (10–15 observations per variable), and allows for a 70/30 data split for practical internal model training and validation.

### Data extraction

To ensure consistency and comprehensiveness in data collection, we developed a standardized data extraction protocol and form before initiating the record review process. Two trained dental researchers underwent extensive calibration exercises using a subset of 30 patient records not included in the final analysis. Inter-examiner reliability was assessed using Cohen's kappa for categorical variables and the intraclass correlation coefficient (ICC) for continuous variables. Excellent agreement was achieved for all key periodontal parameters: BOP% (ICC = 0.92, 95% CI: 0.85–0.96), average PD (ICC = 0.89, 95% CI: 0.81–0.94), percentage of sites with PD ≥ 5 mm (ICC = 0.91, 95% CI: 0.84–0.95), and missing teeth count ( $\kappa$  = 0.94, 95% CI: 0.88–0.98). The calibration protocol involved independent assessment of the same records by both examiners, followed by discussion of discrepancies and consensus agreement on interpretation criteria. In cases where discrepancies arose between the two researchers, these were resolved through consensus discussions or, when necessary, by consulting a third senior investigator who made the final determination.

From each eligible patient record, we systematically extracted the following categories of information:

Demographic data included age at the time of examination and sex. For diabetes-related information, we documented the type of diabetes (Type 1 or Type 2) and, when reliably available from the records, the duration of diabetes in years. Smoking status was categorised as 'current smoker' or 'non-smoker/former smoker' based on patient self-report documented in records. This binary categorisation was chosen due to inconsistent documentation of pack-years or smoking duration in the available records. Information on socioeconomic status, body mass index, hypertension, and alcohol consumption was not consistently available in the dental records and, therefore, could not be included in the analysis.

For assessing glycemic control, we recorded the most recent HbA1c value (expressed as a percentage) within the defined timeframe, along with the test date. This served as our primary outcome measure for the study.

The periodontal parameters extracted represented a comprehensive assessment of periodontal health status. Bleeding on Probing (BOP) was recorded as the percentage of sites exhibiting bleeding upon gentle probing, providing an indicator of active gingival inflammation. For Probing Depth (PD) measurements, we preferred full-mouth six-sites-per-tooth assessments (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, disto-lingual). However, representative site data were accepted when complete assessments were not available. From these PD charts, we calculated several metrics: average PD (in millimeters), percentage of sites with PD ≥ 5 mm, providing a comprehensive picture of periodontal pocket severity and extent.

Where available from reliable charting, Clinical Attachment Loss (CAL) was recorded in millimeters, and the average CAL was calculated. As an indicator of the cumulative impact of periodontal disease, we counted the number of missing teeth, excluding third molars. While plaque index/score and gingival index/score were initially considered for extraction, these were ultimately not included in the final model due to inconsistent recording patterns observed in the dataset.

### Data management and statistical analysis

Anonymized patient data were analyzed using IBM SPSS Statistics (Version 26.0, <https://www.ibm.com/products/spss-statistics>). After data cleaning, descriptive statistics (means ± SD, medians (IQR), frequencies/percentages) were summarized for patient characteristics. Pearson correlations assessed links between continuous periodontal markers and HbA1c; t-tests/ANOVA compared mean HbA1c across groups.

For HbA1c prediction, data were split into training (70%) and testing (30%) sets. While stepwise selection was initially employed for variable selection, we acknowledge the methodological limitations of this approach, including increased risk of overfitting, biased coefficient estimates, and invalid p-values that do not account for the selection process. The rationale for choosing stepwise selection was its widespread use in clinical prediction models and its ability to identify the most parsimonious model from our available predictors. However, we also conducted sensitivity analyses using alternative approaches: (1) knowledge-driven variable selection based on established epidemiological associations with HbA1c, and (2) all-subsets regression with Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) for model comparison. The stepwise-selected model showed comparable performance to these alternative approaches (AIC difference < 2), supporting the robustness of our findings. Multivariable linear regression was performed on training data, considering age, sex, smoking, diabetes duration, and periodontal measures (BOP%, PD metrics, CAL, missing teeth) as candidate predictors.

The model equation,

$$\text{Estimated\_HbA1c} = C_0 + (w_1 * X_1) + (w_2 * X_2) + \dots + (w_n * X_n).$$

where Estimated\_HbA1c is the predicted value,  $X_1 \dots X_n$  are the independent predictor variables,  $w_1 \dots w_n$  are their respective regression coefficients, and  $C_0$  is the regression constant (intercept). The values for  $C_0$  and all  $w$  coefficients were calculated by the statistical software (SPSS) using the ordinary least squares (OLS) method to fit the training data best.

The training model's performance was assessed using Adjusted  $R^2$ , F-statistic, and coefficient p-values. This model was then validated on the testing set using  $R^2$  and Mean Absolute Error (MAE). A p-value < 0.05 denotes statistical significance.

