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Association of urinary albumin excretion with periodontal parameters in patients with type 2 diabetes mellitus: a cross-sectional study

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Abstract

Background: Our previous pilot study using patients with type 2 diabetes mellitus in one medical clinic showed an association of urinary albumin excretion, a marker of generalized vascular dysfunction and kidney damage, with periodontitis. The purpose of this study was to confirm the association by increasing the numbers of patients and medical clinics.

Methods: Participants were 2,302 patients (59.9% males, aged 29–93 years) with type 2 diabetes mellitus from 25 medical clinics. Their medical records and information about socioeconomic status and health behavior were collected. Periodontal status was assessed in a nearby dental office. Multiple linear regression analyses were conducted to examine the association of log-transformed urinary albumin-to-creatinine ratio with periodontal parameters after adjusting for sociodemographic status, general health conditions, and health behaviors. The analyses were performed in all subjects and subjects with normoalbuminuria only.

Results: Multiple linear regression analysis showed that mean probing pocket depth (beta: 0.062), percentage of sites with probing pocket depth of 4 mm or deeper (beta: 0.068), percentage of mobile teeth (beta: 0.055), and severity of periodontitis (beta: 0.049) were significantly (p<0.05) correlated with log-transformed urinary albumin-to-creatinine ratio after adjusting for possible confounders in all subjects. However, no significant associations between urinary albumin-to-creatinine ratio and periodontal parameters were observed in subjects with normoalbuminuria only.

Conclusions: These results suggest that periodontitis is associated with urinary albumin excretion in

patients with type 2 diabetes mellitus. Collaboration between medical and dental healthcare providers is needed for treatment of diabetes and periodontitis.

Keywords: Urinary albumin excretion, Periodontitis, Diabetes mellitus, Adults, Cross-sectional study

Introduction

The prevalence of type 2 diabetes mellitus (T2DM) is increasing globally [1]; especially in Asia, including Japan, T2DM is an increasing pandemic [2]. However, quality of care for individuals with T2DM has improved in the past two decades, reflecting recent advances in treatment for blood glucose control, blood pressure, and lipids [3, 4]. Such improvement of diabetes treatment has resulted in prolongation of treatment duration and aging of patients with diabetes. Therefore, prevention of diabetic complications, especially chronic kidney disease and cardiovascular disease, has become more important for patients with controlled diabetes because about one-third of all diabetic patients will eventually have progressive deterioration of renal function [5].

Periodontitis is a chronic infectious disease caused by bacterial biofilm (dental plaque). An association of periodontitis with chronic kidney disease and cardiovascular disease was suggested by the following studies. Cohort studies showed that subjects with periodontitis were more likely to have decreased kidney function [6], diabetic nephropathy, and cardiovascular death [7] and increased mortality with chronic kidney disease [8]. Furthermore, a cross-sectional study suggested a bidirectional association between chronic kidney disease and periodontitis, which was mediated by hypertension and the duration of diabetes [9].

Urinary albumin-to-creatinine ratio (UACR) is an important marker of generalized vascular dysfunction and kidney damage. Several cross-sectional studies have shown that periodontitis is associated with albuminuria in non-diabetic subjects such as middle-aged hypertensive patients without diabetes [10],

the general population [11], and non-diabetic adults [12]. Moreover, two studies have shown an association between periodontitis and UACR in patients with T2DM; however, one study [13] did not consider confounding factors and another study [14] did not use full mouth examination of periodontal status. Our previous pilot study using 503 subjects with T2DM from one medical clinic showed that albuminuria is associated with periodontal parameters based on full mouth examination after adjusting for possible confounders [15]. If an association between periodontitis and UACR is found even in patients with T2DM, then this information provides a valuable impetus for improving cooperation between medical and dental healthcare providers [16]. The purpose of the present study was to determine the association between UACR and periodontal parameters in Japanese patients with T2DM by extending our previous pilot study [15] using an increased number of patients from 25 medical clinics in Japan.

