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Investigating the Correlation of Glycosylated Hemoglobin A1c with Oral Streptococcus Mutans Count in Patients with Type 2 Diabetes

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ABSTRACT

Introduction: The leading cause of tooth decay is Streptococcus mutans bacteria. Diabetes is also a condition that can impact the mouth's microbiology and the composition of saliva. The studies on the relationship between these two variables are limited; therefore, the present study was conducted to investigate the correlation between glycosylated hemoglobin A1c and the count of mutans streptococci in the mouths of patients with type 2 diabetes.

Materials and Methods: The present study was a cross-sectional analytical study conducted in the specialized diabetes clinic of Hamadan University of Medical Sciences, Iran. Sixty people with type 2 diabetes, non-smokers, who were willing to participate in the study to check the count of Streptococcus mutants, had samples collected from three different locations. Hemoglobin A1c and other relevant information were also extracted from the patients' files, and the data were analyzed using SPSS 24.

Results: There were significant differences in Streptococcus mutans counts among the dorsal surface of the tongue, the gingival groove and the mandibular buccal vestibule (p=0.001), the buccal vestibule and the dorsal surface of the tongue (r=0.337, p=0.008) and the buccal vestibule of the lower jaw and the gingival groove (r=0.361, p=0.004). No significant relationship was observed between the number of Streptococcus mutans bacteria on the dorsal surface of the tongue and the gingival groove (r=-0.197, p=0.137).

Conclusion: According to the findings of this study, although HbA1c is associated with poor control of diabetes mellitus, there was no significant correlation between Streptococcus mutans counts and HbA1c levels. Furthermore, it can be concluded that Streptococcus mutans counts are closely related to specific areas within the oral cavity.

Keywords: Diabetes mellitus; Type 2; Glycated hemoglobin; Hb A1c; Streptococcus mutans.

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Introduction

Diabetes is an increasingly widespread metabolic disorder characterized by elevated blood glucose levels. According to the International Diabetes Federation (IDF) report, approximately 537 million adults worldwide were affected by diabetes in 2021, a number projected to rise to 783 million by 2045. Notably, type 2 diabetes (T2D) accounts for over 90% of all diabetes cases [1]. Hemoglobin A1c (HbA1c) is a form of glycosylated hemoglobin commonly used to estimate blood glucose control in diabetic patients by reflecting average blood glucose levels over the past three months. This index is crucial for managing diabetes and controlling its complications. The American Diabetes Association advises that most nonpregnant adults with diabetes maintain an HbA1c level of less than 7%, as this is associated with a reduction in diabetes-related complications [2].

The oral cavity is colonized by a diverse and complex microbiome, with over 700 identified species, including various bacterial and fungal species [3]. A balanced microbial flora is essential for maintaining both oral and general health. Disruption of this balance can lead to the overgrowth of pathogenic bacteria or opportunistic pathogens, resulting in oral diseases such as dental caries and periodontal disease. Maintaining microbial balance is critical for preserving mucosal barrier function and supporting the immune response to pathogen invasion [4]. Furthermore, microorganisms associated with the oral cavity have been found in distant organs, including the small intestine, heart, lungs, placenta, and brain, influencing both local and systemic responses [5].

Among this complex microbiome, the most common pathogen associated with poor oral health is Streptococcus mutans, a gram-positive bacterium that produces acid. This microorganism can disrupt endothelial cell function and is linkassociated with atherosclerosis, one of the early indicators of cardiovascular disease. Additionally this bacterium is the most significant microorganism related to tooth decay, a risk factor for systemic diseases such as diabetes. Current evidence indicates that diabetes can increase the risk of dental caries through various mechanisms, for example, elevated glucose levels in saliva can significantly impact the activity of microorganisms [7]. Previous studies have demonstrated that diabetes can also lead to alterations in the oral microbiota. Uncontrolled diabetes is associated with notable cariogenic changes in the oral environment, including reduced resting and stimulated salivary flow, diminished salivary buffer capacity, increased acidity of saliva, and high proportion of Streptococcus mutans [8]. Given the established role of HbA1c as a key indicator of diabetes control, alongside the suggested bidirectional relationship between diabetes and oral microbiota—particularly Streptococcus mutans, a major contributor to prevalent oral diseases—understanding the potential relationship between Glycosylated Hemoglobin A1c (HbA1c) and Oral Streptococcus mutans in individuals with Type 2 diabetes is essential. This knowledge is crucial for developing comprehensive care strategies that address both glycemic control and oral health. Therefore, this study aimed to evaluate the correlation between HbA1c levels and Oral Streptococcus mutans in patients with Type 2 diabetes.