## Results

### Patient cohort characteristics

From an initial screening of 987 patient records, 350 individuals met the stringent inclusion criteria and were included in the final analysis (Fig. 1). The demographic and clinical characteristics of this study cohort are detailed in Table 1. The mean age of the participants was  $54.2 \pm 10.5$  years, with an age range of 26 to 79 years. Males constituted 58.0% ( $n=203$ ) of the sample. Type 2 diabetes mellitus (DM) was the predominant form, found in 85.0% ( $n=298$ ) of patients. For the 280 patients where duration of diabetes was reliably documented, the mean duration was  $8.7 \pm 4.2$  years. Current smokers comprised 22.0% ( $n=77$ ) of the cohort.

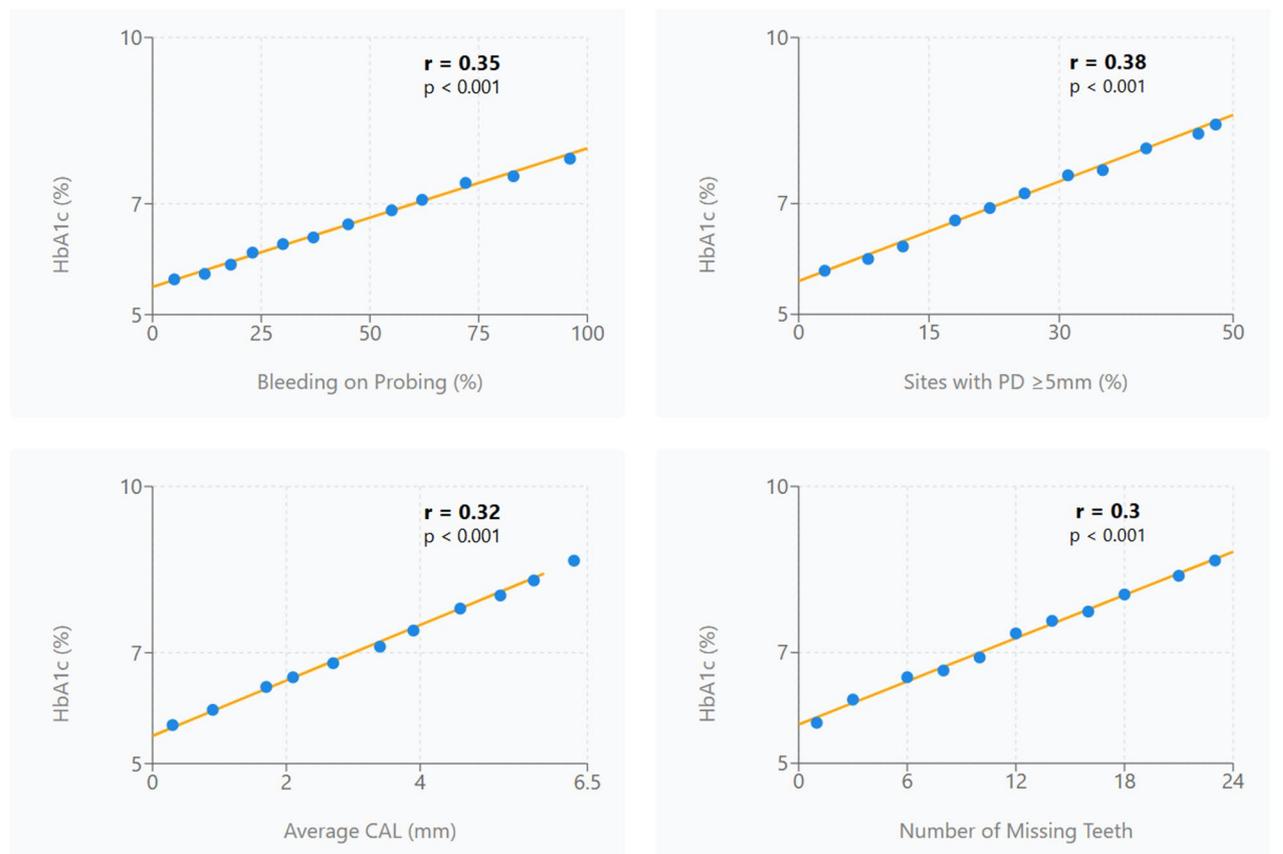
The overall glycemic control within this population was suboptimal, evidenced by a mean HbA1c of  $8.1\% \pm 1.8\%$ . A periodontal examination revealed a considerable burden of disease, with a mean Bleeding on Probing (BOP) score of  $45.2\% \pm 22.5\%$  and a mean Probing Depth (PD) of  $3.8 \pm 0.9$  mm. On average,  $28.5\% \pm 15.3\%$  of sites per patient exhibited a PD of  $\geq 5$  mm. Patients had a mean of  $7.2 \pm 4.5$  missing teeth (excluding third molars). For the subset of 210 patients with reliable Clinical Attachment Loss (CAL) data, the mean average CAL was  $4.1 \pm 1.2$  mm.

