ORIGINAL

Factors associated with diabetes control : results of a 2-year cohort study of outpatients with type 2 diabetes

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Abstract : Type 2 diabetes is a typical lifestyle disease. We aimed to identify the factors affecting glycemic control in 64 outpatients with type 2 diabetes over a 2-year period. We defined poor glycemic control using a change in glycosylated hemoglobin (ΔHbA1c) of ≥0.5% over 2 years and/or HbA1c ≥7.5% at the end of the study period. We used a questionnaire to collect information on oral health behavior and lifestyle, including eating and smoking habits, and analyzed the relationships between indices of diabetes control and responses to the questionnaire. The mean (SD) HbA1c of the participants was 6.87% (0.77%) at a baseline, and 6.93% (0.69%) after 2 years. Twenty-three participants (36.0%) had poor glycemic control. ΔHbA1c and the change in body mass index (ΔBMI) correlated (Spearman's rank correlation, r=0.350, $p<0.01$). The HbA1c at baseline was associated with eating slowly/chewing well, and ΔBMI was associated with perceived oral symptoms. Binominal logistic regression analysis revealed that poor glycemic control was associated with ΔBMI and a smoking habit (odds ratio : 1.62, 95% confidence interval : 1.08–2.42 ; and 4.01, 1.12–14.36, respectively). These findings imply that weight gain and a smoking habit are associated with poor glycemic control in patients with type 2 diabetes. J. Med. Invest. 70 : 28-33, February, 2023

Keywords **:** *poor glycemic control, HbA1c, body mass index, smoking habit, oral symptom*

INTRODUCTION

Type 2 diabetes is predisposed to lifestyle factors, such as overeating, insufficient exercise, and obesity. In addition, eating rapidly without chewing well has recently been reported to be a risk factor for diabetes in the Japanese general population (1). In a previous study of outpatients with type 2 diabetes, we found that a glycosylated hemoglobin (HbA1c) < 7.5% is associated with 'eating slowly and chewing well every day' (2). Furthermore, oral health-related parameters, especially the presence of periodontal inflammation, is related to glycemic control in patients with type 2 diabetes, and many previous intervention studies have shown improvements in glycemic control following periodontal treatment (3-5).

Smoking is also a well-known common risk factor for type 2 diabetes and periodontal disease. In a systematic review by Akter *et al*., it was shown that cigarette smoking is associated with a higher risk of type 2 diabetes in Japanese individuals (6). The amount of time elapsed since the cessation of smoking has also been reported to be inversely related to the risk of type 2 diabetes (6). Dental professionals are expected to participate in programs aimed at stopping smoking (7), and guidance regarding the cessation of smoking is included in dental insurance coverage in Japan. Thus, dental professionals should provide appropriate information to smokers with type 2 diabetes concerning the relationships between smoking and both type 2 diabetes and periodontal disease. In the present study, we aimed to identify factors mediating the relationship between poor glycemic control and lifestyle, including smoking and oral health behaviors, in outpatients with type 2 diabetes.

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PATIENTS AND METHODS

We conducted a 2-year cohort study of outpatients with type 2 diabetes. The subjects were recruited consecutively from the Department of Diabetes at Kawashima Hospital, Tokushima, Japan, between May 2018 and March 2019. The study cohort comprised 64 patients undergoing treatment and regularly visiting a medical department specializing in diabetes. Patients who were using insulin, undergoing dialysis, and/or required hospitalization were excluded. A structured questionnaire comprising questions related to oral health behaviors, including smoking habits, was administered (Figure 1). This questionnaire was developed by the Japanese Dental Association for use during standard dental check-ups for adults (8). We obtained clinical data (HbA1c and body mass index [BMI]) from the clinical records of the participants at baseline and 2 years later, and calculated the changes in HbA1c (ΔHbA1c) and BMI (ΔBMI). We defined poor glycemic control using ΔHbA1c ≥ 0.5% and/or HbA1c ≥ 7.5% at the 2-year time point. The relationships of HbA1c at baseline, ΔHbA1c, BMI at baseline, and ΔBMI with responses to the questionnaire were analyzed using Spearman's rank correlation. The relationships between ΔBMI and responses to the questionnaire were analyzed using the Mann-Whitney U-test. The relationships between the responses to the questionnaire and poor glycemic control were investigated using the chi-square test. Binominal logistic regression analysis was used to identify factors associated with poor glycemic control. Statistical analyses were performed using IBM SPSS 24.0 (IBM, Tokyo, Japan), and statistical significance was accepted when $p < 0.05$.

