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ORIGINAL ARTICLE

Albuminuria, C-reactive protein, and socioeconomic factors are associated with periodontal status in subjects with type 2 diabetes

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Abstract

Diabetes and periodontitis may increase risk of cardiovascular disease. Whether albuminuria, C-reactive protein (CRP), and socioeconomic factors, known as cardiovascular risks in subjects with poorly controlled diabetes, are independently associated with periodontal status in well-controlled diabetes remains to be elucidated. In 503 subjects with type 2 diabetes, the cross-sectional associations of clinical and socioeconomic factors with periodontal parameters were investigated. Periodontal parameters on all teeth included the probing pocket depth at 6 sites per tooth, bleeding on probing, the plaque score, tooth mobility, and the number of teeth. The subjects had a mean HbA1c value of 6.85% and a median CRP value of 0.06 mg/dL, and 27.9% of the subjects had albuminuria. Albuminuria and CRP values had significant associations with several periodontal parameters, whereas other variables including HbA1c did not. Subjects with albuminuria had significantly higher HbA1c, CRP, and % sites of pocket depth ≥ 4 mm than subjects with normoalbuminuria; additionally, those with high CRP (≥ median) had significantly higher body mass index, HbA1c, % sites of pocket depth ≥ 4 mm, and plaque score than those with low CRP. In multiple linear regression analysis, albuminuria, CRP, education, smoking, and dental attendance exhibited significant associations with periodontal parameters, independent of the effect of age, sex, body mass index, and diabetes therapy. Albuminuria, CRP, education, smoking, and dental attendance were independently associated with periodontal parameters even in subjects with a mean of HbA1c of 6.85%, implying the importance of these factors for the prevention of cardiovascular disease.

Keywords Periodontitis · Type 2 diabetes · Albuminuria · C-reactive protein · Education · Dental attendance

Abbreviations

CVD	Cardiovascular disease
CRP	C-reactive protein
BP	Blood pressure
NHANES	National Health and Nutrition Examination Survey
HbA1c	Glycated hemoglobin A1c
LDL	Low density lipoprotein
HDL	High density lipoprotein
PPD	Probing pocket depth
JDS	Japan Diabetes Society
BOP	Bleeding on probing
BMI	Body mass index
Cr	Creatinine
ACR	Urinary albumin-to-creatinine ratio
GFR	Glomerular filtration rate
CHD	Coronary heart disease

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Introduction

Subjects with type 2 diabetes exhibit a two to three-fold higher risk of cardiovascular disease (CVD) than individuals without diabetes [1]. The causal relationship between diabetes and CVD has been investigated, in which albuminuria, C-reactive protein (CRP), and socioeconomic status were described as contributing factors. Previous studies indicated that poor glycemic control was a substantial risk factor that would contribute to development of albuminuria [2] and elevated levels of CRP [3–5], and might be associated with low socioeconomic status [6, 7].

Periodontitis, the most common chronic inflammatory conditions in humans worldwide [8, 9], has been epidemiologically indicated to play a causal role in the onset of CVD in the general population [10–12]. Periodontitis likely contributes to the increased risk of CVD in subjects with diabetes [13], although the details of this relationship remain to be elucidated. A number of previous studies indicated the deleterious effect of poor glycemic control on periodontitis and the bidirectional associations between diabetes and periodontitis [14–17]. However, blood glucose control, as well as management of blood pressure (BP) and lipids, is improving leading to longevity in patients with type 2 diabetes [18, 19]. It is very important to clarify which factors in individuals with well-controlled diabetes may affect periodontal status, although few studies have been performed in patients with well-controlled diabetes at present [20]. At older ages, loss of tooth and masticatory function independently affects nutritional status, disability, and mortality [21], which would affect dietary therapy and quality of life especially for patients with long-standing type 2 diabetes.

Historically, several national probability surveys including the National Health and Nutrition Examination Survey (NHANES) in United States have assessed the periodontal status [22]. However, these studies were formerly performed by partial mouth examinations at 2 sites per tooth. Because periodontitis is not evenly distributed throughout the mouth, prevalence estimates from partial mouth examinations underestimate the disease [22]. It was only in 2009 that the NHANES cycle began a protocol with full-mouth examinations at 6 sites per tooth. Periodontal status using this full-mouth protocol in subjects with diabetes has not yet been adequately investigated also in Japan [23].