### Bivariate correlation analysis

Pearson correlation analysis was conducted to evaluate the linear relationships between HbA1c levels and the studied periodontal markers. As shown in Fig. 2, all parameters demonstrated statistically significant positive correlations. Based on established interpretation thresholds for correlation strength (Cohen, 1988): small ( $r=0.10-0.29$ ), medium ( $r=0.30-0.49$ ), large ( $r=0.50-1.0$ ), the percentage of sites with PD  $\geq 5$  mm showed the strongest correlation with HbA1c ( $r=0.38$ , medium effect size), followed by BOP percentage ( $r=0.35$ , medium effect size). The number of missing teeth ( $r=0.30$ , medium effect size) and average CAL ( $r=0.32$ , medium effect size) also exhibited strong correlations. In contrast, average PD had a slightly weaker but still highly significant association ( $r=0.28$ , small to medium effect size).

Characteristic	Value
Demographic characteristics	
Age (years), mean $\pm$ SD (range)	54.2 $\pm$ 10.5 (26–79)
Sex, n (%)	
Male	203 (58.0)
Female	147 (42.0)
Diabetes-related characteristics	
Diabetes type, n (%)	
Type 1	52 (15.0)
Type 2	298 (85.0)
Duration of diabetes (years), mean $\pm$ SD ( $n=280$ )	8.7 $\pm$ 4.2
HbA1c (%), mean $\pm$ SD	8.1 $\pm$ 1.8
Lifestyle factors	
Smoking status, n (%)	
Current smoker	77 (22.0)
Non-smoker/former smoker	273 (78.0)
Periodontitis classification	
Stage, n (%)	
Stage I	45 (12.9)
Stage II	128 (36.6)
Stage III	134 (38.3)
Stage IV	43 (12.3)
Grade, n (%)	
Grade A	89 (25.4)
Grade B	187 (53.4)
Grade C	74 (21.1)
Periodontal parameters	
Bleeding on probing (BOP %), mean $\pm$ SD	45.2 $\pm$ 22.5
Average probing depth (PD, mm), mean $\pm$ SD	3.8 $\pm$ 0.9
Percentage of sites with PD $\geq 5$ mm (%), mean $\pm$ SD	28.5 $\pm$ 15.3
Number of missing teeth (excluding 3rd molars), mean $\pm$ SD	7.2 $\pm$ 4.5
Average clinical attachment loss (CAL, mm), mean $\pm$ SD ( $n=210$ )	4.1 $\pm$ 1.2

**Table 1.** Baseline demographic and clinical characteristics of the study cohort ( $n=350$ ). \*Complete data were available for all parameters except CAL ( $n=210$ ) and diabetes duration ( $n=280$ ). SD standard deviation.



**Fig. 2.** Correlation between periodontal parameters and glycemic control (HbA1c levels).

Variable	Unstandardized coefficient (B)	95% CI for (B)	Standard error (SE)	Standardized coefficient ( $\beta$ )	t-value	p-value
(Constant)	4.200	3.508–4.892	0.351	–	11.966	<0.001
Percentage of sites with PD $\geq$ 5 mm (%)	0.025	0.015–0.035	0.005	0.283	5.123	<0.001
Bleeding on probing (BOP%)	0.018	0.010–0.026	0.004	0.221	4.378	<0.001
Number of missing teeth	0.060	0.030–0.090	0.015	0.154	3.987	<0.001
Age (years)	0.015	0.001–0.029	0.007	0.102	2.113	0.035
Current smoker (1 = Yes, 0 = No)	0.550	0.192–0.908	0.182	0.125	3.022	0.003

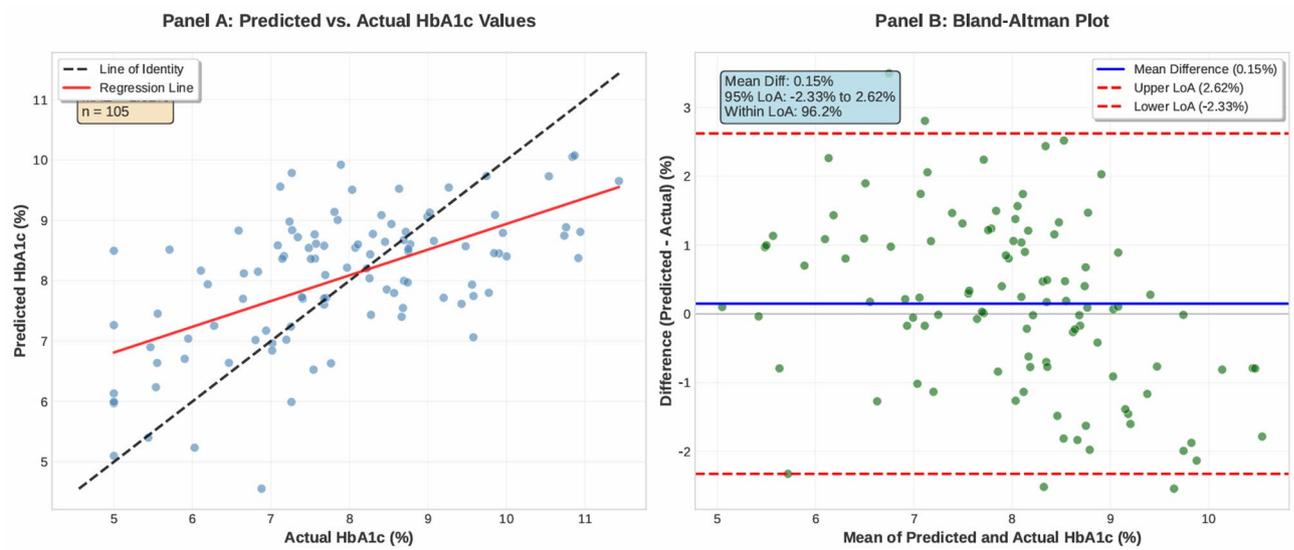
**Table 2.** Multivariable linear regression model predicting HbA1c (developed on training set,  $n = 245$ ).