This study was performed in accordance with Declaration of Helsinki. The study was approved by the ethics committee of

Questionnaire

Q1 Are you worried anything in your mouth? (No, Yes)
Q1-2 If Yes on Q1, what is it? Please check the applicable ones. (1) bite (2) appearance (3) speech (4) bad breath (5) pain (6) other
Q2 How many present teeth do you have? Do you have 20 teeth and more? (Yes, No)
Q3 Can you chew firmly with your back teeth? (both side; one side, not both)
Q4 Do your gum bleed on toothbrushing? (No; sometimes, usually)
Q5 Is your gum swelling? (No; sometimes, usually)
Q6 Are your teeth sensitive to the cold or the hot? (No, sometimes, usually)
Q7 Do you have a primary dentist? (Yes, No)
Q8 Are you sometimes too busy to go to dentist? (No, Yes)
Q9 Are you treated for these diseases? (Diabetes/ Stroke/Heart disease)
Q10 Do your family and/or people around are interested in oral health? (Yes, unclear, No)
Q11 Do you have confidence in your teeth, or have you ever been praised on your teeth? (Yes, unclear, No)
Q12 Do you brush your teeth at your workplace or outside? (every time, sometimes; No)
Q13 Do you have snacks (sweet food and/or drink)? (No, sometimes, every day)
Q14 Do you smoke? (No, Yes)
Q15 Do you brush your teeth before bedtime? (every day; sometimes, No)
Q16 Do you use toothpaste containing fluoride? (Yes, No, unclear)
Q17 Do you use interdental brush or dental floss? (every day, sometimes; No)
Q18 Do you eat slowly and with well chewing during meal? (every day; sometimes, No)
Q19 Have you ever been received tooth brushing instruction at dental office? (Yes, No)
Q20 Do you receive a periodical checkup at dental office more than once a year? (Yes, No)

Figure 1. Questionnaire
The possible options are shown in parentheses. Datasets were compared using the chi-square test.

Kawashima Hospital (No. 0366) and all the participants proved their written informed consent prior to inclusion.

RESULTS

Characteristics of the participants and the distributions of clinical parameters

The characteristics of the study participants are shown in Table 1. They comprised 44 men and 20 women aged 63.9 (standard deviation [SD] 11.9) years (range 34-85 years). The mean duration of diabetes was 8.3 (SD 6.5) years. The distributions of the clinical parameters for the study participants are shown in Table 2. Types of antihyperglycemic, antihyperlipidemic, and antihypertensive agents prescribed for them are shown in Supplemental Tables 1, 2, and 3, respectively.

The changes in HbA1c and BMI over the 2 years of the study are shown in Supplemental Tables 4 and 5. Of the 64 participants, 16 (25.0%) showed a ΔHbA1c of ≥ 0.5% and 11 (17.2%) showed a ΔBMI of ≥ 1. Of the 22 participants with HbA1c < 6.5% at baseline, nine showed a ΔHbA1c ≥ 0.5%.

Table 1. Characteristics of the study participants (n=64)

Age (years)	63.9± 11.9
Women	31.3%
Treatment for glycemic control	
Diet and exercise only	7.8%
Diet, exercise, and antihyperglycemic agents	92.2%
Administration of antihyperlipidemic agents	54.7%
Administration of antihypertensive agents	57.8%
Exercise habit	28.1%
Smoking habit	29.7%
Frequent alcohol consumption	18.8%

Data are mean ± SD or percentage.

Relationships of HbA1c at baseline, ΔHbA1c, BMI at baseline, and ΔBMI with responses to the questionnaire

The Spearman rank correlation coefficients are shown in Table 3. A significant positive correlation was found between ΔHbA1c and ΔBMI ($r = 0.350$, $p = 0.005$). An analysis of the 38 participants with baseline HbA1c < 7.0 yielded a correlation

Table 2. Distributions of clinical parameters for the study participants (n=64)

	Minimum	Maximum	Mean	SD
Age (years)	34	85	63.9	11.9
Duration of diabetes (years)	0.2	35.0	8.3	6.5
BMI (kg/m^2) at baseline	17.8	33.9	25.6	3.2
BMI (kg/m^2) after 2 years	17.0	33.7	25.2	3.4
HbA1c (%) at baseline	5.4	9.2	6.9	0.8
HbA1c (%) after 2 years	5.6	8.6	6.9	0.7

BMI, body mass index; HbA1c, glycosylated hemoglobin.