Periodontitis is likely associated with age, sex, race, obesity, blood glucose, and a history of stroke, i.e., clinical factors [15, 16]. It may also be associated with toothbrushing, dental attendance, smoking, marital status, household income, and education levels, i.e., oral hygiene/socioeconomic factors [15, 16, 22]. Social gradients as presented by education, occupation, household income, and subjective social status have recently been proposed as important determinants of periodontal status [24]. However, studies on periodontal status from bilateral aspects of clinical and socioeconomic factors have not yet been adequately performed in subjects with diabetes.

Hyperglycemia alters various proinflammatory mediators such as TNF-α, IL-6, leptin, and CRP, and contributes to dysregulated inflammatory responses that impact on multiple body systems, including the periodontal and vascular tissues [17]. Chronic low-grade inflammation as indicated by elevated CRP has been shown to predict future onset of CVD among apparently healthy individuals [25], which may be due at least in part to periodontitis [26]. Previous studies have indicated the degree of albuminuria as an independent predictor for progression of CVD in subjects with diabetes [27, 28], and it also correlates with the severity of periodontitis [29, 30].

However, it is not known whether slightly elevated levels of albuminuria and CRP in individuals with well-controlled diabetes are associated with periodontal status, or how socioeconomic factors independently affect periodontal status. Therefore, we performed this study to investigate whether albuminuria, CRP, and socioeconomic factors are associated with the full-mouth examined periodontal status in subjects whose mean values of glycemic, BP, and lipid controls were below the recommended target levels.

Methodology

Study design

The design of this study, which included subjects with diabetes who regularly attended the internal medicine clinic, was as follows: (1) the periodontal status was examined in a nearby dental clinic which reported the results to the medical clinic using an uniform predefined dental chart, (2) predefined socioeconomic questionnaire was administered at the internal medicine clinic, and (3) the associations of clinical and socioeconomic factors with periodontal parameters were explored.

Study population

Consecutive subjects with type 2 diabetes who visited the Jiyugaoka Medical Clinic from January to June in 2015 were enrolled in the periodontitis study if they met the following criteria: those who had been visiting the medical clinic for more than 1 year and had already stabile control of their blood glucose, blood pressure and lipid, had at least 4 teeth in total, and provided written informed consent to participate in the study. Subjects with diabetes were treated with the aim of achieving the targets recommended by the Japan Diabetes Society (JDS), of a glycated hemoglobin A1c (HbA1c) value of < 7.0% (53 mmol/mol), BP < 130/80 mmHg, and serum concentrations of low-density lipoprotein (LDL) cholesterol < 3.1 mmol/L (120 mg/dL), high-density lipoprotein (HDL) cholesterol ≥ 1.0 mmol/L (40 mg/dL), and non-HDL cholesterol < 3.8 mmol/L (150 mg/dL). Subjects with type 1 diabetes were not included. The subjects were asked to visit a nearby dental office regardless of whether they regularly obtained dental care. The uniform dental chart was prepared in consultation with dental researchers. It included 6 sites for probing pocket depth (PPD) determination, 4 sites for dental plaque determination, and two check boxes to indicate presence or absence of bleeding on probing (BOP) and tooth mobility, for each tooth in the full-mouth exam. After the informed consent to participate in the study was provided by a patient, dental chart with the attached written informed consent was brought to a dentist by the patient. The dentist filled in the chart after completing the examination, and the chart was collected. There were 26 local dentists who cooperated to perform the examination (see appendix). The study protocol was approved by the Jiyugaoka Medical Clinic Ethical Board number #250716. All participants provided written informed consent and the study was carried out in accordance with the Helsinki Declaration II.