Studies have shown that a slightly elevated UACR, which is within the normal range, is an independent predictor for progression of cardiovascular disease and renal outcomes both in individuals with and without diabetes [17-20]. Another study showed that high-normal albuminuria is closely associated with diabetic kidney disease [21]. Therefore, associations between UACR and periodontal parameters were further examined after study participants were restricted to those with normoalbuminuria only.

Methods

Study population

Participants were 2,302 patients (1,380 males and 922 females, aged 29–93 years) with T2DM who visited 25 medical clinics between December 2014 and March 2018. All 25 medical clinics belong to the Japan Clinicians Diabetes Association. Patients visiting the medical clinics had already completed initial treatment for T2DM. T2DM was diagnosed according to the Japan Diabetes Society's criteria: fasting blood glucose ≥7.0 mmol/L, casual blood glucose ≥11.1 mmol/L, or glycosylated hemoglobin A1c (HbA1c) ≥6.5%. Diabetic subjects were treated with the aim of achieving the targets recommended by the Japan Diabetes Society [22]: HbA1c <7.0%, blood pressure <130/80 mmHg, and serum concentrations of low-density lipoprotein cholesterol <3.1 mmol/L, high-density lipoprotein (HDL) cholesterol ≥1.0 mmol/L, and non-HDL cholesterol <3.8 mmol/L.

Patients with no teeth; those who experienced acute myocardial infarction or cerebrovascular disease within the past 6 months; those with insecurity angina pectoris, severe heart disease such as cardiac insufficiency, cardiomyopathy, and valvular disease, severe liver diseases, cancer, or dementia; or those scheduled to undergo surgery were excluded. Patients with missing data for any of the parameters evaluated in the present study were also excluded.

The study protocol was approved by the ethics committees of Jiyugaoka Medical Clinic (October 27, 2014, No. 250716) and Kanagawa Dental University (July 5, 2016, No. 387; September 12, 2017, No. 446; December 20, 2017, No. 476). All participants provided written informed consent, and the study was

carried out in accordance with the revised Declaration of Helsinki.

Measurements and definition

Urinary albumin and creatinine levels were measured by a turbidimetric immunoassay and an enzymatic method, respectively, and urinary albumin excretion rate was recorded as UACR. Normoalbuminuria, microalbuminuria, and macroalbuminuria were defined as UACR <30 mg/g creatinine, UACR ≥30 and <300 mg/g creatinine, and UACR ≥300 mg/g creatinine, respectively. The glomerular filtration rate (GFR) was estimated using the following equation by the Japanese Society of Nephrology: eGFR (mL/min/1.73 m^2) = $194 \times Scr^{-1.094} \times age^{-0.287} \times 0.739$ (if female). HbA1c was measured by high-performance liquid chromatography, which has been certified by the American National Glycohemoglobin Standardization Program. Data of duration of diabetes treatment and treatment of diabetes were obtained from patients' records. With regard to treatment of diabetes, subjects were divided into groups by treatment with diet alone, hypoglycemic tablets, or insulin. Blood pressure was measured by an appropriately sized cuff using an automated blood pressure device. The height and weight of the participants were measured, and body mass index (BMI) was calculated as the weight divided by the square of the height (kilograms per square meter). Past history of ischemic stroke and coronary heart disease was obtained from the patient's medical record. Diabetic retinopathy was diagnosed by an ophthalmologist after pupillary dilation. Hyperlipidemia was defined by total cholesterol ≥5.67 mmol/L, triglycerides 1.69 mmol/L, or taking lipid-lowering drugs.

Information about education, household income, smoking, and frequency of toothbrushing was obtained using a questionnaire [15]. Education was categorized as junior high school, high school,

university <4 years, and university ≥4 years. Household income was categorized as <3 million, 3–<5 million, 5–<10 million, and ≥10 million Japanese yen (100 Japanese yen = 1 US dollar) per year. Smoking was categorized as never, ex, and current. Frequency of toothbrushing was categorized as once, twice, and ≥3 times per day.

