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Original Article

The Effect of Non-Surgical Periodontal Therapy on Glycosylated Hemoglobin Levels in Non-Diabetic Individuals

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ABSTRACT

Non-surgical periodontal treatment (NSPT) is the primary approach to managing periodontal infections. Our study aimed to evaluate and compare HbA1c levels between non-diabetic subjects with chronic periodontitis and subjects with a healthy periodontium. In addition, this study evaluated the effect of NSPT on blood glucose regulation in non-diabetic patients with chronic periodontitis. This clinical trial divided participants into two groups: an intervention group consisting of 20 non-diabetic subjects with a diagnosis of chronic periodontitis and a control group consisting of 20 non-diabetic individuals with healthy periodontal tissues. Periodontal clinical parameters, including gingival index (GI), probing pocket depth (PPD), clinical attachment loss (CAL), and HbA1c levels, were recorded. The intervention group underwent NSPT, and after three months, their periodontal parameters and HbA1c levels were reassessed and compared with baseline values. Before treatment, the HbA1c levels in the intervention group were significantly higher than those in the control group ($P < 0.001$). In the intervention group, a significant decrease in HbA1c levels was observed after treatment ($P < 0.001$), whereas the control group showed no significant change ($P > 0.001$). These findings suggest that chronic periodontitis may affect blood sugar levels even in non-diabetic individuals. Furthermore, NSPT not only improves periodontal health but also helps to reduce HbA1c levels.

Keywords: Periodontal treatment, Hemoglobin level, Non-diabetic individuals, Blood sugar

Introduction

Chronic periodontitis and diabetes mellitus are two prevalent chronic conditions that share a bidirectional relationship and exhibit similarities in their underlying pathobiology. Diabetes mellitus is recognized as a significant risk factor for periodontitis, contributing to increased severity, prevalence, and disease progression [1, 2]. Periodontal disease is often regarded as the sixth major complication of diabetes, alongside retinopathy, neuropathy, nephropathy, macrovascular disease, and impaired wound healing. Moreover, emerging evidence suggests that periodontitis itself may serve as a potential risk factor for diabetes [3, 4].

Glycosylated hemoglobin (HbA1c) is widely employed as a diagnostic marker for diabetes. Elevated HbA1c levels hold clinical significance in both pre-diabetic and diabetic individuals, with a range of 5.7–6.4% being indicative of a pre-diabetic state [5-7]. Chronic periodontitis is a progressive infectious disease that leads to the deterioration of periodontal tissues and can ultimately result in tooth loss. It has also been identified as a contributing factor in the onset and progression of various systemic diseases [8, 9].

One of the key mechanisms linking chronic periodontitis to systemic health issues is its role in triggering the production of inflammatory mediators, such as tumor necrosis factor-alpha (TNF-α), interleukin-6, interleukin-1β, and interferon-gamma. These mediators are known to influence both glucose and lipid metabolism. TNF-α, in particular, plays a crucial role in fat metabolism and acts as an insulin antagonist, while interleukin-6 and interleukin-1β also exhibit insulin-antagonistic properties [10]. Although extensive research has established a connection between diabetes and an increased severity of periodontal disease, relatively few studies have explored the relationship between periodontitis and blood glucose regulation in individuals without diabetes [11].

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Numerous studies have highlighted the adverse impact of periodontal infections on blood sugar regulation and the beneficial effects of non-surgical periodontal treatment (NSPT) in improving glycemic control among diabetic individuals [12]. Limited research has focused on how periodontal infections influence blood sugar levels in individuals without diabetes. Nibali *et al*. [13] found that individuals with periodontitis exhibited significantly higher non-fasting glucose levels compared to those with a healthy periodontium. Some studies suggest that while the effect of periodontitis on glucose metabolism is more pronounced in diabetic patients, it may still contribute to metabolic disturbances in non-diabetic individuals, though to a lesser degree [3]. The findings show that periodontal infections in individuals without diabetes could potentially disrupt the regulation of blood sugar [4].

Research conducted by Wolff *et al*. [3] reported higher mean HbA1c levels in individuals with periodontitis compared to healthy individuals. Additionally, large-scale population-based studies have indicated that the presence of chronic periodontal infections at baseline is positively associated with changes in HbA1c levels over time [14]. Current evidence suggests that HbA1c testing could serve as an objective tool for assessing the risk of diabetes in individuals with periodontitis or for evaluating the progression and severity of periodontal disease in diabetic patients [4].

NSPT remains the primary recommended intervention for controlling periodontal infections. This study aimed to compare HbA1c levels in non-diabetic individuals with chronic periodontitis to those with healthy periodontal tissue. Additionally, the study sought to assess the impact of NSPT on blood sugar regulation in non-diabetic patients affected by chronic periodontitis.