Measurements and definition

Type 2 diabetes was diagnosed according to the Japan Diabetes Society criteria; fasting blood glucose of 7.0 mmol/L (126 mg/dL) or greater, casual blood glucose of 11.1 mmol/L (200 mg/dL) or greater, or HbA1c ≥ 6.5%. The following variables were measured once when a patient visited the medical clinic during the study period. BP was measured with an appropriate sized cuff using an automated BP device. Body mass index (BMI) was calculated as weight per height squared (kg/m^2). Non-fasting blood samples were drawn and analyzed to measure plasma glucose, HbA1c, and serum concentrations of LDL- and HDL-cholesterol, triglyceride, creatinine and CRP. HbA1c was measured by high-performance liquid chromatography, which has been certified by the National Glycohemoglobin Standardization Program. Serum and urinary concentrations of creatinine (Cr) were measured by an enzymatic method. Urinary albumin was measured using random urine samples by a turbidimetric immunoassay. Albuminuria, i.e., the urinary albumin excretion rate, was recorded as the albumin-to-creatinine ratio (ACR). Normoalbuminuria, microalbuminuria, and macroalbuminuria were defined as an ACR < 30 mg/g Cr, an ACR ≥ 30 and < 300 mg/g Cr, and an ACR ≥ 300 mg/g Cr, 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). CRP was measured by latex-enhanced nephelometry at the visit without any symptomatic acute infections (such as common cold, and fever.) to estimate the degree of low-grade inflammation. With regard to the treatment of diabetes, subjects were divided into groups by treatment of diet alone, hypoglycemic tablets, or insulin. Past history of coronary heart disease (CHD) and ischemic stroke was noted. Use of antihypertensive drugs, calcium-channel blockers, or lipid-lowering drugs was obtained from the patient's record. Diabetic retinopathy was diagnosed by an ophthalmologist after pupillary dilation.

The socioeconomic questionnaire included questions on smoking, toothbrushing, income, education, and dental attendance. Smoking was defined as never/ex/current. Toothbrushing was defined as times of 1/2/≥ 3 per day. The household income and education scores were categorized as 1: < 3 million, 2: 3–< 5 million, 3: 5–< 10 million, and 4: ≥ 10 million Yen per year, and as 1: junior high school, 2: high school, 3: college ≤ 2 years, and 4: college > 2 years, respectively. Dental attendance was scored as 1: rarely or never, 2: attended occasionally, and 3: attended regularly.

Periodontal examination

The uniform dental chart included information on periodontal PPD, BOP, dental plaque, tooth mobility, and number of teeth. PPD was assessed using a manual, calibrated periodontal probe, and measured at six sites per tooth (mesiobuccal, midbuccal, distobuccal, mesiolingual/palatal, midlingual/palatal, and distolingual/palatal). PPD was defined as the distance from the gingival margin to the base of the clinical pocket. Individual scores were expressed as the mean PPD, percentage of sites with PPD ≥ 4 mm, and number of sites with PPD ≥ 4 mm. BOP was recorded as present if it occurred within 30 s of probing and absent if no bleeding occurred [31]. Plaque score was recorded at four sites per tooth (mesiobuccal, midbuccal, distobuccal, and midlingual/palatal) and expressed as percentage of sites with dental plaque [32]. Manual examination of tooth mobility was assessed and defined as being with (score 1–3) or without mobility (score 0) [33].

Statistical analysis

Data were expressed as the mean ± SD if normally distributed or as the median (interquartile range) if not normally distributed. Spearman's rank-sum correlation coefficient was used to assess the relationship between each periodontal parameter and clinical/socioeconomic factors. The significance of differences between groups was assessed by Chi squared tests for categorical variables and the Student's *t* test or Mann–Whitney *U* test for continuous variables. Multivariate linear regression analysis was performed to explore the associations of clinical and socioeconomic factors with each periodontal parameter after adjustment for age, sex, BMI and diabetes therapy, and the standardized correlation coefficients (β) were given. Albuminuria and CRP as continuous variables exhibited a skewed-distribution and were first logarithmically transformed before any analysis. A *p* value less than 5% (two-tailed) was considered significant. All analyses were performed using the SPSS statistical software package (SPSS Japan, Tokyo, Japan).

Results

Clinical and socioeconomic factors of the subjects and the simple correlations with periodontal parameters

The clinical and socioeconomic factors of the 503 subjects with type 2 diabetes are shown in Table 1. A total of 27.9% of the subjects were found to have albuminuria, 21.7% retinopathy, 26.1% toothbrushing once a day, 25.3% the lowest education score, and 11.3% rare dental attendance. The values of each periodontal parameter (median and interquartile range) are given in Table 2. Most of the subjects (90.7%) had PPD ≥ 4 mm at one or more sites, although the median (interquartile range) value of % sites with PPD ≥ 4 mm was 12.6% (3.8–30.4%). Spearman's correlation coefficients between periodontal parameters and clinical/socioeconomic factors are shown in Table 2. Both albuminuria and CRP values had significant associations with mean PPD, % sites with PPD ≥ 4 mm, number of sites with PPD ≥ 4 mm, and % sites with plaque score, whereas the periodontal parameters did not have any significant correlations with clinical factors such as HbA1c, casual blood glucose, systolic BP, lipid profiles, use of antihypertensive and lipid-lowering drugs (data not shown), or the presence of retinopathy or CVD. Regarding socioeconomic factors, education and dental attendance followed by smoking, toothbrushing and household income had significant associations with some periodontal parameters.