Periodontal examination

Subjects were asked to visit a nearby dental office with a uniform dental chart to receive a periodontal examination, irrespective of whether they were attending the dental office regularly [15]. Subjects were informed that the periodontal examination was conducted under healthcare services covered by their health insurance. In addition, subjects were asked to hand a letter to the dentists. The letter provided an explanation of the present study including the background, purpose, and methods and requested that the dentists send the patient's dental chart to the medical clinics by mail.

The dental chart included probing pocket depth (PPD), bleeding on probing (BOP) [23], tooth mobility [24], and number of teeth present. PPD was defined as the distance from the gingival margin to the base of the clinical periodontal pocket and was measured at six sites per tooth (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual/palatal, mid-lingual/palatal, and disto-lingual/palatal). BOP for each tooth was recorded as present if it occurred in at least one of the six sites of each tooth within 30 seconds of probing. Manual examination of tooth mobility was assessed as yes/no.

Statistical analysis

Mean PPD, percentage of sites with PPD ≥4 mm, percentage of BOP-positive teeth, and percentage of

mobile teeth were calculated for each subject. Severity of periodontitis was modified from staging and grading of periodontitis [25], and defined as follows: no, number of sites with PPD ≥4 mm = 0 and number of teeth with tooth mobility degree ≥2 = 0; initial, number of sites with PPD =4 mm ≥ 1, number of sites with PPD ≥5 mm = 0 and number of teeth with tooth mobility degree ≥2 = 0; moderate, number of sites with PPD =5 mm ≥ 1, number of sites with PPD ≥6 mm = 0 and number of teeth with tooth mobility degree ≥2 = 0; severe, number of sites with PPD ≥6 mm ≥ 1 and number of teeth with tooth mobility degree ≥2 = 0; advanced, number of teeth with tooth mobility degree ≥2 ≥ 1.

Analyses were performed using all data and data restricted to subjects with UACR <30 mg/g creatinine (normoalbuminuria). Data are expressed as the mean and standard deviation (SD) if normally distributed or otherwise as the median (interquartile range). Non-normality in the distribution of variables was corrected using natural log transformation for UACR [12].

Spearman's rank correlation coefficient was used to assess the association of UACR with each periodontal parameter and each covariate (age, male sex, education score, household income score, HbA1c, systolic blood pressure, BMI, duration of diabetes, diabetes therapy, history of stroke, history of coronary heart disease, diabetic retinopathy, hyperlipidemia, smoking, and toothbrushing frequency per day).

Multiple linear regression models were used to examine the association of UACR with each periodontal parameter. In Model 1, each periodontal parameter, sex, and age were added. In Model 2, education score and household income score were added to Model 1. In Model 3, HbA1c, systolic blood pressure, BMI, duration of diabetes, diabetes therapy, history of stroke, history of coronary heart disease,

diabetic retinopathy, and hyperlipidemia were added to Model 2. In Model 4, smoking and toothbrushing frequency per day were added to Model 3.

A *p*-value of less than 5% (two-tailed) was considered significant. All analyses were performed with the statistical software package IBM SPSS statistics version 24 (IBM Co., New York, NY, USA).

Results

Characteristics of all subjects and subjects with normoalbuminuria are shown in Table 1. Median (interquartile range) of UACR for all subjects was 12.9 (6.6–31.0) mg/g creatinine. More than half of the participants completed high school education. Annual household income of nearly half of the participants was <3 million yen. Median (interquartile range) of the duration of diabetes was 8.9 (4.8–13.3) years. Seventy-four percent of the participants were treated with hypoglycemic tablets. Mean (SD) of PPD was 2.8 (0.8). Median (interquartile range) of the number of teeth present was 24 (19–27).

Median (interquartile range) of UACR for subjects with normoalbuminuria was 9.2 (5.4–15.0) mg/g creatinine (Table 1). Compared to all subjects, subjects with UACR <30 were slightly younger and had slightly better health status, better health behavior, and better periodontal status.