Materials and Methods

Ethical considerations

Initially, all participants received a thorough explanation of the study's purpose and procedures. They signed informed consent forms, and their demographic information and medical history were documented. The study protocol was approved by the Ethics Committee of Hamadan University of Medical Sciences, under the code IR.UMSHA.REC.1402.047.

Participants and the relevant factors

In this cross-sectional study, 60 patients with diabetes were recruited. All participants were referred to the Hamadan Diabetes Clinic in 2024, Iran, and met the inclusion criteria without any exclusion criteria.

Inclusion Criteria

All participants were selected from individuals aged 30 and older. Diabetic participants were verified to have type 2 diabetes according to the following criteria:

- Fasting Plasma Glucose (FPG) of ≥ 126 mg/dL (confirmed by two separate tests).
- HbA1c of ≥ 6.5% (confirmed by two separate tests).

Exclusion Criteria

The exclusion criteria included immune system deficiencies, xerostomia, AIDS, a history of radiotherapy or chemotherapy within the past month, cardiovascular diseases, smoking, and the use of medications that reduce salivary flow, as well as systemic conditions such as hypothyroidism and Cushing's disease. Additionally, participants with chronic or genetic diseases that could affect their nutritional status were excluded.

Sampling and Counting Streptococcus mutans

To assess the count of Streptococcus mutans, samples were collected from three specific sites: 1) the dorsal surface of the tongue, 2) the gingival groove, and 3) the mandibular buccal vestibule. Tongue samples were taken from the central groove area of the middle third of the tongue, while vestibular samples were obtained from the area aligned with the mandibular premolar teeth. For the gingival groove samples, sterile endodontic papers No. 15 were used to collect samples from the interproximal region, ensuring a maximum pocket depth of 3mm. A subculture was prepared from Streptococcus mutans bacteria. Using a sterile loop, 5 to 6 similar colonies were transferred and dissolved in Brain Heart Infusion Broth (Merck, Germany) contained in test tubes. The test tubes were then placed in an incubator (Memmert, Germany) at of 37°C for 2 hours. To determine the concentration of bacteria, the tube containing the bacterial suspension was placed in a spectrophotometer (Biorad/USA), and the optical density was measured at a wavelength of 600 nm. In the next step, the number of colonies that grew in each culture medium was reported as CFU/mL [9].

Statistical Analysis

First, the data were summarized using descriptive statistics. The normality of the data for each group was assessed using the Shapiro-Wilk test. Pearson correlation coefficient tests were utilized to assess the relationship between HbA1c levels and the concentration of Streptococcus mutans. Data analysis was conducted using SPSS 24, with a significance level set at P≤0.05.

Results

Sixty patients with diabetes were recruited, comprising 22 males and 38 females. Various characteristics of the study population, including weight, height, body mass index (BMI), fasting plasma sugar, and HbA1c, are presented in Table 1. Descriptive statistics for variables such as history of diabetes (newly diagnosed or previously diagnosed), history of hypertension, use of blood glucose-lowering medications, and insulin injection are shown in Figure 1. The average duration of hypertension among the research participants was 2.37±4.84 years. The average systolic and diastolic blood pressures of the participants in this study were 120.5±15.47 mmHg and 82.5±4.26 mmHg, respectively. Figure 2 illustrates the mean and standard deviation of Streptococcus mutans counts in three different sites in the oral cavity: the dorsal surface of the tongue, the gingival groove, and the mandibular buccal vestibule. One-way ANOVA revealed a significant difference in Streptococcus mutans counts among the different locations (p=0.001), and the Tukey test indicated that the gingival groove had significantly higher counts (p=0.001).

Table 1. Characteristics of the study population.

