Clinical implications of age and sex in the prevalence of periodontitis in Korean adults with diabetes

KYUNGDO HAN[1] and JUN-BEOM PARK[2]

Departments of [1]Biostatistics and [2]Periodontics, College of Medicine,
The Catholic University of Korea, Seoul 06591, Republic of Korea

Abstract. The present study was performed to assess the risk factors for periodontitis in Korean adults with diabetes. Data from the Korean National Health and Nutrition Examination Survey of the Korean population, conducted between January 2012 and December 2014 were used in the investigation. The presence of periodontitis in participants with diabetes in association with demographic variables and the anthropometric characteristics of the participants was investigated. Multiple logistic regression analyses were used to assess the associations between periodontitis and age, sex, diabetic control and duration of diabetes, following adjustment for confounding factors. The odds ratio of periodontitis was higher in individuals ≥65 years old compared with individuals <65 years old (1.152). The odds ratio of periodontitis was significantly higher in males compared with females (1.774). The number of patients with moderate and severe periodontitis differed significantly between different age groups. The present study revealed that age, sex and oral health behavior are risk indicators for periodontitis in patients with diabetes. The present study suggests that that an increased age, being male and engaging in poor oral health behavior increases the risk of periodontitis in participants with diabetes.

Introduction

Diabetes mellitus is a complex metabolic disorder. A key feature of diabetes mellitus is the reduced function of the β cells in the islets of Langerhans in the pancreas. These β cells produce insulin and their reduced function may decrease insulin secretion and lead to increased blood glucose levels (1). The synthesis of advanced glycosylation end-products and the induction of oxidative stress may exacerbate early pathological vascular changes (2). In patients with diabetes, associated complications may contribute to increased morbidity and premature mortality (3). Retinopathy, neuropathy, cardiovascular disease, nephropathy and encephalopathy are considered to be the primary complications of diabetes (4) and periodontal disease has been implicated as the sixth complication of diabetes (5). Periodontitis is a common, chronic, inflammatory disease that induces the gradual destruction of the supporting apparatus of the teeth, causing teeth to become mobile, which may ultimately result in tooth loss (6). It has been reported that the prevalence of periodontal disease in diabetic patients is >85% (27.3% of patients had gingivitis and 59.5% had periodontitis) whereas the prevalence of periodontitis in the general population is 46% (1,7). Diabetes is a known risk factor of periodontal disease and patients with diabetes have an increased prevalence of severe periodontitis compared with healthy adults (8). Indeed, it has been demonstrated that the susceptibility to periodontitis increases by ~3-fold in patients with diabetes (6). Among individuals with chronic periodontitis, patients with diabetes exhibit enhanced lipopolysaccharide-induced immune responsiveness, implicating an exacerbated inflammatory response (9).

It has been suggested that diabetes and periodontitis are biologically linked (10) Hyperglycemia associated with diabetes has been previously studied due to its association with adverse periodontal outcomes (3). However, to the best of our knowledge, the risk factors for periodontitis specifically in patients with diabetes have not yet been identified. Therefore, the present study was performed to assess the risk factors for periodontitis in Korean adults with diabetes using nationally representative data.

Materials and methods

Survey and subjects. The results of the present study were obtained by secondary analysis of data obtained during the Korean National Health and Nutrition Examination Survey (KNHANES) between January 2012 and December 2014. The KNHANES was approved by the Institutional Review Board of the Korea Center for Disease Control and all participants provided written informed consent. The Institutional Review Board at the Catholic University of Korea approved the present study (KC14EISI0636).

A total of 23,626 individuals participated in the KNHANES survey. The number of individuals included in the present

Correspondence to: Dr Jun-Beom Park, Department of Periodontics, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seoul 06591, Republic of Korea
E-mail: jbassoonis@yahoo.co.kr

study was reduced to 1,630 following the exclusion of partici-pants <30 years old, individuals that had only undergone <8 h fasting prior to examination, participants with missing values, individuals without diabetes mellitus and participants that did not undergo an oral examination (Fig. 1).

Demographic variables. The sociodemographic and life-style variables of the participants were evaluated by a self-administered questionnaire that assessed education level, household income, smoking, alcohol intake and physical exercise. Regarding smoking status, patients were classified as non-smokers, ex-smokers or current smokers. Non-smokers were those who had never smoked or had smoked <100 ciga-rettes during their lifetime, whereas ex-smokers were those who had smoked >100 cigarettes in their entire life but were not smoking at the time of the study. Regarding alcohol consump-tion, patients were categorized as non-drinkers, mild to moderate drinkers (1-30 g/day) or heavy drinkers (>30 g/day). Physical activity was measured using the international physical activity questionnaire as part of the KNHANES. Subjects who exercised for ≥5 occasions per week for 30 min per session, or those who participated in strenuous physical activity for ≥3 occasions per week for 20 min per session, were defined as regular exercisers. Education level was categorized as either high school education (≥10 years schooling) or middle school graduate or lower (<10 years schooling). The number of household members was evaluated. Household income was divided by the number of included family members and categorized into quartiles. The lowest quartile of household income was <USD 1,092.40 per month and patients were cate-gorized as being in the lowest quartile or not. The participant's self-reported health status was categorized as good or not good (which consisted of patients reporting their health as average or bad).