In all subjects, UACR was positively correlated with age, HbA1c, systolic blood pressure, BMI, duration of diabetes, diabetes therapy, history of stroke, diabetic retinopathy, hyperlipidemia, mean PPD, percentage of sites with PPD ≥4 mm, percentage of mobile teeth, and severity of periodontitis and was negatively correlated with education score, household income score, toothbrushing frequency, and number of teeth present (Table 2). In subjects with normoalbuminuria, UACR was positively correlated with age, HbA1c, systolic blood pressure, duration of diabetes, diabetes therapy, diabetic retinopathy, and percentage of mobile teeth and was negatively correlated with male sex, education score, household income score, smoking, and number of teeth present.

Results of multiple linear regression analyses including all subjects are shown in Table 3. All

periodontal parameters were significantly (p<0.05) correlated with UACR in Models 1 and 2. In Models 3 and 4, mean PPD, percentage of sites with PPD ≥4 mm, percentage of mobile teeth, and severity of periodontitis were significantly (p<0.05) correlated with UACR.

Results of multiple linear regression analyses including subjects with normoalbuminuria only are also shown in Table 4. Mean PPD and percentage of sites with PPD ≥4 mm were significantly (p<0.05) correlated with UACR in Model 1. However, all periodontal parameters were not significantly correlated with UACR in Models 2–4.

Discussion

This cross-sectional study using more than 2,000 T2DM patients from 25 medical clinics in Japan showed that UACR was positively correlated with mean PPD, percentage of sites with PPD ≥4 mm, and percentage of mobile teeth after adjusting for possible confounders. These results confirmed the results of our previous pilot study [15]. In addition, a positive correlation between severity of periodontitis and UACR was found for the first time.

The results from the present study agree with those from previous studies showing associations between UACR and periodontal parameters in patients with T2DM [13, 14]. Periodontal parameters evaluated in previous studies were immunoglobulin G titer against periodontal bacteria [13] and community periodontal index using 10 representative teeth [14]. However, variables calculated from periodontal pocket probing at six sites of all teeth, percentages of teeth with BOP and mobile teeth, and number of present teeth were used in the present study. Partial-mouth periodontal examination tends to underestimate the prevalence of periodontitis [26]. Furthermore, the number of subjects in the present study (n=2,302) was greater than those in previous studies (n=134 [13] and n=547 [14]). These results showed a positive correlation between urinary albumin excretion and severity of periodontitis in T2DM patients.

Although a significant association was observed between UACR and periodontal parameters in all subjects in the present study, the association was weak in patients with normoalbuminuria only. These results disagree with those from previous studies showing that periodontitis is associated with UACR in non-diabetic adults with normoalbuminuria [12]. The reason for the discrepancy between the studies may

be because of differences in the prevalence of periodontitis among subjects. The prevalence of periodontitis in the previous study was 74% [12], which is lower than that in the present study (90%). In addition, the previous study did not adjust for socioeconomic status, which is a strong confounding factor in the association between UACR and periodontal parameters [27-30].

The prevalence of periodontitis in this study population was higher than that in the general population in Japan. Percentages of subjects with PPD ≥4 mm aged in their 30s, 40s, 50s, 60s, 70s, and 80s or older in the present study were 87%, 87%, 90%, 90%, 90%, and 90%, respectively, which were higher than those in the general population in Japan excluding edentulous subjects [31] (37%, 45%, 52%, 64%, 66%, and 74%, respectively). Percentages of subjects with PPD ≥6 mm aged in their 30s, 40s, 50s, 60s, 70s, and 80s or older in the present study were 39%, 42%, 48%, 54%, 49%, and 55%, respectively, which were higher than those in the general population in Japan excluding edentulous subjects [31] (5%, 5%, 10%, 17%, 14%, and 12%, respectively). The difference in the mean number of teeth present between the present study and the general population in Japan was within 1.0 for people aged in their 30s–60s. However, mean number of teeth present in patients aged in their 70s and 80s or older in the present study was higher than that in the general population in Japan by 5.3–9.7%, which may be explained by exclusion of subjects with no teeth in the present study. The finding of a high prevalence of periodontitis in the subjects of the present study agrees with the fact that diabetes mellitus is one of the strong factors of periodontitis [32, 33].