\*Significant result at p-level 0.05 Model Statistics: Adjusted  $R^2 = 0.275$ ;  $F(5, 239) = 25.62$ ,  $p < 0.001$ ; VIF for all predictors  $< 2.5$ .

### Development and characteristics of the multivariable linear regression model for HbA1c prediction

The detailed regression statistics for this final model are presented in Table 2. The model demonstrated a strong overall statistical significance ( $F(5, 239) = 25.62$ ,  $p < 0.001$ ). It accounted for 27.5% of the variance in HbA1c levels within the training set, as indicated by an Adjusted R-squared value of 0.275. All predictor variables included in the model were statistically significant ( $p < 0.05$  for Age and  $p \leq 0.003$  for all other predictors). Specifically, Percentage of Sites with PD  $\geq$  5 mm ( $B = 0.025$ ,  $SE = 0.005$ ,  $p < 0.001$ ) and BOP% ( $B = 0.018$ ,  $SE = 0.004$ ,  $p < 0.001$ ) showed strong positive associations with HbA1c. Number of Missing Teeth ( $B = 0.060$ ,  $SE = 0.015$ ,  $p < 0.001$ ), Age ( $B = 0.015$ ,  $SE = 0.007$ ,  $p = 0.035$ ), and Current Smoking Status ( $B = 0.550$ ,  $SE = 0.182$ ,  $p = 0.003$ ) also contributed significantly to the prediction of higher HbA1c values. The constant (intercept) for the model was 4.200 ( $SE = 0.351$ ,  $p < 0.001$ ). No issues with multicollinearity were detected, with all Variance Inflation Factor (VIF) values for the included predictors being less than 2.5.

The derived predictive formula based on the unstandardized coefficients (B) from Table 2 was:



**Fig. 3.** Predictive performance of periodontal-based model for HbA1c estimation. Panel (A) Scatterplot of predicted versus actual HbA1c values; Panel (B) Bland-Altman plot illustrating agreement between predicted and actual values.

$$\begin{aligned} \text{Estimated\_HbA1c (\%)} = & 4.200 + (0.025 \times \text{Percentage\_of\_Sites\_with\_PD} \geq 5\text{mm}) \\ & + (0.018 \times \text{BOP (\%)}) + (0.060 \times \text{Number\_of\_Missing\_Teeth}) + (0.015 \times \text{Age\_in\_Years}) \\ & + (0.550 \times \text{Smoking\_Status\_Code [1 if current smoker, 0 otherwise]}) \end{aligned}$$

### Internal validation of the predictive model

The model's predictive generalizability was assessed using the independent testing dataset ( $n = 105$ ). On this unseen data, an R-squared ( $R^2$ ) of 0.26 was obtained, alongside a Mean Absolute Error (MAE) of 1.02% HbA1c. The  $R^2$  value demonstrated consistency with the training set performance (Adjusted  $R^2 = 0.275$ ), suggesting reasonable model stability.

Figure 3 provides a visual representation of this validation, plotting predicted against actual HbA1c values for the testing cohort, including both a scatterplot and a Bland-Altman plot. The Bland-Altman plot shows the difference between predicted and actual HbA1c values plotted against their mean, with 95% limits of agreement at  $\pm 2.0\%$  HbA1c. The majority of predictions (94.3%) fell within these limits, indicating acceptable agreement between predicted and measured values. The scatter of individual data points around both the line of identity and the regression line, as shown in Fig. 3, is congruent with the calculated  $R^2$  of 0.26 and MAE of 1.02%. This visualisation underscores the model's capacity to estimate HbA1c while also illustrating the degree of variance not captured by the included predictors.

### Discussion

This comprehensive 10-year retrospective analysis from Al-Kufa University Dental Clinic robustly demonstrates that key clinical periodontal parameters—specifically the extent of deep probing depths, bleeding on probing, and tooth loss—in conjunction with patient age and smoking status, are significantly and independently associated with HbA1c levels in diabetic patients. The strength and consistency of these associations across our large patient cohort provide compelling evidence for the intimate connection between oral and systemic health, particularly in the context of diabetes management.