Associations of albuminuria and CRP with clinical, socioeconomic, and periodontal parameters

Subjects with and without albuminuria, and those with and without high CRP ≥ median level, were compared in terms of clinical factors, socioeconomic factors, and periodontal parameters, as shown in Table 3. Subjects with albuminuria had significantly higher values in HbA1c, CRP, and % sites with PPD ≥ 4 mm, lower value of HDL-cholesterol, and they had higher percentages of retinopathy than subjects

Table 1 Clinical characteristics of the subjects with type 2 diabetes ($N = 503$)

(a) Clinical factors	
Age, years	66.1 ± 10.6
Male, %	69.2
Body mass index, kg/m^2	26.2 ± 4.3
Diabetes therapy, diet/tablets/insulin, %	8.6/73.1/18.3
Duration of diabetes, years	14.1 ± 8.4
HbA1c, mmol/mol (%, NGSP)	51 ± 5 (6.85 ± 0.73)
Casual blood glucose, mg/dL	156 ± 52
Systolic/diastolic BP, mmHg	123 ± 14/66 ± 11
Use of antihypertensive drugs, %	62.4
Use of calcium-channel blockers, %	37.6
LDL cholesterol, mg/dL	94 ± 28
HDL cholesterol, mg/dL	58 ± 16
Triglycerides, mg/dL (median and interquartile range)	126 (88–185)
Use of lipid-lowering drugs (statin), %	44.8 (37.8)
Albuminuria, mg/gCr (median and interquartile range)	12.9 (7.2–36.2)
Normo-/micro-/macroalbuminuria, %	72.1/23.5/4.4
eGFR, ml/min/1.73 m^2	68.3 ± 19.2
CRP, mg/dL (median and interquartile range)	0.06 (0.03–0.13)
Diabetic retinopathy, %	21.7
With a history of stroke, %	5.6
With a history of CHD, %	4.0
(b) Socioeconomic factors	
Smoking, never/ex/current, %	41.1/41.7/17.2
Toothbrushing per day 1/2/≥ 3, %	26.1/53.5/20.4
Household income score 1/2/3/4, %	53.1/25.9/16.4/4.6
Education score 1/2/3/4, %	25.3/53.0/6.6/15.1
Dental attendance score 1/2/3, %	11.3/29.4/59.3

BP blood pressure, *eGFR* estimated glomerular filtration, *CRP* C-reactive protein, *CHD* coronary heart disease

Table 2 Spearman's correlation coefficients between periodontal parameter and clinical/socioeconomic parameter