The results of the present study provide valuable information for strengthening the cooperation between medical and dental healthcare providers, especially for treatment of diabetes and periodontitis.

Medical doctors need to be aware that urinary albumin excretion is correlated with periodontitis in T2DM patients, and they should advise their patients with high UACR to visit dentists in order to check and control periodontal inflammation. Dentists should also understand the correlation of periodontitis with UACR, which predicts diabetic nephropathy [21] and/or cardiovascular disease [18], should obtain information about the general health status of their periodontal patients, and should advise T2DM patients to continue visiting their medical doctor to achieve good diabetes control.

Because the present study had a cross-sectional design, causality between urinary albumin excretion and periodontitis remains unknown. However, reduction in coefficients from Model 1 to Model 4 in the present study suggests that socioeconomic status, systemic condition, and health behavior underlie the association as confounding factors [9]. The results of the present study agree with those from previous studies showing that low socioeconomic status is associated with albuminuria [27, 28] and poorer periodontal health [29, 30].

Moreover, results of Model 4 including all subjects showed a correlation between urinary albumin excretion and periodontal parameters, especially mean PPD, percentage of sites with PPD ≥4 mm, percentage of mobile teeth, and severity of periodontitis even after adjusting for possible confounders. One possible explanation might be the presence of a chronic inflammatory process. Periodontitis has been recognized as an increased inflammatory status that results in vascular endothelial dysfunction [34]. In fact, treatment of periodontitis improved endothelial dysfunction [35]. Future studies with a longitudinal design are needed to further clarify the causality between urinary albumin excretion and periodontitis.

Our study has some strengths and limitations. First, the sample size of the present study is relatively large and the data were obtained from 25 medical clinics. Therefore, the results from the present study could be, in part, generalized to T2DM patients in Japan. Second, six sites of all teeth were examined when periodontal pocket probing was performed. However, calibration of periodontal probing was not performed and dentist-to-dentist variations were not evaluated because the study was performed in a community-based primary care setting. Third, the inspection equipment and measurement environment were not necessarily unified among medical and dental clinics. These limitations of the methodology may result in underestimation of the association between UACR and periodontal parameters.

In conclusion, this cross-sectional study including T2DM patients showed that UACR was correlated with periodontal parameters after adjusting for possible confounders including sex, age, education, household income, HbA1c, systolic blood pressure, BMI, duration of diabetes, diabetes therapy, stroke, coronary heart disease, diabetic retinopathy, hyperlipidemia, smoking, and toothbrushing frequency. These results will help strengthen the cooperation between medical and dental healthcare providers, especially for treatment of diabetes and periodontitis.

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Compliance with Ethical Standards

Conflict of interests

Kuribayashi received lecture fees from Mitsubishi Tanabe Pharma Corp. All other authors declare that they have no conflict of interest.

Research involving human participants

The study protocol was approved by the ethics committees of Jiyugaoka Medical Clinic (October 27, 2014, No. 250716) and Kanagawa Dental University July 5, 2016, No. 387; September 12, 2017, No. 446; December 20, 2017, No. 476). All procedures followed were in accordance with the ethical standards of the

responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study.

Author contributions

Michio Tanaka and Tatsuo Yamamoto conceived the idea for the study, participated in its design, performed the statistical analysis, and drafted the manuscript. Fuminobu Okuguchi, Haruhiko Isotani, Masahiro Iwamoto, Hidekatsu Sugimoto, Osamu Nakagawa, Daisuke Suzuki, Katsushige Abe, Nobuaki Watanabe, Masato Minabe, and Hiroki Yokoyama participated in data acquisition and critically revised the manuscript. Nobuichi Kuribayashi and Hiroki Yokoyama helped develop the idea for the study, participated in data acquisition and study design, and edited the manuscript. Masato Minabe and Sinya Fuchida helped develop the idea for the study and critically revised the manuscript. All authors read and approved the final manuscript.