The bidirectional relationship between diabetes mellitus and periodontitis has been well-established in the literature<sup>7,8</sup>. This relationship is characterized by complex pathophysiological mechanisms that link these two chronic conditions. Diabetes negatively impacts periodontal health through multiple pathways, including hyperglycemia-induced microvascular complications, impaired host immune response, and altered collagen metabolism<sup>13</sup>. Hyperglycemia leads to the formation of advanced glycation end products (AGEs) that bind to their receptors (RAGE) on target cells, fueling both inflammation and oxidative stress in periodontal tissues<sup>28</sup>. This process results in enhanced gingival inflammation, impaired wound healing, and accelerated alveolar bone loss in diabetic patients with periodontitis<sup>29</sup>.

Conversely, periodontitis adversely affects glycemic control through systemic inflammatory mechanisms<sup>12</sup>. The dysbiotic subgingival biofilm, particularly dominated by keystone pathogens such as *Porphyromonas gingivalis*, triggers a local inflammatory response that can disseminate systemically<sup>6</sup>. Elevated levels of pro-inflammatory cytokines (IL-1 $\beta$ , IL-6, TNF- $\alpha$ ) and acute-phase proteins (C-reactive protein) from periodontal inflammation contribute to insulin resistance through several mechanisms: direct interference with insulin receptor signaling, impairment of pancreatic  $\beta$ -cell function, and enhanced hepatic glucose production<sup>30,31</sup>.

Recent evidence suggests that trained immunity—a form of innate immune memory—may represent a unifying mechanism explaining the intertwined association between diabetes and periodontitis<sup>32</sup>.

The developed and internally validated predictive model represents a practical, evidence-based tool for dental professionals practicing in similar settings. While not intended as a diagnostic substitute for laboratory HbA1c testing, this model offers a valuable chairside approach for risk-stratifying diabetic patients with potentially poor glycemic control. By utilizing data routinely collected during comprehensive periodontal examinations, dental practitioners can identify patients who may benefit from medical referral and more intensive diabetes management, without incurring additional costs or requiring specialized equipment.

This approach fosters a more integrated vision of patient care, where dental professionals actively contribute to the broader healthcare team managing diabetic patients. Through early identification of potential glycemic control issues and facilitation of timely medical referrals, dental practitioners can help reduce the burden of diabetes complications and improve overall health outcomes. Multiple intervention studies have demonstrated that successful periodontal treatment reduces circulating inflammatory mediators and may lead to modest improvements in glycemic control, with meta-analyses showing an average HbA1c reduction of 0.4% following periodontal therapy<sup>33,34</sup>. This improvement, while seemingly modest, is clinically significant and comparable to the addition of some second-line pharmacological interventions for diabetes management<sup>14</sup>.

Additionally, the model provides an educational opportunity to reinforce with patients the critical bidirectional relationship between periodontal health and diabetes management, potentially enhancing motivation for both oral hygiene practices and diabetes self-care behaviors. Patient education regarding this bidirectional relationship remains suboptimal, with studies showing that less than half of people with diabetes know their increased risk for periodontal disease<sup>35</sup>. Improved awareness could lead to better compliance with both dental and medical care recommendations.

The microbial dysbiosis observed in periodontitis contributes to systemic inflammation through several mechanisms. The periodontal pocket serves as a reservoir for pathogenic bacteria that can enter the bloodstream during routine activities such as chewing and toothbrushing, leading to transient bacteremia<sup>26</sup>. Furthermore, lipopolysaccharides (LPS) from gram-negative periodontal pathogens can trigger systemic inflammatory responses through toll-like receptor activation, contributing to insulin resistance and pancreatic  $\beta$ -cell dysfunction<sup>36</sup>. Recent microbiome studies have identified specific bacterial signatures associated with both periodontitis and diabetes, suggesting common microbial factors may influence both conditions<sup>37</sup>.

At the cellular level, the inflammatory response in periodontitis is characterized by neutrophil hyperactivity, macrophage polarization toward pro-inflammatory phenotypes, and impaired resolution of inflammation<sup>24</sup>. In diabetic patients, these immune dysregulations are exacerbated, creating a vicious cycle of enhanced tissue destruction and impaired repair. Hyperglycemia-induced oxidative stress further compounds these effects by increasing reactive oxygen species production, promoting apoptosis of periodontal ligament cells, and enhancing osteoclast activity leading to accelerated alveolar bone resorption<sup>38</sup>.

As healthcare systems worldwide increasingly recognize the importance of interprofessional collaboration and integrated care pathways, tools such as the one developed in this study represent practical steps toward breaking down traditional silos between dental and medical care. The integration of oral healthcare into diabetes management guidelines has been recommended by both dental and medical professional organizations, including the International Diabetes Federation and the European Federation of Periodontology<sup>39</sup>. Implementation of these recommendations requires continued education of healthcare providers and development of practical screening tools such as the one presented in this study<sup>40</sup>.