Anthropometric measurements. Anthropometric measurements of individuals that participated in the present study were taken by the trained staff members. Participants wore light, indoor clothing without shoes for the measurement of body weight and height, as previously described (11). The narrowest point between the iliac crest and the lower border of the rib cage was used to determine waist circumference. The following formula of weight/height^2 (kg/m^2) was used to calculate body mass index. A standard mercury sphygmomanometer (Baumanometer; W.A. Baum Co., Inc., Copiague, NY, USA) was used to measure systolic and diastolic blood pressure in the right arm. Blood pressure measurements were performed twice with a 5 min interval and the average of the two measurements was used for analysis. Blood samples were collected from the antecubital vein of each participant to measure the white blood cell count. The white blood cell count was measured using an automated hematology analyzer (XE-2100D; Sysmex Corporation, Kobe, Japan).

Definition of diabetes mellitus and hypertension. A high waist circumference was categorized as ≥90 cm in men and ≥80 cm in women. Hypertension was diagnosed if an individual had a systolic blood pressure of >160 mm Hg or a diastolic blood pressure of >90 mm Hg, or if the individual was using systemic antihypertensive drugs. A fasting blood

cholesterol level >240 mg/ml or the use of medication for the condition was considered to indicate the presence of hyper-cholesterolemia. The level of kidney function was determined by estimating the glomerular filtration rate (eGFR) using the following equations: eGFR (ml/min/1.73 m^2)=186.3x (serum creatinine$^{-1.154}$) x (age$^{-0.203}$) for males and 186.3x (serum creati-nine$^{-1.154}$) x (age$^{-0.203}$) x0.742 for females. Serum creatinine was measured by the colorimetric method using a Hitachi 7600 modular chemistry analyzer (Hitachi, Ltd., Tokyo, Japan). The eGFR was categorized as either ≥60 or not as previously described (12). Cardiovascular disease was considered present if the individual had experienced a stroke or had a congenital heart defect (13).

Diabetes was defined as a fasting blood sugar >126 mg/dl or the individual was currently using anti-diabetic medica-tion (14). The recognition, treatment and control of diabetes was self-evaluated, as well as insulin injection. Glucose and glycated hemoglobin levels were categorized into five levels. Patients were classified into the following 5 groups based on their glycated hemoglobin levels: <6, 6≤x<6.5, 6.5≤x<7, 7≤x<7.9 and ≥8 and into the following 5 groups based on their glucose levels: <100, 100≤x<120, 120≤x<140, 140≤x<160 and >160.

Periodontitis and oral health behaviors. The oral health status of the participants was evaluated using the World Health Organization Community Periodontal Index (CPI) (15,16). The index teeth according to the Federation Dentaire Internationale system were 11, 16, 17, 26, 27, 31, 36, 37, 46 and 47 (17). Periodontitis was defined as CPIs of 3 and 4. The CPI score was 3 in cases of a shallow pocket with a depth of 3.5-5.5 mm and 4 in cases of a deep pocket with a depth ≥5.5 mm (18). Moderate periodontitis was defined as a CPI of 3 and severe periodontitis was defined as a CPI of 4.

The frequency of daily tooth brushing and the use of secondary oral products were used to evaluate oral health behavior. Dental floss, interdental brushes, electric toothbrushes, irrigation devices, end-tufted brushes, tongue cleaners, mouth-wash and special devices for dentures were considered to be secondary oral products. The survey also recorded the partici-pant's self-reported oral status, the presence of any toothache, chewing discomfort, speech discomfort and whether patients had undergone a dental checkup within that year.

Statistical analysis. The results are presented as the mean ± standard error of the mean for continuous variables and as proportions (standard errors) for categorical variables. To assess differences in characteristics as categorized by body mass index, a χ^2 test was performed to assess categorical variables and an independent t test was used to assess continuous variables. The risk factors for periodontitis in diabetes were evaluated following adjustments for age, sex, smoking, drinking, number of household members, income, self-reported health, medication, self-reported oral status, tooth pain, frequency of tooth brushing per day and the use of secondary oral products. Multiple logistic regression analyses were used to assess the associations between periodontitis and age, sex, diabetic control and duration of diabetes, following adjustment for confounding factors. P<0.05 was considered to indicate a statistically significant difference. All statistical
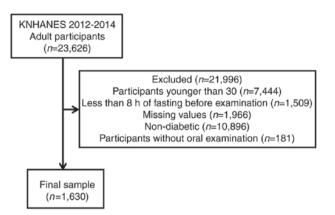
Figure 1. Flow chart of participants included and excluded from the study. KNHANES, Korean National Health and Nutrition Examination Survey.

analyses were performed using SAS software version 9.2 for Windows (SAS Institute, Inc., Cary, NC, USA).