	Weight (Kg)	*Height (Cm)*	*BMI (Kg/M2)*	*FPG (mg/dl)*	*HbA1c (mmol/dl)*
*Mean & SD**	*77.66±9.99*	*164±7.18*	*28.90±2.90*	*172.34±60.15*	*10.26±4.35*

Standard Deviation *

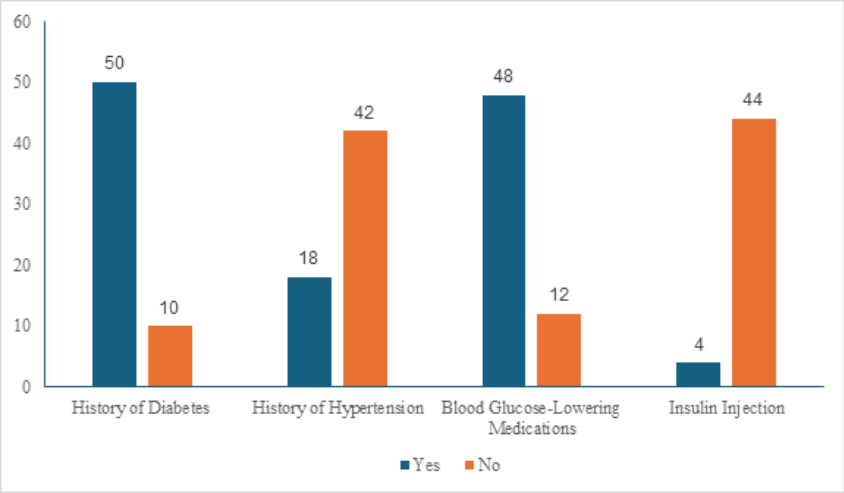


Figure 1. Descriptive statistics for history of diabetes, history of hypertension, blood glucose-lowering medications, and insulin injection.

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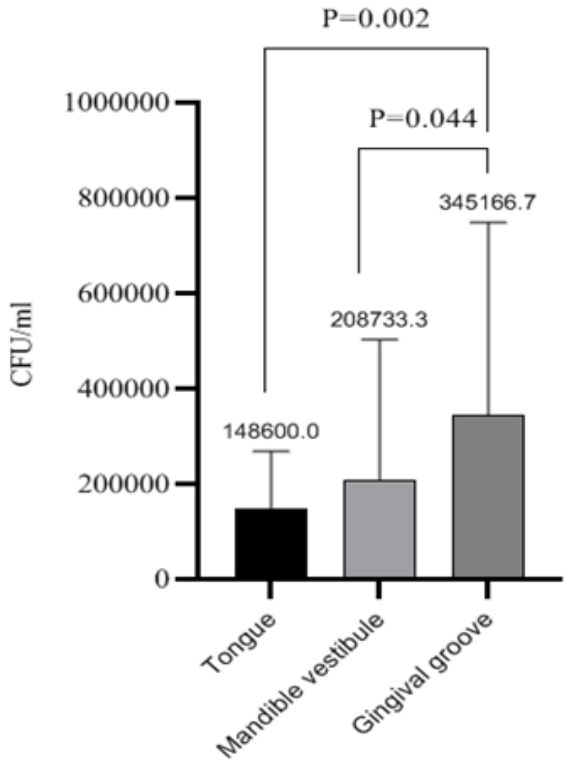
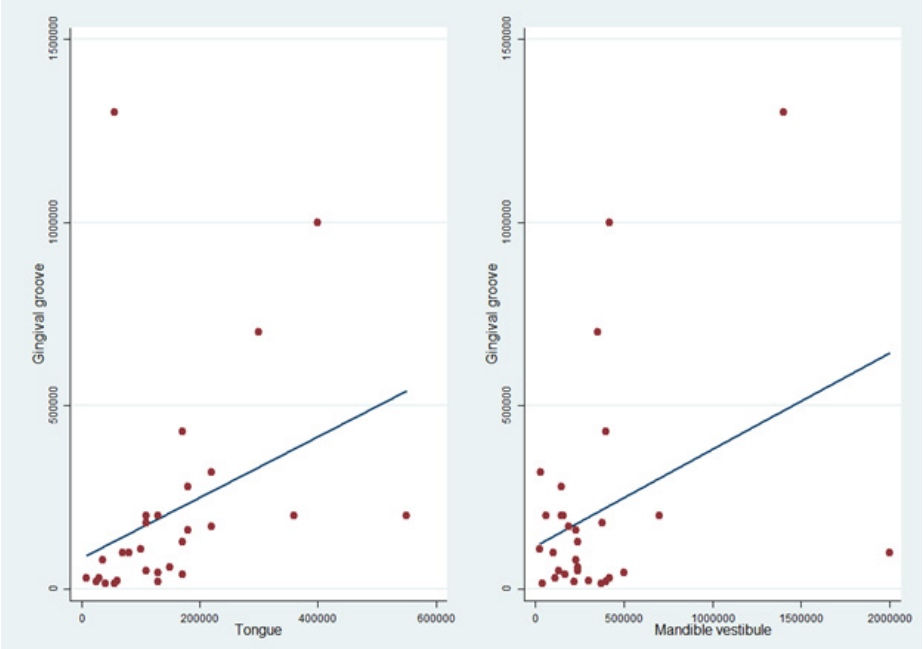