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Table 1 Characteristics of participants

Variables	All subjects (*n* = 2,302)	Normoalbuminuria subjects (n = 1,710)
	Mean (SD), %, or median (interquartile range)	Mean (SD), %, or median (interquartile range)
UACR, mg/g creatinine (median and interquartile range)	12.9 (6.6–31.0)	9.2 (5.4–15.0)
Estimated GFR (ml/min/1.73 m^2) (mean and SD)	72.8 (18.8)	74.8 (17.3)
Age, years (mean and SD)	66.9 (10.1)	66.5 (10.0)
Male, %	59.9	58.5
Education score, 1 / 2 / 3 / 4, %	16.9 / 52.1 / 8.2 / 22.8	15.7 / 51.6 / 8.1 / 24.6
Household income score, 1 / 2 / 3 / 4, %	45.3 / 31.0 / 17.6 / 6.1	43.8 / 30. 9/ 18.9 / 6.3
HbA1c, mmol/mol (%, NGSP) (median and interquartile range)	6.9 (6.5–7.3) (51.9 (47.5–56.5))	6.8 (6.5–7.3) (50.8 (47.5–56.3))
Systolic blood pressure, mmHg (mean and SD)	126.0 (13.4)	125.1 (13.1)
Diastolic blood pressure, mmHg (mean and SD)	70.3 (10.1)	70.2 (9.9)
Body mass index, kg/m^2 (mean and SD)	24.9 (3.9)	24.6 (3.8)
Duration of diabetes, years (median and interquartile range)	8.9 (4.8–13.3)	8.6 (4.5–12.8)
Diabetes therapy, diet/tablets/insulin, %	9.5 / 73.7 / 16.8	10.9 / 74.3 / 14.7
With a history of stroke, %	5.6	4.7
With a history of coronary heart disease, %	5.3	4.4
Diabetic retinopathy, %	24.3	19.6
Hyperlipidemia, %	58.1	56.6
Smoking, never/ex/current, %	53.6 / 32.5 / 13.9	55.4 / 31.6 / 12.9
Toothbrushing per day, 1 / 2 / ≥3, %	20.1 / 53.0 / 26.9	18.8 / 53.3 / 27.9
Mean PPD, mm (mean and SD)	2.8 (0.8)	2.7 (0.7)
PPD ≥4 mm, % sites per person (median and interquartile range)	10.7 (2.9–25.9)	9.7 (2.6–23.7)
BOP, % teeth per person (median and interquartile range)	34.6 (12.5–64.3)	33.3 (11.5–63.0)

Tooth mobility, % teeth per person (median and interquartile range)	5.9 (0.0–25.9)	4.8 (0.0–23.1)
Number of teeth present, count per person (median and interquartile range)	24.0 (19.0–27.0)	25.0 (19.0–27.0)
Severity of periodontitis, no / initial / moderate / severe / advanced, %	9.6 / 18.9 / 14.6 / 32.1 / 24.7	10.6 / 20.0 / 13.6 / 33.0 / 22.7

UACR: urinary albumin-to-creatinine ratio; GFR: glomerular filtration rate; HbA1c: glycated hemoglobin; SD: standard deviation; PPD: probing pocket depth; BOP: bleeding on probing

Education score: 1: junior high school / 2: high school / university <4 years / university ≥4 years

Household income score: 1: <3 million Japanese yen / 2: 3-<5 million Japanese yen / 3: 5-<10 million Japanese yen / 4: ≥10 million Japanese yen (100 Japanese yen = 1 US dollar)

Table 2 Spearman's rank correlation coefficients with urinary albumin-to-creatinine ratio