Materials and Methods

This study was designed as a not random controlled clinical trial involving non-diabetic individuals. Based on the findings of Perayil *et al*. [15] and considering a 95% confidence level, a test power of 80%, and an accuracy margin of 0.3, a sample size of 15 participants per group was determined. To account for a potential 25% dropout rate, a total of 20 participants were included in each group: an intervention group (individuals with chronic periodontitis) and a control group (individuals with a healthy periodontium). The participants' ages ranged from thirty to 50 years. Patients for the intervention group were recruited from the periodontology department, whereas individuals for the control group were taken from other departments. The selection process followed Non-probability Sampling and Convenience Sampling techniques.

The inclusion criteria for the intervention group required participants to be free of systemic diseases, have a clinical attachment loss (CAL) of at least 3 millimeters or probing pocket depth (PPD) of 5 millimeters or more in at least 30 percent of their teeth, possess a minimum of 20 teeth, have normal fasting blood sugar levels, and maintain a body mass index (BMI) within the normal range ($18.5 < BMI < 25$). Similarly, the control group was composed of individuals with at least 20 teeth, normal fasting blood sugar levels, and a BMI within the same range, without any systemic diseases.

The exclusion criteria included a prior diagnosis of diabetes mellitus, as well as the consumption of non-steroidal anti-inflammatory drugs, antibiotics, or immunosuppressive medications for a minimum of one week within the last three months, recent periodontal treatment within the last six months, excessive bleeding within the past month, pregnancy or breastfeeding, smoking, alcohol or drug addiction, the presence of a removable prosthesis or long dental bridge, and lack of patient cooperation following treatment (scaling and root planing). Additionally, participants diagnosed with diabetes or any systemic conditions affecting glucose metabolism or periodontal health were excluded from the study at any stage of its implementation.

Patients were informed about the objectives of the study, and each participant provided written consent before enrollment. A fasting blood glucose experiment was conducted as a prerequisite for inclusion in the study. Blood sugar levels were measured using a glucometer (Caresens, Isens, Germany) at the dental unit. Only individuals with fasting blood sugar (FBS) levels within the normal range (70-110 mg/dL) were selected. To validate the accuracy of the glucometer, blood sugar readings were taken from three individuals before the study commenced. Their FBS levels were then rechecked in a laboratory the following day. The comparison of results confirmed that the glucometer had an accuracy of over 98%.

For participants meeting the inclusion criteria, a trained medical nurse collected two milliliters of peripheral venous blood from the antecubital vein using a 5 ml syringe before initiating non-surgical periodontal treatment. The samples were transferred to tubes containing ethylenediaminetetraacetic acid (EDTA) as an anticoagulant. These samples were then analyzed in a laboratory to determine HbA1c levels using a 32 ml HbA1c kit with high-

performance liquid chromatography. After three months of non-surgical periodontal treatment, HbA1c levels were reassessed.

Periodontal clinical parameters were recorded both before the intervention and three months post-treatment in both groups. A dental student, under the guidance of a periodontist, conducted the measurements. Examiner reliability (intra-examiner reliability) was assessed by evaluating five patients twice, with a 24-hour interval between sessions. The results demonstrated a measurement accuracy of over 87% within a 1-millimeter range.

PPD, defined as the distance from the gingival margin to the base of the pocket, and CAL, which measures the distance from the enamel-cementum junction to the pocket base, were recorded at six sites per tooth (mesiobuccal, distobuccal, midbuccal, mesiopalatal, midpalatal, and distopalatal) for all teeth except third molars and remaining roots. These measurements were taken using a Williams periodontal probe (Hu-Friedy, Chicago, IL, USA).

To assess gingival inflammation, the gingival index (GI) by Löe and Silness was utilized. This index assigns scores ranging from 0-3, evaluating the severity of inflammation separately at the gingival margin and interproximal parts. Bleeding was assessed by gently inserting a periodontal probe into the gingival sulcus and carefully moving it within the sulcus to observe the bleeding response.

Participants included in the study were provided with oral hygiene education by a periodontist, which covered using interdental tools for controlling microbial plaque. For the intervention group, training was conducted in two separate sessions by a dental student under the supervision of a periodontist. Following the 1st session, and after observing a reduction in inflammation, hopeless teeth along with microbial plaque-related factors, such as overhanging restorations and caries near the gumline, were removed from the oral cavity. The 2nd session of scaling and root planing (SRP) took place two weeks later, performed under local anesthesia without a time limit for each individual. The control group, which had no plaque or microbial plaque-related issues and exhibited healthy periodontal tissue, only received oral hygiene education without any additional periodontal treatment. Both groups were monitored through monthly check-ups to assess oral hygiene and control microbial plaque, as well as to evaluate their overall health, but no periodontal treatments were performed during these visits. After 3 months, periodontal clinical parameters and HbA1c levels were re-assessed by the primary examiner for both groups.