Figure 2. Mean and standard deviation of Streptococcus mutans counts in different sites.



Pearson's statistical test revealed a statistically significant correlation between the number of Streptococcus mutans bacteria in the buccal vestibule and the dorsal surface of the tongue (r=0.337, p=0.008). Additionally, a statistically significant relationship was found between the number of Streptococcus mutans bacteria in the buccal vestibule of the lower jaw and the gingival groove (r=0.361, p=0.004). However, no significant relationship was observed between the number of Streptococcus mutans bacteria on the dorsal surface of the tongue and the gingival groove (r=-0.197, p=0.137).

Discussion

This study evaluated the relationship between HbA1c levels and the counts of Streptococcus mutans in individuals with Type 2 diabetes. We found that participants exhibited elevated HbA1c levels (mean 10.26±4.35 mmol/dL), indicating poor glycemic con-

trol. However, contrary to our initial hypothesis, there was no significant correlation between Streptococcus mutans counts and HbA1c levels. Additionally, no relationship was found between Streptococcus mutans counts and fasting plasma glucose (FPG). Interestingly, a statistically significant relationship was found between the number of Streptococcus mutans bacteria in the buccal vestibule of the lower jaw and the gingival groove. However, no significant relationship was observed between the number of Streptococcus mutans bacteria on the dorsal surface of the tongue and the gingival groove. Our analysis revealed that the gingival groove had the highest counts of Streptococcus mutans, significantly surpassing counts from the dorsal surface of the tongue and the mandibular buccal vestibule. This finding suggests that specific oral sites may be more conducive to the growth of cariogenic bacteria, independent of glycemic control measures such as HbA1c and FPG.

Despite the established links between diabetes and oral health 10, the lack of a significant correlation between Streptococcus mutans counts and HbA1c levels was notable. Elevated HbA1c is often associated with altered salivary composition, including increased glucose levels that can promote the growth 11of cariogenic bacteria. However, our findings suggest that while Streptococcus mutans is a known pathogen in the oral cavity, its counts may not directly correlate with glycemic control, as measured by HbA1c, in this population. One possible explanation for this discrepancy could be the complexity of the oral microbiome and the various factors influencing microbial populations beyond glucose levels, such as pH, salivary flow, and individual oral hygiene practices [12]. Additionally, dietary habits can significantly affect the oral environment [13]; high sugar intake can exacerbate the growth of cariogenic bacteria [14], potentially confounding the relationship with HbA1c. Oral hygiene plays a significant role in maintaining microbial balance and may potentially influence oral bacterial counts more than systemic conditions, including fasting plasma glucose (FPG) levels [15]. The significant relationship observed between Streptococcus mutans counts in the buccal vestibule and gingival groove, but not with the dorsal surface of the tongue, underscores the importance of site-specific assessments in oral microbiome studies. This suggests that certain anatomical sites may harbor higher bacterial loads, potentially increasing the risk for dental caries and periodontal disease, irrespective of overall glycemic control. While elevated HbA1c levels are indicative of poor diabetes management, the relationship with Streptococcus mutans may be more complex than previously thought. Factors such as oral hygiene habits and dietary choices might play critical roles, highlighting the need for further research into the interplay between diabetes and oral health. The lack of a direct correlation between Streptococcus mutans counts and HbA1c levels emphasizes the necessity for a multi-aspect approach to patient care that encompasses both glycemic control and oral health.