Supplemented Table 1 Medication type of antihyperglycemic agents[a]

Class	number	%[b]
Biguanides	40	62.5%
Thiazolidine diones	1	1.6%
Sulfonylureas	10	15.6%
Meglitinides	11	17.2%
DPP-4 inhibitor	38	59.4%
α -Glucosidase inhibitors	20	31.3%
SGLT-2 inhibitor	24	37.5%
GLP-1 receptor agonists	10	15.6%

[a] Compounding agents are counted for both classes.
[b] Percentage to all study participants

Supplemented Table 2 Medication type of antihyperlipidemic agents

Class	number	%[a]
Statins	28	43.8%
Fibrates	5	7.8%
Ezetimibe	2	3.1%

[a] Percentage to all study participants

Supplemented Table 3 Medication type of antihypertensive agents[a]

Class	number	%[b]
Calucium blocker	24	37.5%
ACE inhibitor	4	6.3%
ARB	23	35.9%
Diuretic	2	3.1%
β -blocker	2	3.1%

[a] Compounding agents are counted for both classes.
[b] Percentage to all study participants

Supplemental Table 4. Relationship between baseline HbA1c and change in HbA1c over the 2 years of the study (n=64)

	After 2 years			
At baseline	HbA1c < 6.5	6.5 ≤ HbA1c < 7.0	7.0 ≤ HbA1c < 7.5	7.5 ≤ HbA1c
HbA1c < 6.5	10	10	1	1
6.5 ≤ HbA1c < 7.0	3	5	5	3
7.0 ≤ HbA1c < 7.5	1	3	3	4
7.5 ≤ HbA1c	1	4	4	6

HbA1c, glycosylated hemoglobin (%).

Supplemental Table 5. Relationship between baseline BMI and change in BMI over the 2 years of the study (n=64)

	After 2 years			
At baseline	BMI < 18.5	18.5 ≤ BMI < 23	23 ≤ BMI < 25	25 ≤ BMI
BMI < 18.5	1	0	0	0
18.5 ≤ BMI < 23	1	8	2	0
23 ≤ BMI < 25	0	3	9	5
25 ≤ BMI	0	0	5	30

BMI, body mass index (kg/ m^2).

coefficient of 0.605 ($p < 0.001$).

HbA1c at baseline was negatively associated with eating slowly/chewing well, and because ΔHbA1c negatively correlated with HbA1c at baseline, it was positively associated with eating slowly/chewing well.

ΔBMI was associated with perceived oral symptoms. The median ΔBMI was higher in the group with perceived oral symptoms than in the group without, as shown in Figure 2 (Mann-Whitney U test, $p < 0.01$).

An investigation of the relationships between answers to the questionnaire using Spearman rank correlation analysis showed that the perceived oral symptoms (Q1) significantly correlated with chewing firmly with the back teeth (Q3), being too busy to go to the dentist (Q8), and with brushing the teeth before going to bed (Q15) ($r = 0.338$, $p = 0.006$; $r = 0.262$, $p = 0.036$; and $r = 0.298$, $p = 0.022$; respectively).

Relationships between questionnaire responses and poor glycemic control

As shown in Figure 1, the participants were divided into two groups according to their questionnaire responses and their relationships with poor glycemic control were analyzed using the chi-square test. We found that only a smoking habit was significantly associated with poor glycemic control. Of the 19 smokers, 11 (57.9%) had poor glycemic control, and of the 45 non-smokers, 12 (26.7%) had poor glycemic control (Figure 3). Of the 19 smokers, only two were women.