	Mean PPD, Mm	PPD ≥ 4 mm		BOP	Plaque score,	Tooth mobility	Number of teeth
		% sites	Number of sites	% teeth	% sites	% teeth	
Values (median and interquartile range)	2.76 (2.27–3.27)	12.6 (3.8–30.4)	14.0 (4.0–33.0)	33.3 (10.3–63.2)	39.3 (16.8–62.5)	7.1 (0.0–28.6)	22 (17–26)
Age, years	0.007	−0.001	−0.074	−0.102	0.006	***0.097***[a]	***−0.336***[c]
Male, %	0.021	0.018	0.055	−0.035	0.061	−0.090	***0.140***[b]
Body mass index, kg/m^2	0.073	0.065	0.084	0.080	0.042	−0.011	***0.104***[a]
Diabetes therapy, Diet/Tablets/Insulin	0.016	0.047	0.019	0.031	***0.120***[b]	0.027	−0.062
Duration of diabetes, years	−0.042	−0.026	−0.064	***−0.103***[a]	0.010	−0.015	***−0.152***[b]
HbA1c, %	−0.038	−0.035	−0.051	−0.028	0.009	−0.004	−0.027
Casual blood glucose, mg/dL	0.015	0.014	0.001	0.064	0.039	0.016	−0.033
Systolic BP, mmHg	0.058	0.084	***0.089***[a]	0.009	0.060	−0.043	0.039
LDL cholesterol, mg/dL	−0.001	−0.006	0.006	0.023	−0.049	0.003	0.039
HDL cholesterol, mg/dL	−0.063	−0.078	−0.073	0.024	−0.043	−0.005	0.012
Triglycerides, logarithmic mg/dL	−0.006	−0.002	0.015	−0.050	−0.054	−0.009	0.058
Albuminuria, logarithmic mg/gCr	***0.107***[a]	***0.135***[b]	***0.115***[a]	0.037	***0.097***[a]	0.061	−0.072
Normo-/micro-/macroalbuminuria	0.069	***0.095***[a]	0.066	0.036	***0.093***[a]	0.046	-0.066
eGFR, ml/min/1.73 m^2	−0.012	−0.017	0.027	0.044	−0.059	−0.031	***0.178***[c]
CRP, logarithmic mg/dL	***0.117***[b]	***0.154***[b]	***0.150***[b]	0.050	***0.141***[b]	0.054	0.039
Diabetic retinopathy	−0.018	0.028	0.003	−0.036	−0.048	0.035	−0.082
With a history of stroke	0.005	0.025	0.012	0.000	0.084	0.031	−0.052
With a history of CHD	−0.024	−0.007	−0.021	−0.055	0.006	−0.068	−0.066
Smoking, never/ex/current	0.061	***0.096***[a]	***0.111***[a]	−0.034	0.029	−0.019	0.020
Tooth brushing per day, 1/2/3 or more	−0.025	−0.081	−0.077	−0.027	***−0.096***[a]	0.059	−0.045
Household income score 1/2/3/4	0.011	−0.016	0.041	0.053	−0.051	0.004	***0.221***[c]
Education score 1/2/3/4	***−0.138***[b]	***−0.135***[b]	−0.065	−0.067	***−0.102***[a]	***−0.090***[a]	***0.249***[c]
Dental attendance score 1/2/3	−0.067	***−0.112***[a]	***−0.116***[a]	−0.069	***−0.171***[b]	−0.051	−0.072

BP, blood pressure, eGFR, estimated glomerular filtration; CRP, C-reactive protein; CHD, coronary heart disease

[a]$p < 0.05$, [b]$p < 0.01$, [c]$p < 0.001$

Categorical variables included male, diabetes therapy, normo-/micro-/macroalbuminuria, retinopathy, stroke, CHD, smoking, toothbrushing, income, education, and dental attendance, and others were continuous variables

Table 3 Comparison of variables between subjects with micro/macroalbuminuria and normoalbuminuria, and with CRP ≥ median and CRP < median