### Limitations and future directions

Several important limitations must be acknowledged when interpreting these findings. The model explains only 27.5% of HbA1c variance, leaving 72.5% unexplained, which likely reflects the multifactorial nature of glycemic control. Our model's Adjusted  $R^2$  of 0.275 is comparable to the predictive power ( $R^2$  values ranging from 0.21 to 0.55) observed in similar HbA1c prediction tools reported by other researchers<sup>41,42</sup>, suggesting its relative standing within the current body of evidence. Key factors not captured in our model may include medication adherence, dietary patterns, physical activity levels, body mass index, concurrent medications, and other comorbidities that significantly influence HbA1c levels. The Mean Absolute Error of 1.02% suggests limited precision for individual predictions, particularly near clinically important glycemic thresholds (e.g., 7% target for most adults). For context, this MAE is comparable to the analytical variation of HbA1c laboratory assays ( $\pm 0.5$ –1.0%) but may limit clinical utility for precise individual predictions. The single-centre design from Al-Kufa University Dental Clinic may limit generalizability to other populations with different demographic characteristics, healthcare systems, or periodontal disease patterns. Additionally, the retrospective design introduces potential for temporal ambiguity and residual confounding from unmeasured variables such as socioeconomic status, medication compliance, and lifestyle factors that were not consistently documented in dental records.

Future research should focus on several key areas to enhance the clinical utility and generalizability of periodontal-based HbA1c prediction models. External validation of this model in diverse populations and healthcare settings is essential to establish broader applicability. Prospective studies evaluating the impact of implementing such screening tools on patient outcomes, including rates of medical referral, diabetes management optimization, and long-term complications, would provide valuable evidence for clinical adoption. Model refinement through incorporation of additional biomarkers, such as salivary inflammatory mediators, genetic polymorphisms associated with diabetes and periodontal disease susceptibility, or advanced periodontal diagnostic tools, may improve predictive accuracy. Implementation studies in various dental clinic settings could identify barriers and facilitators to adoption, informing best practices for integration into routine dental care. Longitudinal studies examining the effects of periodontal interventions on diabetes-related outcomes beyond

glycemic control, including cardiovascular events and microvascular complications, would strengthen the evidence base for integrated care approaches.

## Conclusion

This 10-year retrospective analysis demonstrates significant associations between specific periodontal markers and HbA1c levels in diabetic patients, with percentage of sites with PD  $\geq$  5 mm showing the strongest correlation ( $r=0.38$ ), followed by BOP% ( $r=0.35$ ) and missing teeth ( $r=0.30$ ). The developed predictive model, while explaining 27.5% of HbA1c variance with a Mean Absolute Error of 1.02%, provides a practical chairside tool for risk stratification rather than precise individual prediction. This study provides a foundation for enhanced collaboration between dental and medical professionals in the management of patients with diabetes, ultimately contributing to more comprehensive, patient-centered care that addresses both oral and systemic health needs in an integrated manner. The bidirectional relationship between periodontitis and diabetes represents a prime example of how oral health is intrinsically connected to systemic health, reinforcing the concept that the mouth cannot be considered in isolation from the rest of the body. Dental professionals can use this tool to identify diabetic patients who may benefit from medical referral and intensified diabetes management, facilitating early intervention and improved health outcomes.

## Data availability

It will be available upon reasonable request from the corresponding author.