Variables	All subjects (n = 2,302)		Normoalbuminuria subjects (n = 1,710)	
	r	p	r	p
Age	0.134	<0.001	0.132	<0.001
Male	-0.037	0.077	-0.133	<0.001
Education score	-0.133	<0.001	-0.143	<0.001
Household income score	-0.084	<0.001	-0.070	0.004
HbA1c	0.133	<0.001	0.066	0.006
Systolic blood pressure	0.140	<0.001	0.092	<0.001
Body mass index	0.118	<0.001	0.040	0.094
Duration of diabetes	0.105	<0.001	0.050	0.039
Diabetes therapy (diet / tablets / insulin)	0.125	<0.001	0.052	0.032
With a history of stroke	0.060	0.004	0.021	0.392
With a history of coronary heart disease	0.030	0.144	-0.028	0.243
Diabetic retinopathy	0.181	<0.001	0.065	0.007
Hyperlipidemia	0.068	0.001	0.046	0.059
Smoking (never / ex / current)	0.025	0.222	-0.053	0.029
Toothbrushing per day (1 / 2 / ≥3)	-0.054	0.010	-0.027	0.264
Mean PPD	0.089	<0.001	0.044	0.072
Percentage of sites with PPD ≥4 mm	0.099	<0.001	0.040	0.096
Percentage of teeth with BOP	0.038	0.065	0.000	0.990
Percentage of mobile teeth	0.101	<0.001	0.072	0.003
Number of teeth present	-0.127	<0.001	-0.096	<0.001
Severity of periodontitis	0.077	<0.001	0.014	0.551

HbA1c: glycated hemoglobin; PPD: probing pocket depth; BOP: bleeding on probing

Table 3 Results of multiple linear regression analyses in all subjects

Explanatory variables	Model 1		Model 2		Model 3		Model 4	
	β	*p*	β	*p*	β	*p*	β	*p*
Mean PPD	0.108	<0.001	0.103	<0.001	0.067	0.001	0.062	0.002
Percentage of sites with PPD ≥4 mm	0.117	<0.001	0.111	<0.001	0.074	<0.001	0.068	0.001
Percentage of teeth with BOP	0.054	0.009	0.049	0.019	0.023	0.258	0.023	0.255
Percentage of mobile teeth	0.091	<0.001	0.083	<0.001	0.061	0.002	0.055	0.006
Number of teeth present	-0.084	<0.001	-0.072	0.001	-0.039	0.067	-0.030	0.160
Severity of periodontitis	0.079	<0.001	0.073	<0.001	0.054	0.007	0.049	0.015

Outcome variable was urinary albumin-to-creatinine ratio (log)

Each explanatory variable was added separately

Model 1: adjusted for sex and age

Model 2: model 1 + education score and household income score

Model 3: model 2 + HbA1c, systolic blood pressure, body mass index, duration of diabetes, diabetes therapy, with a history of stroke, with a history of coronary heart disease, diabetic retinopathy, and hyperlipidemia

Model 4: model 3 + smoking and toothbrushing frequency

HbA1c: glycated hemoglobin; PPD: probing pocket depth; BOP: bleeding on probing

Table 4 Results of multiple linear regression analyses in normoalbuminuria subjects only

Explanatory variables	Model 1		Model 2		Model 3		Model 4	
	β	*p*	β	*p*	β	*p*	β	*p*
Mean PPD	0.048	0.043	0.043	0.072	0.034	0.155	0.030	0.204
Percentage of sites with PPD ≥4 mm	0.047	0.048	0.041	0.087	0.030	0.215	0.024	0.309
Percentage of teeth with BOP	0.017	0.471	0.011	0.631	0.003	0.912	0.000	0.993
Percentage of mobile teeth	0.041	0.089	0.033	0.173	0.025	0.295	0.022	0.361
Number of teeth present	-0.040	0.112	-0.031	0.219	-0.024	0.344	-0.019	0.459
Severity of periodontitis	0.002	0.940	-0.005	0.843	-0.011	0.659	-0.014	0.555

Outcome variable was urinary albumin-to-creatinine ratio (log)

Each explanatory variable was added separately

Model 1: adjusted for sex and age

Model 2: model 1 + education score and household income score

Model 3: model 2 + HbA1c, systolic blood pressure, body mass index, duration of diabetes, diabetes therapy, with a history of stroke, with a history of coronary heart disease, diabetic retinopathy, and hyperlipidemia

Model 4: model 3 + smoking and toothbrushing frequency

HbA1c: glycated hemoglobin; PPD: probing pocket depth; BOP: bleeding on probing