We processed data using SPSS version 23 software. The Shapiro-Wilk test was applied to test for the normality of the data. For normally distributed data, paired t-tests were used to compare pre and post-treatment means, while the Wilcoxon test was employed for non-normally distributed data. The Mann-Whitney test was used to compare the means between the two groups for PPD and HbA1c data, which were not normally distributed. For the GI data, an independent t-test was used, as it followed a normal distribution. Statistical significance was considered at P-value < 0.05.

Results and Discussion

In this research, 40 participants were assigned to either the intervention or control group. The intervention group had 12 females and 8 males, while the control group had 11 females and 9 males. Gender distribution between the groups showed no significant difference (P = 0.75), according to the chi-square test. The average age of the intervention group was 39.28 ± 1.88 years, whereas the control group had an average age of 38.70 ± 1.86 years, with a statistically significant difference (P = 0.015) as determined by the Mann-Whitney test. BMI averages in the intervention group were 23.81 ± 1.56 and 23.42 ± 1.34 in the control group, with no statistically significant difference (P = 0.94). The intervention group showed a significant change in HbA1c (0.22% ± 0.13%) following non-surgical periodontal treatment compared to the control group (0.01% ± 0.05%), with a huge difference between the two (P < 0.001) **(Table 1)**.

Table 1. The mean ± SD of HbA1C

	Intervention group	**Control group**	**Test result**
Before	5.45 ± 0.62	5.12 ± 0.33	P-value** = 0.66
After	5.23 ± 0.69	5.11 ± 0.32	P-value** = 0.058
Differences	0.22 ± 0.13	0.01 ± 0.05	P-value** < 0.001
Test result	P-value* < 0.001	P-value* = 0.66	

The evaluation of periodontal parameters in the intervention group revealed a significant improvement post-treatment. Specifically, the GI fell by 0.57 in the intervention group, while the control group showed a minimal change of 0.01 ($P < 0.001$). Similarly, the probing pocket depth (PPD) was reduced by 0.54 millimeters in the intervention group, compared to a 0.03 millimeter decrease in the control group ($P < 0.001$) **(Tables 2 and 3)**.

Table 2. The mean ± SD of GI

	Intervention group	Control group	Test result
Before	2.42 ± 0.22	0.63 ± 0.20	t**** = 28.61 df = 38 P-value < 0.001
After	1.85 ± 0.30	0.62 ± 0.18	t**** = 15.19 df = 38 P-value < 0.001
Differences	0.57 ± 0.24	0.01 ± 0.08	P-value** < 0.001
Test result	t*** = 10.59 df = 19 P-value < 0.001	P-value* = 0.56	

Table 3. The mean ± SD of PPD

	Intervention group (mm)	Control group (mm)	Test result
Before	3.38 ± 0.34	2.33 ± 0.49	P-value** < 0.001
After	2.84 ± 0.38	2.30 ± 0.46	P-value** < 0.001
Differences	0.54 ± 0.27	0.03 ± 0.06	P-value** < 0.001
Test result	t*** = 10.59 df = 19 P-value < 0.001	P-value* = 0.02	

In the intervention group, the mean clinical attachment level (CAL) was 3.06 ± 0.38 millimeter before treatment, and after three months, it decreased to 2.42 ± 2.42 millimeter, showing a significant reduction of 0.64 ± 0.38 millimeter ($P < 0.001$).

This study demonstrated that non-diabetic individuals with periodontitis had higher HbA1c levels compared to those with healthy periodontal tissue and that non-surgical periodontal treatment (NSPT) resulted in a reduction of HbA1c. Periodontal disease is often referred to as the sixth complication of diabetes, as it is linked to neuropathy, macrovascular disease, nephropathy, retinopathy, and impaired wound healing [3]. Furthermore, periodontitis has been recognized as a factor that exacerbates blood sugar control issues in diabetic patients, likely due to the bacteria and their by-products from infected periodontal pockets entering the bloodstream [13]. In addition, inflammatory cytokines, particularly IL-1β and TNF-α, are released from the infected periodontal tissue into circulation, potentially reducing insulin sensitivity [3, 10].