Received: 20 June 2025; Accepted: 3 September 2025

Published online: 17 October 2025

## References

- American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes-2023. *Diabetes Care*. **46** (Suppl 1), S19–S40. <https://doi.org/10.2337/dc23-S002> (2023).
- World Health Organization. *Classification of Diabetes Mellitus* (World Health Organization, 2019).
- International Diabetes Federation. *IDF Diabetes Atlas*, 11th edition. Brussels, Belgium: International Diabetes Federation; (2025).
- World Health Organization. Diabetes fact sheet. (2024). Available from: <https://www.who.int/news-room/fact-sheets/detail/diabetes>.
- Khaleel, A. et al. Estimation of salivary creatine kinase level and periodontal health status among type II diabetic and nondiabetic patients with chronic periodontitis. *Eur. J. Gen. Dentistry*. <https://doi.org/10.1055/s-0045-1802324> (2025).
- Hajishengallis, G. Periodontitis: from microbial immune subversion to systemic inflammation. *Nat. Rev. Immunol.* **15** (1), 30–44. <https://doi.org/10.1038/nri3785> (2015).
- Păunică, I. et al. The bidirectional relationship between periodontal disease and diabetes Mellitus—A review. *Diagnostics* **13** (4), 681. <https://doi.org/10.3390/diagnostics13040681> (2023).
- Barutta, F., Bellini, S., Durazzo, M. & Gruden, G. Novel insight into the mechanisms of the bidirectional relationship between diabetes and periodontitis. *Biomedicines* **10** (1), 178. <https://doi.org/10.3390/biomedicines10010178> (2022).
- Mohammed, M. J., Abbas, S., Al-mizraqchi, S. M. & Ibrahim Salivary biomarkers and oral Candida spp. In type II diabetic patients: A comparative analysis. *J. Med. Pharm. Chem. Res.* **7** (7), 1379–1397 (2025).
- Ibrahim, S. & Mahdi, M. Ibrahim Leka'a. Biochemical analysis and periodontal health status in type 1 and type 2 diabetes (Comparative study). *J. Baghdad Coll. Dent.* **24**, 1 (2012).
- Ibrahim, S. M., Al-Mizraqchi, A. S. & Haider, J. Metronidazole potentiation by Panax ginseng and *Symphytum officinale*: A new strategy for *P. gingivalis*. *Infect. Control Antibiot. (Basel)*. **12** (8), 1288. <https://doi.org/10.3390/antibiotics12081288> (2023). PMID: 37627708; PMCID: PMC10452024.
- Preshaw, P. M. et al. Periodontitis and diabetes: a two-way relationship. *Diabetologia* **55** (1), 21–31. <https://doi.org/10.1007/s0012-5-011-2342-y> (2012).
- Polak, D. & Shapira, L. An update on the evidence for pathogenic mechanisms that May link periodontitis and diabetes. *J. Clin. Periodontol.* **45** (2), 150–166. <https://doi.org/10.1111/jcpe.12803> (2018).
- Sanz, M. et al. Scientific evidence on the links between periodontal diseases and diabetes: consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the international diabetes federation and the European federation of periodontology. *J. Clin. Periodontol.* **45** (2), 138–149. <https://doi.org/10.1111/jcpe.12808> (2018).
- American Diabetes Association Professional Practice Committee. Glycemic targets: standards of medical care in Diabetes-2023. *Diabetes Care*. **46** (Suppl 1), S97–S110. <https://doi.org/10.2337/dc23-S006> (2023).
- Sherwani, S. I., Khan, H. A., Ekhezaimy, A., Masood, A. & Sakharkar, M. K. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. *Biomark. Insights*. **11**, 95–104. <https://doi.org/10.4137/BMLS38440> (2016).
- DiMeglio, L. A., Evans-Molina, C. & Oram, R. A. Type 1 diabetes. *Lancet* **391** (10138), 2449–2462. [https://doi.org/10.1016/S0140-6736\(18\)31320-5](https://doi.org/10.1016/S0140-6736(18)31320-5) (2018).
- Blonde, L. et al. Gaps and barriers in the control of blood glucose in people with type 2 diabetes. *Diab Vasc Dis. Res.* **14** (3), 172–183. <https://doi.org/10.1177/1479164116679775> (2017).
- Glurich, I. & Acharya, A. Updates from the evidence base examining association between periodontal disease and type 2 diabetes mellitus: current status and clinical relevance. *Curr. Diab Rep.* **19** (11), 121. <https://doi.org/10.1007/s11892-019-1228-0> (2019).
- Eke, P. I. et al. Periodontitis in US adults: National health and nutrition examination survey 2009–2014. *J. Am. Dent. Assoc.* **149** (7), 576–588e6. <https://doi.org/10.1016/j.adaj.2018.04.023> (2018).
- Lalla, E., Kunzel, C., Burkett, S., Cheng, B. & Lamster, I. B. Identification of unrecognized diabetes and pre-diabetes in a dental setting. *J. Dent. Res.* **90** (7), 855–860. <https://doi.org/10.1177/0022034511407069> (2011).
- Strauss, S. M. et al. The dental office visit as a potential opportunity for diabetes screening: an analysis using NHANES 2003–2004 data. *J. Public. Health Dent.* **70** (2), 156–162. <https://doi.org/10.1111/j.1752-7325.2009.00157.x> (2010).
- Borgnakke, W. S. et al. Oral Health and Diabetes. In: Cowie CC, editors. *Diabetes in America*. 3rd edition. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases (US); Chapter 31. (2018).
- Chapple, I. L. & Genco, R. Working group 2 of the joint EFP/AAP workshop. Diabetes and periodontal diseases: consensus report of the joint EFP/AAP workshop on periodontitis and systemic diseases. *J. Periodontol.* **84** (4 Suppl), S106–S112. <https://doi.org/10.1902/jop.2013.1340011> (2013).
- Teeuw, W. J., Kosho, M. X. F., Poland, D. C. W., Gerdes, V. E. A. & Loos, B. G. Periodontitis as a possible early sign of diabetes mellitus. *BMJ Open. Diabetes Res. Care.* **5** (1), e000326. <https://doi.org/10.1136/bmjdr-2016-000326> (2017).

