Relationship Between Periodontal Status and HbA1c in Nondiabetics

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Abstract

Objectives: *Many studies have reported an association between diabetes and periodontitis. We analyzed the periodontal status and glycosylated hemoglobin (HbA1c) level in nondiabetic subjects to investigate the relationship between periodontitis and glucose control in nondiabetics.* ***Methods:*** *Periodontal status, HbA1c, serum cholesterol, triglyceride, body mass index (BMI), and demographic variables were assessed in 141 Japanese adults. The difference in the HbA1c level was evaluated among subjects according to periodontal status.* ***Results:*** *After adjusting for age, gender, BMI, and smoking, alcohol, and exercise habits as covariates, the mean HbA1c was significantly elevated with periodontal deterioration (*$P = 0.023$*).* ***Conclusions:*** *There was a significant relationship between periodontal status and HbA1c levels in nondiabetics.*

Key Words: hemoglobin A, glycosylated, periodontitis, epidemiology

Introduction

Periodontitis is more prevalent in diabetics and worsens with the disease (1). Some studies have used a fasting 75-g oral glucose tolerance test to examine the relationship between periodontal status and glycemic control in nondiabetics (2,3). One of these studies demonstrated that deep periodontal pockets were closely related to the current glucose tolerance status and the development of glucose intolerance in nondiabetics (2). Another study showed that the extent of alveolar bone loss was associated with impaired glucose tolerance (IGT), suggesting that periodontitis with alveolar bone loss has an adverse effect on glucose metabolism (3). Glycosylated hemoglobin (HbA1c) is considered a beneficial indicator of long-term glucose homeostasis, reflecting an average blood glucose concentration for the past 2-3 months, and an increase in HbA1c is thought to be related to glucose intolerance (4). Several studies have shown that periodontal treatment of diabetic patients decreased HbA1c levels (5-7). However, it remains unclear whether periodontal status effects on the HbA1c in nondiabetics. In this community-based study, we examined the cross-sectional relationship between periodontal status and HbA1c level in nondiabetics.

Materials and Methods

Subjects. The study included 141 dentate subjects (59 men, 41-91 years old; 82 women, 41-90 years old) who attended a mass health examination, which included a periodontal assessment, conducted from 2005 to 2006 on four small islands, each with a population of a few hundred people, in the southwestern part of Nagasaki Prefecture, Japan. One man and four women with self-reported diabetes, and one man with HbA1c >6.5 percent, were excluded from the analysis. Ultimately, 57 men and 78 women were included in the analysis. Each subject signed an informed consent form approved by the Committee for Ethics in Epidemiology at Nagasaki University.

Oral Examination. Four calibrated dentists examined the periodontal status of the subjects using a modification of the Community Periodontal Index (CPI) based on partial-mouth recordings for representative teeth. The subjects were categorized into three groups according to the highest CPI value among the representative teeth: ≤2, normal/gingivitis; 3, mild/moderate periodontitis; and 4, severe periodontitis.

Systemic Condition. The subjects completed a questionnaire regarding their medical history and their smoking, alcohol, and exercise habits. A blood sample was collected from the antecubital vein to measure biochemical parameters. HbA1c was measured using high-performance liquid chromatography (HLC-723G7, TOSOH, Tokyo, Japan). Serum cholesterol, serum triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were measured using an

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Table 1
Characteristics of Subjects According to Periodontal Status ($n = 135$)

Characteristics*	Healthy/gingivitis ($n = 18$)	Mild/moderate periodontitis ($n = 73$)	Severe periodontitis ($n = 44$)	P†
Continuous variables				
HbA1c (%)‡	5.02 ± 0.37	5.08 ± 0.38	5.20 ± 0.32	0.098
Total cholesterol (mg/dL)	223.67 ± 43.18	199.90 ± 30.43	202.32 ± 39.05	0.194
HDL cholesterol (mg/dL)	61.72 ± 16.08	57.05 ± 16.29	56.18 ± 14.06	0.431
LDL cholesterol (mg/dL)	143.78 ± 43.50	125.27 ± 27.61	127.32 ± 35.23	0.556
Triglycerides (mg/dL)	124.50 ± 67.16	121.62 ± 77.30	127.05 ± 66.76	0.925
Categorical variables		Number of subjects		
Age				0.819
40-64	7	24	13	
65-74	6	20	18	
≥75	5	29	13	
Gender				0.007
Male	2	32	23	
Female	16	41	21	
BMI¶				0.109
<25	10	52	34	
≥25	8	21	10	
Hypertension§				0.398
No	7	27	13	
Yes	11	46	31	
Smoking habit				0.035
Never	16	52	27	
Current/former	2	21	17	
Alcohol habit				0.706
Never	14	50	31	
Current/former	4	23	13	
Exercise habit				0.132
Yes	11	37	18	
No	7	36	26	