Factors associated with poor glycemic control

We next performed binominal logistic regression analysis using poor glycemic control (ΔHbA1c ≥ 0.5% and/or HbA1c ≥ 7.5% after 2 years) as the outcome variable and five other variables (age, duration of diabetes, ΔBMI, use of a hypoglycemic agent, and smoking) as independent variables. The presence of a smoking habit is strongly associated with gender in Japan ; and in fact, there were only two female smokers in our study subjects. Therefore, sex was not included among the independent variables. We found that ΔBMI was significantly associated with poor glycemic control (Table 4). Smokers were found to be approximately four times more likely to have poor glycemic control than non-smokers (Table 4). When gender was included as an explanatory variable instead of smoking, no significant association was

Table 3. Correlations between clinical parameters and responses to the questionnaire (n=64)

	HbA1c at baseline	Δ HbA1c	BMI at baseline	Δ BMI
HbA1c at baseline	—	−0.512** <0.001	0.161 0.203	−0.131 0.301
Δ HbA1c	−0.512** <0.001	—	−0.155 0.220	0.350** 0.005
BMI at baseline	0.161 0.203	−0.155 0.220	—	−0.202 0.109
Δ BMI	−0.131 0.301	0.350** 0.005	−0.202 0.109	—
Q1 Perceived oral symptoms (No or Yes)	−0.106 0.406	0.045 0.723	−0.009 0.942	0.331** 0.008
Q18 Eating slowly and chewing well (every day, sometimes, or no)	0.325** 0.009	−0.404** <0.001	0.106 0.402	0.004 0.975

Upper row: Spearman's rank correlation coefficient
Lower row: *p*-value
HbA1c, glycosylated hemoglobin; Δ HbA1c, change in HbA1c; BMI, body mass index; Δ BMI, change in BMI; Q, question.

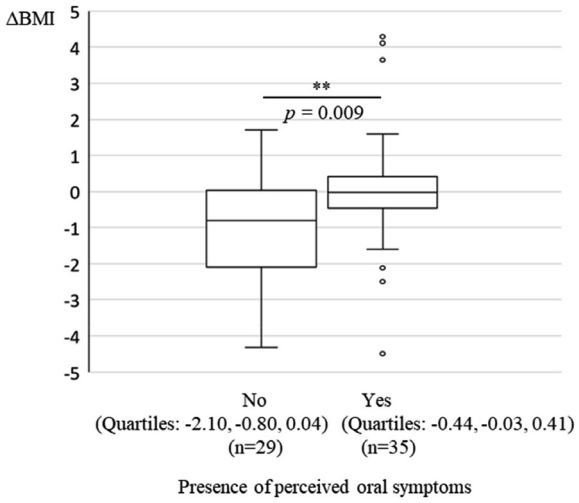

Figure 2. Relationship between the presence of perceived oral symptoms and the change in body mass index (ΔBMI)
**$p < 0.01$ (Mann-Whitney U-test).

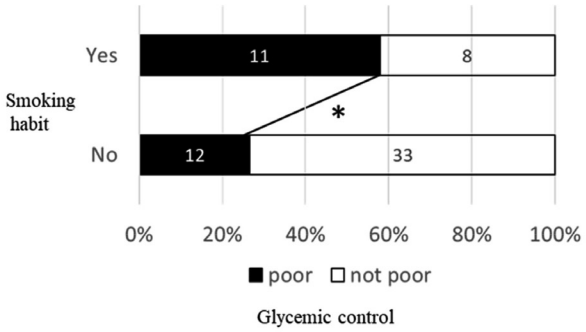

Figure 3. Relationship between the existence of a smoking habit and poor glycemic control
*$p < 0.05$ (chi-square test). Poor glycemic control : change in glycosylated hemoglobin level (ΔHbA1c) ≥ 0.5% and/or HbA1c ≥ 7.5% after 2 years.

Table 4. Odds ratios and 95% confidence intervals for poor glycemic control, according to binominal logistic regression analysis (n=64)

Variable		OR	95% CI	*p*-value
Age (years)		1.014	0.962–1.068	0.615
Duration of diabetes (years)		1.038	0.951–1.134	0.403
Δ BMI (kg/m^2)		1.617	1.081–2.419	0.019
Administration of a hypoglycemic agent				
	Yes	0.925	0.112–7.650	0.942
	No (ref.)			
Smoking habit				
	Yes	4.005	1.117–14.356	0.033
	No (ref.)			

a: According to the forced entry method
ref.: reference category
OR, odds ratio; CI, confidence interval; Δ BMI, change in body mass index.

found for gender.

The similar logistic regression analysis was performed for only 44 male subjects. As a result, it was found that the risk of poor glycemic control was about 4.4 times higher in smokers than in non-smokers (odds ratio : 4.41, 95% confidence interval : 1.04-18.7).