According to our findings, integrating regular dental assessments into diabetes management is essential, as elevated HbA1c levels do not always correlate with increased Streptococcus mutans counts. Dental professionals should monitor oral health proactively to reduce the risk of dental complications. Patient education on good oral hygiene practices, including proper brushing, flossing, and dietary counselling to reduce sugar intake, is vital. When comparing the results of the present study to existing literature, several key similarities and differences emerge regarding the relationship between HbA1c levels and Streptococcus mutans counts in individuals with Type 2 diabetes.

Similar to our findings, Almeida-Santos reported that although some bacteria are associated with higher blood sugar levels, as indicated by HbA1c, there was no significant correlation between the count of Streptococcus mutans and HbA1c. Their findings suggest that the connection between the oral microbiome and diabetes, especially regarding oral diseases, is mainly influenced by lifestyle factors or a result of inadequate disease management, rather than the presence of diabetes itself. They recommended that future studies examining the relationship between type 2 diabetes (T2D) and the oral microbiome should incorporate dietary and lifestyle habits as two essential variables for analysis 16. In line with our study, Taylor observed that the periodontal microbiota seems unaffected by diabetes and that there is limited evidence suggesting it influences glycaemic control; however, there is substantial information on potential mechanistic pathways indicating a close relationship between diabetes and periodontitis [17]. In contrast to the present study, some studies have shown a positive correlation between elevated HbA1c levels and increased counts of Streptococcus mutans, supporting the notion that poor glycemic control can lead to an environment conducive to the growth of cariogenic bacteria. For instance, Jensen reported that the plaque microbiota showed a significant association with glycemic control in children with type 1 diabetes, revealing that poorer glycemic control correlated with higher early markers of periodontal disease. Further-

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more, the complexity and richness of the microbiota increased as HbA1c levels rose 18. Ganesan reported that certain bacterial species are more dominant in diabetes, including Fusobacterium, Parvimonas, Peptostreptococcus, Gemella, Streptococcus, Leptotrichia, Filifactor, Veillonella, TM7, and Terrahemophilus. Additionally, these bacterial communities show distinct patterns based on the level of HbA1c, which is a measure of blood sugar control, categorizing individuals into three groups: pre-diabetic, diabetic, and severely diabetic [19]. This discrepancy may suggest that the relationship is not as straightforward as previously thought. Factors such as individual variations in oral hygiene practices, dietary habits, and other systemic health issues could influence microbial populations independently of glycemic control.

Moreover, while some studies have focused on the general relationship between diabetes and oral health, our findings emphasize the importance of site-specific assessments. We observed significantly higher counts of Streptococcus mutans in the gingival groove compared to other sites, a nuanced aspect that is not always highlighted in the existing literature. This suggests that localized factors may play a crucial role in shaping oral microbiota dynamics, thereby complicating the relationship with systemic health indicators, such as HbA1c. Additionally, it's essential to consider that different methodologies, sample sizes, and patient populations can yield varying results. Some studies may have included broader populations or employed different criteria for diabetes classification, which could impact the observed outcomes.

This study has several limitations that should be taken into account when interpreting the findings. The cross-sectional design restricts our ability to determine causation between glycemic control and oral microbial populations, suggesting that longitudinal studies would be beneficial. The sample size of 60 participants, while sufficient for some outcomes, limits the generalizability of the results, and a more diverse population could provide deeper insights. Additionally, focusing solely on Streptococcus mutans overlooks other pathogenic bacteria in the complex oral microbiome. Future research would be better served by exploring several key areas based on the current study to investigate the causal relationships between glycemic control, Streptococcus mutans counts, and oral health through longitudinal studies. Additionally, examining a broader range of oral pathogens will provide a more comprehensive view of the oral microbiome's role in diabetes management. Assessing the impact of targeted interventions, such as improved oral hygiene and dietary changes, on Streptococcus mutans counts and glycemic control can offer valuable clinical insights. Studying diverse populations will help determine how factors such as diet and access to healthcare influence the relationship between diabetes and oral health. Lastly, evaluating the effectiveness of patient education initiatives on oral hygiene practices can inform best practices for integrating oral health into diabetes management. These directions will deepen our understanding of the connections between diabetes and oral health, ultimately improving patient care strategies.

Conclusion

According to the results of the present study, although elevated HbA1c levels indicated poor glycemic control, there was no significant correlation with Streptococcus mutans counts and HbA1c levels. Moreover, it can be concluded that Streptococcus mutans counts are highly correlated with the sites of the oral cavity.

Conflict of Interest

There is no conflict of interest to declare.

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