* Mean ± standard deviation; number of subjects are represented.
† Continuous variables were subjected to one-way analysis of variance or the Kruskal–Wallis test according to distribution of each variable. The chi-squared tests were used for categorical variables.
‡ The mean of HbA1c of all subjects was 5.11 ± 0.36, range 4.10-6.10.
¶ BMI was categorized into two groups: <25 and ≥25.
§ Hypertension was defined as a systolic blood pressure of ≥140 mm Hg, and/or a diastolic blood pressure of ≥90 mm Hg, or current use of antihypertensives.
BMI, body mass index; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Autoanalyzer (JCA-BM1250, JEOL, Tokyo, Japan). The body mass index (BMI), an indicator of obesity, was defined as weight in kilograms divided by the square of the height in meters. BMI was categorized into two groups, <25 and ≥25, based on the obesity criterion for Japanese (8). Hypertension was defined as a systolic blood pressure ≥140 mm Hg, and/or a diastolic blood pressure ≥90 mm Hg, or current use of antihypertensive medication. Age was divided into three groups: ≤64, 65-74, and ≥75 years.

Statistical Analysis. SPSS version 12.0J (SPSS Japan, Tokyo, Japan) was used for the statistical analyses. In the bivariate analyses, continuous variables were subjected to one-way analysis of variance or the Kruskal–Wallis test according to distribution of each variable. The chi-squared tests were used for categorical variables. Analysis of covariance was performed to adjust for age, gender, BMI, and smoking, alcohol, and exercise habits, which are known risk factors for type 2 diabetes (2,3,9).

Results

The characteristics of the subjects according to periodontal status are shown in Table 1. The mean HbA1c was associated with periodontal status, but this did not reach statistical significance ($P = 0.098$). Gender and smoking were significantly associated with the periodontal condition ($P = 0.007$ and $P = 0.035$, respectively). None of the other variables differed significantly among subjects of each periodontal status.

The adjusted mean HbA1c values of 4.97, 5.08, and 5.22 in subjects with normal/gingivitis, mild/moderate periodontitis, and severe periodontitis, respectively, differed significantly with periodontal status ($P = 0.023$) (Table 2). In this model,

Table 2
Adjusted Mean of HbA1c in Subjects According to Periodontal Status

Periodontal status (CPI code)	HbA1c	*P*
Healthy/gingivitis (≤2)	4.97 ± 0.08	0.023
Mild/moderate periodontitis (3)	5.08 ± 0.04	
Severe periodontitis (4)	5.22 ± 0.05	

Mean ± standard error is represented.
Analysis of covariance was performed to adjust for age, gender, body mass index, and smoking, alcohol, and exercise habits.
CPI, Community Periodontal Index; HbA1c, glycosylated hemoglobin.

age ($P = 0.041$), alcohol habit ($P = 0.041$), and BMI ($P = 0.018$) were significant covariates correlated with HbA1c.

Discussion

In the present community-based study, periodontal status was significantly associated with the HbA1c level after adjusting for known risk factors for type 2 diabetes. A previous study reported a relationship between deep periodontal pockets and IGT; deep pockets were more closely related to a past deterioration of glucose tolerance from normal to IGT rather than the IGT condition itself on the examination day, suggesting that having deep pockets is a risk factor for glucose intolerance (2).

A recent study on the effect of exposure to multiple infections on insulin sensitivity in healthy middle-aged men reported that exposure to multiple pathogens could cause a chronic low-grade infection, resulting in insulin resistance (10). Recently, Cani *et al.* (11) identified lipopolysaccharide (LPS) as an important factor triggering insulin resistance. LPS strongly stimulated the release of tumor necrosis factor-α (TNF-α) and interleukin-6 in the liver, representing the first target of LPS-induced insulin resistance. Engebretson *et al.* (12) reported that the severity of chronic periodontitis and the plasma levels of LPS were associated with the plasma TNF-α level in their type 2 diabetic cohort study. However, no correlation was found between the plasma TNF-α and HbA1c in these diabetic subjects, suggesting that periodontitis in subjects with type 2 diabetes influenced the TNF-α level to such a low degree that glucose levels were not influenced. Further studies are needed to clarify whether TNF-α is associated with HbA1c in periodontitis in the case of nondiabetics.

Although we cannot be sure of a causal relationship between periodontitis and HbA1c from this cross-sectional study, previous studies have reported that IGT has no effect on periodontal status (9). The use of the CPI for representative teeth might have underestimated the periodontal condition of the subjects in the present study, and we could not assess whether attachment loss or alveolar bone loss was associated with HbA1c. Additionally, the small number of subjects, especially in some cells in Table 1, may affect the results. In conclusion, periodontal status was related to HbA1c in nondiabetic subjects, independently of other risk factors for type 2 diabetes. Chronic periodontitis may be associated with the glucose control in nondiabetics. Prospective large cohort studies with full measurements of pocket depth and attachment loss, and intervention by periodontal treatment, are needed to clarify the causal relationship between periodontitis and glucose condition in nondiabetics.

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