DISCUSSION

Many previous studies have shown that type 2 diabetes is associated with lifestyle factors, such as an inappropriate diet, low physical activity, and smoking (9, 10). All of these are modifiable factors and are associated with both the persistence of prediabetes and its progression to type 2 diabetes (11). In a cross-sectional study that we reported previously, we found that eating slowly and chewing well are advantageous for glycemic control (HbA1c < 7.5%) in patients with type 2 diabetes (2), and in the present study, participants with low baseline HbA1c values ate more slowly and chewed their food more thoroughly (Table 3).

A few previous studies have shown relationships between lifestyle and glycemic control in Asian patients with type 2 diabetes. For example, Jiang *et al*. found that tobacco use and obesity predicted the rapid worsening of glycemia in 7,091 Chinese patients with type 2 diabetes (12). In the present study, we also found that smoking and weight gain are associated with poor glycemic control in Japanese patients with type 2 diabetes. Given that smoking and obesity lead to insulin resistance, a smoking habit and weight gain might reduce the efficacy of diabetes treatment (13, 14). Ohkuma *et al*. performed a cross-sectional study of the relationships of glycemia with indices of insulin resistance and secretion in Japanese patients with type 2 diabetes mellitus, and found dose- and time-dependent relationships of smoking and its cessation with glycemic control and insulin resistance (15). The cessation of smoking should be recommended as standard for all patients with diabetes (16). However, in the present study, ～30% of the participants were smokers, implying that guidance on the cessation of smoking in patients with diabetes is inadequate. Because guidance regarding the cessation of smoking is covered by dental insurance, it is desirable that a comprehensive medical system that includes dental professionals is designed.

In the present study, we found that weight gain over a 2-year period (ΔBMI) correlates with ΔHbA1c over the same period, and that ΔBMI is associated with poor glycemic control. Koga *et al*. reported that ΔBMI over 5 years correlates with both the change in C-reactive protein concentration (ΔCRP) and ΔHbA1c in individuals with obesity but no diabetes mellitus (17), and hypothesized that the correlation between ΔBMI and ΔCRP might be the result of greater secretion of proinflammatory cytokines by adipose tissue with increasing BMI (18). Therefore, it is possible that glycemic control might be improved by a reduction in BMI. When data for participants with baseline HbA1c < 7.0 were analyzed separately, a higher correlation coefficient (r = 0.605) was obtained than that obtained using data collected for all the participants. This might imply that weight control is more likely to be effective in patients with only mild hyperglycemia.

In the present study, we found that ΔBMI is associated with perceived oral symptoms. The causes of symptoms related to the mouth are thought to be diverse. Because the perceived oral symptoms correlated with chewing firmly with back teeth, being too busy to go to the dentist, and not brushing the teeth before going to bed, this may reflect inadequate oral health measures. Thus, it is possible that proper oral management and appropriate weight control are linked.

We defined poor glycemic control using a ΔHbA1c of ≥ 0.5% over 2 years and/or an HbA1c of ≥ 7.5% at the 2-year time point in the present study. The treatment goals for people with diabetes should be set individually, considering such factors as age, the presence of complications, and the use of medication. The Japan Diabetes Society suggests that higher glycemic targets should be set for older individuals than for younger individuals (18). Given that the present study cohort included participants with a wide range of ages, we used a compromise HbA1c threshold of ≥ 7.5% after 2 years to define poor glycemic control. A quarter of the participants showed an increase in HbA1c of ≥ 0.5%. Therefore, we used a combination of these two criteria to define poor glycemic control during the study period.

The present study had several limitations. First, the findings may not be generalizable to populations outside of Japan because the prevalence of obesity and/or lifestyle issues, including a smoking habit, differs considerably between countries (19, 20). Second, because the medication being used and the changes made in this over the 2 years of the study were complex, the details of the medication could not be added to the list of explanatory variables, despite most of the participants receiving antihyperglycemic agents. Third, due to the small number of subjects, baseline HbA1c levels and duration of diabetes could not be grouped for analysis. Intervention studies should be performed in the future to determine whether smoking and/or weight gain impair glycemic control.

In conclusion, by means of a 2-year cohort study, we found that ΔHbA1c correlates with ΔBMI. We also found that a smoking habit and weight gain might lead to poor glycemic control. Given that weight control and the cessation of smoking might be advantageous for glycemic control in patients with type 2 diabetes, they should be promoted as part of the health guidance issued by health professionals in multiple disciplines.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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