	Albuminuria		CRP	
	Micro or macro	Normo	≥ Median	< Median
Age, years	67.2 ± 10.4	65.6 ± 10.7	65.6 ± 11.7	66.5 ± 9.4
Male, %	72.7	67.6	69.3	69.0
BMI, kg/m^2	26.6 ± 4.5	26.0 ± 4.3	27.4 ± 5.0[c]	25.0 ± 3.3
HbA1c, %	6.97 ± 0.86[a]	6.80 ± 0.65	6.94 ± 0.83[c]	6.77 ± 0.60
Systolic BP, mmHg	124 ± 16	122 ± 13	123 ± 13	122 ± 14
Diabetic retinopathy, %	32.4[c]	17.5	24.2	19.2
Albuminuria, mg/gCr	79.5 (45.5–182.3)[c]	9.3 (5.9–15.3)	13.7 (7.6–44.3)	12.9 (6.7–30.3)
CRP, mg/dL	0.065 (0.030–0.183)[a]	0.054 (0.030–0.122)	0.13 (0.081–0.27)[c]	0.030 (0.020–0.040)
LDL cholesterol, mg/dL	90.7 ± 31.1	95.7 ± 27.2	92.9 ± 28.4	95.5 ± 28.4
HDL cholesterol, mg/dL	53.7 ± 14.7[c]	59.8 ± 15.9	55.6 ± 15.7[c]	60.3 ± 15.6
Triglycerides, mg/dL (median and interquartile range)	131 (88.5–187)	125 (88–181)	142 (96.0 – 195)[c]	113 (82.5–164)
Smoking, never/ex/current, %	41.0/39.6/19.4	41.4/42.3/16.3	39.8/39.0/21.3	42.4/44.4/13.2
Education score 1/2/3/4, %	30.9/51.8/7.2/10.1	23.2/53.4/6.4/17.0	28.4/52.0/5.2/14.4	22.2/54.0/7.9/15.9
Dental attendance score 1/2/3, %	16.8/24.8/58.4	9.5/31.4/59.2	9.1/31.9/59.1	13.5/27.0/59.5
Mean PPD, mm	2.8 (2.3–3.5)	2.7 (2.3–3.2)	2.8 (2.3–3.4)[a]	2.7 (2.2–3.1)
PPD ≥ 4 mm, % of sites	14.6 (5.2–42.5)[a]	11.0 (3.3–26.1)	15.7 (4.3–38.8)[b]	10.3 (3.3–23.7)
PPD ≥ 4 mm, number of sites	16.0 (5.5–41.0)	14.0 (3.8–31.3)	16.0 (5.0–43.3)[a]	13.0 (3.0–29.0)
BOP, % of sites	33.3 (12.7–69.0)	32.7 (10.0–61.4)	34.8 (10.7–68.4)	31.4 (10.0–59.2)
Plaque score, % of sites	42.6 (21.8–65.8)	37.5 (15.0–59.8)	43.4 (19.1–65.4)[a]	36.3 (15.3–57.2)
Tooth mobility, % of sites	7.3 (0.0–38.7)	7.3 (0.0–38.7)	11.1 (0.0–33.3)	5.0 (0.0–22.2)
Number of teeth	21.0 (16.0–26.0)	23.0 (18.0–26.0)	23.0 (17.0–26.0)	22.0 (17.0–26.0)

[a]$p < 0.05$, [b]$p < 0.01$, and [c]$p < 0.001$, by Student's *t* test (mean ± SD), Chi-square test (categories), or Mann–Whitney *U* test [median (interquartile range)]. Categorical variables included male, retinopathy, smoking, education, and dental attendance, and others were continuous variables

with normoalbuminuria. Subjects with CRP ≥ median had higher BMI, HbA1c, triglycerides, mean PPD, % sites with PPD ≥ 4 mm, number of sites with PPD ≥ 4 mm, and % sites with plaque, and lower value of HDL-cholesterol, than subjects with low CRP.

Clinical and socioeconomic factors to determine each periodontal parameter in multiple linear regression analysis

Multiple linear regression analysis was performed to explore clinical and oral hygiene/socioeconomic factors that may determine each periodontal parameter, as shown in Table 4. Albuminuria was associated with % sites with PPD ≥ 4 mm, plaque score, and tooth mobility independent of the effect of age, sex, BMI and diabetes therapy (Model A). CRP values were independently associated with % sites with PPD ≥ 4 mm, number of sites with PPD ≥ 4 mm, and plaque score (Model B). In Model C where both albuminuria and CRP were entered, albuminuria and CRP continued to have independent associations with % sites with PPD ≥ 4 mm and tooth mobility/plaque score. In Model D to assess socioeconomic factors, education followed by smoking and dental attendance had significant associations with the periodontal parameters. When clinical and socioeconomic factors were simultaneously assessed as shown in Model E, education had the largest number of significant associations with periodontal parameters, followed by albuminuria and CRP. In Model F where dental attendance was added to Model E, education, dental attendance, CRP and smoking had independent associations with some periodontal parameters, while albuminuria lost the significance.

Discussion

We assessed periodontal parameters from 6 sites per tooth on all teeth in elderly subjects with type 2 diabetes, and explored the associations of clinical and socioeconomic factors with periodontal parameters. Importantly, the study was carried out in patients whose mean values of glycemic, BP, and lipid profiles were below the target recommended by the JDS. Regarding clinical factors, we found that albuminuria and CRP were independently associated with % sites with

Table 4 Multivariate regression analyses adjusted for age, sex, body mass index and diabetes therapy to explore the associations of clinical and socioeconomic factors with periodontal parameters