In this study, the findings show that HbA1c levels in the intervention group were significantly higher than those in the control group. Since all factors influencing blood sugar were controlled for in this study, the increased HbA1c levels in the intervention group may be attributed to the infection. This result is consistent with previous research. For example, Banjar *et al*. [4] mentioned that individuals with periodontitis were more likely to experience undiagnosed hypoglycemia compared to those with healthy periodontal tissue. They also found that more severe periodontitis was associated with higher HbA1c levels. Additionally, Taylor *et al*. [16] noted that severe periodontal infections could affect glycemic control in diabetic individuals. Similarly, Wolff *et al*. [3] showed that individuals with periodontitis but no systemic conditions had significantly higher blood glucose levels, indicating that periodontitis might impair blood sugar regulation, putting individuals in a prediabetic state. Furthermore, Demmer *et al*. [17] indicated that moderate periodontal disease may double the risk of developing diabetes. A recent review by Graziani *et al*. [18] also suggested that glycemic control could be compromised in non-diabetic individuals with periodontitis. However, a study by Kebede *et al*. [19] over 11 years found no relationship between periodontitis and the development of diabetes. On the other hand, Ghalaut *et al*. [20] failed to report any significant difference between HbA1c levels and the severity of periodontitis. The infectious nature of periodontal pockets and the release of inflammatory mediators, such as IL-1β and TNF-α, are thought to disrupt

insulin receptor function, reducing insulin sensitivity [3, 10, 21]. Thus, periodontal therapy might improve glycemic control by decreasing these pro-inflammatory mediators.

In this research, the effect of non-surgical periodontal treatment (NSPT) on blood sugar regulation was assessed by measuring HbA1c levels three months after treatment. HbA1c has become a reliable alternative to fasting blood sugar (FBS) for diabetes screening and was recognized as a diagnostic tool by the World Health Organization [4]. HbA1c reflects long-term blood glucose levels, as glucose binds irreversibly to hemoglobin, offering a more stable measurement over a 30-90 day period, unaffected by daily fluctuations in blood sugar levels [3, 21, 22]. NSPT is a well-established procedure for removing microbial plaque from the tooth root surfaces, which leads to a reduction in gingival inflammation, pocket depth, and improvements in clinical attachment levels. While the benefits of NSPT be up to a year, most improvements occur within the first three months [23]. After scaling and root planning (SRP), dentin tubules open, allowing pathogens to infiltrate, which may lead to re-infection after three to four months [24]. Thus, in this research, periodontal clinical parameters were re-evaluated three months after NSPT.

The results showed significant improvements in all periodontal clinical parameters after treatment, suggesting that the reduction in HbA1c in the intervention group could be attributed to the removal of chronic infection and inflammation. Previous studies also demonstrate a decrease in both periodontal clinical parameters and HbA1c levels following NSPT within three months, supporting the findings of this study [17, 21, 22]. Cruz *et al*. [25] reported that NSPT enhances plaque control and reduces gingival inflammation in individuals with chronic periodontitis, regardless of whether they have diabetes. Similarly, Dag *et al*. [26] found that SRP reduced HbA1c levels in individuals with controlled diabetes. However, Smith *et al*. [27] observed that periodontal mechanical treatment alone did not effectively regulate blood sugar in diabetic patients. Periodontitis induces systemic subclinical inflammation through periopathogens and inflammatory mediators, which impact pancreatic β-cells and disrupt insulin signaling. The reduction in HbA1c after periodontal treatment may reflect improved insulin sensitivity and reduced insulin resistance, potentially due to the decrease in pro-inflammatory cytokines and pathogenic bacteria [28].

The results of this study align with previous observational research, which indicates that non-diabetic individuals with periodontitis tend to have elevated blood sugar levels compared to those without periodontitis. Furthermore, the study demonstrates that non-surgical periodontal treatment not only improves periodontal parameters but also leads to a reduction in blood sugar levels in these patients. This supports the concept of a bidirectional association between diabetes and periodontitis.

Conclusion

This study demonstrated that chronic periodontitis can influence blood sugar regulation in individuals without diabetes. Non-surgical periodontal treatment led to improvements in periodontal clinical parameters and a reduction in HbA1c levels within 3 months. However, this study had certain limitations, including a small sample size, reliance on FBS alone to verify the non-diabetic status of participants, a short follow-up duration of only three months, and the absence of measurements for pro-inflammatory mediators such as CRP, IL-6, IF-γ, IL-1β, and TNF-α in serum or gingival crevicular fluid (GCF). Additionally, confounding factors such as race and ethnicity were not accounted for. Future research should explore the correlation between serum or GCF levels of inflammatory markers and HbA1c levels to better understand the underlying mechanisms.

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