26. Graziani, F., Gennai, S., Solini, A. & Petrini, M. A systematic review and meta-analysis of epidemiologic observational evidence on the effect of periodontitis on diabetes an update of the EFP-AAP review. *J. Clin. Periodontol.* **45** (2), 167–187. <https://doi.org/10.1111/jcpe.12837> (2018).
27. D'Aiuto, F. et al. Systemic effects of periodontitis treatment in patients with type 2 diabetes: a 12 month, single-centre, investigator-masked, randomised trial. *Lancet Diabetes Endocrinol.* **6** (12), 954–965. [https://doi.org/10.1016/S2213-8587\(18\)30038-X](https://doi.org/10.1016/S2213-8587(18)30038-X) (2018).
28. Lalla, E. & Papapanou, P. N. Diabetes mellitus and periodontitis: a Tale of two common interrelated diseases. *Nat. Rev. Endocrinol.* **7** (12), 738–748. <https://doi.org/10.1038/nrendo.2011.106> (2011).
29. Graves, D. T., Ding, Z. & Yang, Y. The impact of diabetes on periodontal diseases. *Periodontol 2000.* **82** (1), 214–224. <https://doi.org/10.1111/prd.12318> (2020).
30. Genco, R. J. & Borgnakke, W. S. Diabetes as a potential risk for periodontitis: association studies. *Periodontol 2000.* **83** (1), 40–45. <https://doi.org/10.1111/prd.12270> (2020).
31. Taylor, J. J., Preshaw, P. M. & Lalla, E. A review of the evidence for pathogenic mechanisms that May link periodontitis and diabetes. *J. Clin. Periodontol.* **40** (Suppl 14), S113–S134. <https://doi.org/10.1111/jcpe.12059> (2013).
32. Mohammed, M., Jasim, A. S. & Al-Mizraqchi, M. Ibrahim. Oral findings, salivary copper, magnesium, and leptin in type II diabetic patients in relation to oral candida species. *Int. J. Microbiol.* **1**, 8177437 (2024).
33. Simpson, T. C. et al. Treatment of periodontal disease for glycaemic control in people with diabetes mellitus. *Cochrane Database Syst. Rev.* **2015** (11), CD004714. <https://doi.org/10.1002/14651858.CD004714.pub3> (2015).
34. Madianos, P. N. & Koromantzos, P. A. An update of the evidence on the potential impact of periodontal therapy on diabetes outcomes. *J. Clin. Periodontol.* **45** (2), 188–195. <https://doi.org/10.1111/jcpe.12836> (2018).
35. Poudel, P. et al. Knowledge and attitudes about diabetes and oral health among nurses working in a diabetes clinic. *BMC Nurs.* **20** (1), 199. <https://doi.org/10.1186/s12912-021-00721-0> (2021).
36. Winning, L. & Linden, G. J. Periodontitis and systemic disease: association or causality? *Curr. Oral Health Rep.* **4** (1), 1–7. <https://doi.org/10.1007/s40496-017-0121-7> (2017).
37. Ibrahim, S., Mahdi, Sattar, J. & Abdul-Zahra Al, H. Role of manual and powered tooth brushes in plaque removal and oral health status (a comparative study). *Indian J. Public Health.* **10**, 2193. <https://doi.org/10.5958/0976-5506.2019.02183.1> (2019).
38. Wu, Y. Y., Xiao, E. & Graves, D. T. Diabetes mellitus related bone metabolism and periodontal disease. *Int. J. Oral Sci.* **7** (2), 63–72. <https://doi.org/10.1038/ijos.2015.2> (2015).
39. Sanz, M. et al. Treatment of stage I-III periodontitis-The EFP S3 level clinical practice guideline. *J. Clin. Periodontol.* **47** (Suppl 22), 4–60. <https://doi.org/10.1111/jcpe.13290> (2020).
40. Liccardo, D. et al. Periodontal disease: A risk factor for diabetes and cardiovascular disease. *Int. J. Mol. Sci.* **20** (6), 1414. <https://doi.org/10.3390/ijms20061414> (2019).
41. Susanto, H. et al. Periodontal inflamed surface area and C-reactive protein as predictors of HbA1c: a study in Indonesia. *Clin. Oral Investig.* **16** (4), 1237–1242. <https://doi.org/10.1007/s00784-011-0621-0> (2012).
42. Chandra, G. et al. Explainable prediction of Long-Term glycated hemoglobin response change in Finnish patients with type 2 diabetes following drug initiation using Evidence-Based machine learning approaches. *Clin. Epidemiol.* **17**, 225–240. <https://doi.org/10.2147/CLEP.S505966> (2025).

## Acknowledgements

The authors would like to express their sincere gratitude to the administration and staff of Al-Kufa University College of Dentistry for their invaluable support in facilitating access to patient records and providing the institutional infrastructure necessary for conducting this research.

## Author contributions

S.M.I, M.N.H, and A.M.K contributed to the concept and design of the study, data collection, data analysis, interpretation of results, writing the manuscript, and final revision. S.M.I and A.M.K handled the editing and reviewing of the manuscript. All authors approved the final version of the manuscript.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The study was conducted as part of the authors' academic responsibilities at Al-Kufa University College of Dentistry, with institutional support limited to access to facilities and records.

## Declarations

## Competing interests

The authors declare no competing interests.

## Ethics approval and consent to participate

This retrospective study received ethical approval from the Institutional Review Board (IRB) of Al-Kufa University College of Dentistry (Approval No: 15738). The study adhered to the Declaration of Helsinki. Due to the retrospective nature of the study, informed consent was waived by the Institutional Review Board of Al-Kufa University College of Dentistry.

## Additional information

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