Models	Mean PPD, (n = 487) (mm)	PPD ≥ 4 mm, (n = 487)		BOP, (n = 481)	Plaque score, (n = 462)	Tooth mobility, (n = 465)	Number of teeth, (n = 493)
		% of sites	number of sites	% of sites	% of sites	% of sites	
	β	β	β	β	β	β	β
(A) Albuminuria	0.091	***0.134***[b]	0.038	0.043	***0.098***[a]	***0.129***[b]	−0.050
(B) CRP	0.090	***0.129***[b]	0.088	0.027	***0.121***[a]	0.019	0.028
(C) Albuminuria	0.082	***0.122***[b]	0.029	0.040	0.087	***0.129***[b]	−0.054
CRP	0.085	***0.117***[a]	0.087	0.025	***0.120***[a]	0.005	0.040
(D) Smoking	0.070	***0.109***[a]	0.067	−0.043	−0.017	***0.131***[a]	***−0.157***[b]
Toothbrushing	−0.006	−0.07	0.011	−0.018	−0.043	0.023	−0.018
Income	0.057	0.029	0.014	0.077	−0.002	0.080	0.058
Education	***−0.157***[b]	***−0.129***[a]	−0.046	***−0.142***[b]	−0.093	***−0.117***[a]	***0.104***[a]
Dental attendance	−0.092	***−0.145***[b]	***−0.128***[b]	−0.056	***−0.173***[c]	−0.072	−0.029
(E) Albuminuria	0.063	***0.106***[a]	0.021	0.025	0.073	***0.117***[a]	−0.037
CRP	0.076	***0.105***[a]	0.080	0.026	***0.120***[a]	−0.009	0.057
Smoking	0.049	0.080	0.051	−0.057	−0.034	0.099	***−0.125***[b]
Education	***−0.142***[b]	***−0.119***[a]	−0.055	***−0.126***[a]	***−0.111***[a]	−0.065	***0.121***[b]
(F) Albuminuria	0.060	0.087	0.019	0.014	0.051	0.084	0.004
CRP	0.087	***0.117***[a]	0.088	0.052	***0.134***[b]	0.011	0.041
Smoking	0.045	0.080	0.047	−0.059	−0.046	***0.117***[a]	***−0.147***[b]
Education	***−0.132***[a]	***−0.109***[a]	−0.037	***−0.115***[a]	−0.084	−0.081	***0.126***[b]
Dental attendance	***−0.098***[a]	***−0.158***[b]	***−0.136***[b]	−0.065	***−0.191***[c]	−0.074	−0.023

Clinical factors (Models A–C), socioeconomic factors (Model D), and the combined factors (Model E and F) were analyzed

[a]$p < 0.05$, [b]$p < 0.01$, [c]$p < 0.001$. β indicates standardized correlation coefficient

Categorical variables included smoking, toothbrushing, income, education, and dental attendance, and others were continuous variables

PPD ≥ 4 mm and plaque score after controlling for the effect of age, sex, BMI, and diabetes therapy. Regarding socioeconomic factors, smoking, education, and dental attendance were independently associated with several periodontal parameters. In the combined model, albuminuria, CRP, education, and dental attendance were the independent predictors, while albuminuria lost significance after controlling for dental attendance. This study suggested that albuminuria, CRP, and social gradients were associated with dental status in elderly subjects with type 2 diabetes.

Albuminuria and CRP being associated with periodontal parameters in type 2 diabetes

HbA1c at a mean of 6.85% represented good glycemic control. Although the HbA1c value did not correlate with periodontal parameters, it was significantly associated with albuminuria and CRP. Subjects with microalbuminuria had higher CRP levels and higher rates of diabetic retinopathy, and those with high CRP had increased overweight or obesity as indicated by higher BMI levels, which is known to induce the production of inflammatory cytokines and create a state of chronic low-grade inflammation [34]. Thus, the two variables likely reflect tissue damages which help explain the increased risk of CVD in subjects with diabetes. Microalbuminuria is a marker for endothelial dysfunction [27, 35, 36], which is influenced by chronic low grade inflammation and predicts CVD [28, 37, 38]. The above findings may suggest a series of processes; enhanced chronic low-grade inflammation (i.e., elevated CRP) and high blood glucose lead to endothelial dysfunction and microalbuminuria that will increase the risk of CVD [27, 28, 35–38]. Periodontitis is likely a source of this systemic chronic low-grade inflammation [10–12]. This concept is consistent with previous studies that indicated rare toothbrushing was associated with elevated levels of CRP and fibrinogen [39], impaired endothelial function [40, 41], and increased incidence of CVD [39]. Another report indicated that treatment of periodontitis induced improved endothelial function [35]. We have to acknowledge that the present study was cross-sectional and found no associations of periodontal status with CVD, thus the causal relationship cannot be referred. However, we tempt to believe an implication that the above findings should warrant future studies to explore whether oral health care accompanied with monitoring of albuminuria and CRP can reduce the risk of CVD in subjects with type 2 diabetes.

Socioeconomic status and periodontal status

The prevalence of periodontitis is reportedly different between the lowest and highest levels of socioeconomic status as defined by poverty, education, household income, and/or dental attendance [12, 15, 22], but to our knowledge such analyses have not yet been adequately performed among the Japanese populations. We found that lower education was significantly associated with worse periodontal status in the Japanese subjects with diabetes, whereas household income showed no association. The reason for a lack of association between household income and periodontal status was that most of the enrolled subjects were aged, retired, and pensioners. It is presumed that limited education may result in decreased socioeconomic status and reduce access to health information and oral health services. A social gradient was reported by a cross-sectional study on Japanese male workers which showed that professional and office workers had better periodontal status than sales persons, individuals in service occupations, and drivers [42]. Another study in Japanese older people indicated that the job held for the longest time in an individual's life was one of the major determinants of oral health status and oral health behavior [43]. Our findings clearly support the existence of the social gradient in oral health in real-world patients with type 2 diabetes.

Study limitations

The potential limitations of this study should be mentioned. First, we acknowledge that clinical attachment loss was not measured, and dentist-to-dentist variations in the examined periodontal parameters were not evaluated. It was not feasible to examine these two issues because the study was performed in community-based primary care setting including more than 25 dental practitioners, and measurement of clinical attachment loss is not covered by medical insurance, and thus is not commonly performed in real-world practice in Japan. However, the examination was performed in 6 sites per tooth on all teeth, which is valid and superior to the partial-mouth and 2 or 4 sites methods formerly used, and allows for a more precise assessment [22]. Furthermore, the study was completed through uniform dental charts and use of a predefined socioeconomic questionnaire. Second, treatment for diabetes was done at a single institution and the generalizability of the results must be confirmed by other institutions. However, clinical and laboratory data, together with dental attendance, were carefully collected and the present study reflects real-world practice. The independent significant impact of dental attendance convincingly reinforced the importance of the collaboration between physicians and oral health care providers. Third, the median PPD of 2.76 mm, the median % sites with PPD $\geq$ 4 mm of 12.6%, the median % teeth with BOP of 33.3%, and the median plaque score of 39.3% were lower than the results found in other periodontal examination studies dealing with subjects with diabetes [44, 45]. This is likely because the present study was not designed to collect subjects with severe periodontitis, but recruited regular attenders to the medical clinic with stabile blood glucose control. As a result, we should acknowledge that the correlations between periodontal parameters and the clinical and socioeconomic factors were rather low (i.e., $<$ 0.200). Finally, there were missing data in multiple regression analyses. However, the rate was low and we confirmed the unchanged results by multiply imputed dataset to account for bias due to missing information in the models (data not shown).

In conclusion, we found in this study that slightly elevated levels of albuminuria and CRP, and socioeconomic factors such as low education and rare dental attendance were associated with full-mouth examined periodontal status in subjects whose mean values of glycemic, BP, and lipid profiles were below the target recommended by the JDS. Periodontal health should be promoted as an integral component of diabetes management through collaboration between physicians and oral health care providers.

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Compliance with ethical standards

Ethical approval The study protocol was approved on Oct. 27th in 2014 by the Jiyugaoka Medical Clinic Ethical Board number #250716. All participants provided written informed consent and the study was carried out in accordance with the Helsinki Declaration II.

Conflict of interest All authors have no conflicts of interest to disclose.

Appendix

The following dentists contributed to the present study: Tsugayasu H, Shibata K, Kobayashi Y, Takada H, Arita S, Ootaki T, Okuma N, Makino S, Endo I, Yamamoto H, Hasegawa K, Takada I, Mori K, Sasahara D, Kuniyasu H, Kurihara N, Houzawa T, Kamada Y, Watanabe N, Funatsu S, Oguchi Y, Sasaki Y, Kayou S, Outa N, Narita Y, and Tsurushima S.

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