Results

Baseline characteristics. Table I details the baseline characteristics of the participants included in the study according to the presence of periodontitis. The odds ratio (OR) of periodontitis was higher in individuals aged ≥65 years old compared with individuals aged 30-65 years old (OR 1.152). The OR of periodontitis was significantly higher in males compared with females, with a 95% confidence interval of 1.387-2.269 (P<0.05). Being male, smoking, drinking, have a higher number of household members, being in the lowest income quartile, have an average or bad health status, having problematic self-reported oral status, experiencing tooth pain, experiencing chewing or speech discomfort, having a lower frequency of tooth brushing and not using secondary oral products were significantly associated with the incidence of periodontitis in the diabetic population.

The odds ratio of periodontitis following adjustments for confounding factors. ORs and their 95% confidence intervals for moderate and severe periodontitis categorized by various variables following adjustments for age, sex, smoking, drinking, number of household members, income, self-reported health, medication, self-reported oral status, tooth pain, frequency of tooth brushing per day and use of secondary oral products are presented in Fig. 2. The ORs and 95% confidence intervals of periodontitis were 1.60 (1.05, 2.46) and 2.28 (1.47, 3.52) for ex-smokers and current smokers, respectively when non-smokers were considered as a reference. The ORs and 95% confidence intervals of periodontitis for the individuals were 1.51 (1.01, 2.26) and 1.20 (0.91, 1.58) for the individuals with a toothbrushing frequency of ≤1 and 2, respectively when participants with toothbrushing frequency of 3 was considered as a reference. These results indicate that individuals with current smoking had higher ORs of periodontitis. Similarly, participants with a toothbrushing frequency of ≤1 had higher ORs of periodontitis.

The percentage of moderate and severe periodontitis categorized by different variables. Fig. 3 presents the percentage of moderate and severe periodontitis categorized by age, sex, duration of diabetes and glycated hemoglobin. The percentages of moderate periodontitis in individuals aged 30-39 and ≥70 were 24.1 and 36.8%, respectively. The percentages of moderate periodontitis in male and female were 35.5 and 30.2%, respectively. The percentage of patients with periodontitis differed significantly between different age groups (P=0.0074) and significant differences were also noted between males and females (P<0.0001). There were no significant differences between patients with moderate and severe periodontitis.

Discussion

The present study used nationally representative data to determine that age, sex and oral health behavior were risk factors for periodontitis in Korean adults with diabetes. The effect of age on the prevalence of periodontitis may partially be explained by the onset of chronic inflammation, which is a common feature of aging and age-associated diseases, including periodontitis (19). It has been previously revealed that the prevalence and severity of periodontal disease increased as age increased (1). Similarly, periodontitis occurred at a higher rate in diabetic participants compared with non-diabetic individuals and this phenomenon was positively correlated with age in individuals with diabetes (19). It has been suggested that patients with diabetes aged ≥35 years old experience more rapid destruction of the periodontium (20). Furthermore, it has been demonstrated that age is significantly associated with the increased prevalence and greater severity of destructive periodontal disease in patients with diabetes (21). The results of present study confirmed the importance of age in determining the prevalence of periodontitis in patients with diabetes.

Differences between the two sexes have also been noted in previous studies. A previous report revealed that diabetic males had worse periodontal conditions compared with diabetic females (22). A previous study also revealed statistically significant associations between males and severe periodontitis (23). These results therefore suggest that there is a greater need for the regular periodontal evaluation and effective oral hygiene care among males with diabetes than in females with diabetes to decrease the risk of developing periodontitis and progression of periodontitis into a more severe form (24). The present study revealed that the percentage of patients with moderate and severe periodontitis did not significantly differ between different duration of diabetes or diabetic control. In a previous study, diabetic status was associated with an increased severity and prevalence of destructive periodontal disease in the diabetic population (21). Furthermore, glycemic status influences the prevalence and severity of periodontal disease in diabetic participants (1). Individuals with poorly controlled diabetes and periodontitis are more likely to suffer from gingival bleeding than those with good or moderate control (25). Conversely, no significant correlation was observed between periodontitis and glycated hemoglobin levels in non-diabetic subjects (26). Similarly, glycemic control, defined by fasting plasma glucose (140 mg/dl) and glycohemoglobin value (6.5%), was not significantly associated with periodontal status (27). Diabetic control did not reveal any differences in the periodontal condition (20). A previous report demonstrated

Table I. Baseline characteristics of study participants with moderate and severe periodontitis.

Characteristic	No periodontitis, n=838, % (SEM)	Periodontitis, n=792, % (SEM)	P-value	Odds ratio (95% CI)
Age (years)			0.4059	
30-64	67.4 (1.8)	65.3 (2.1)		1 (reference)
≥65	32.6 (1.8)	34.7 (2.1)		1.152 (0.916, 1.449)
Sex			<0.0001[a]	
Male	49.3 (2.1)	60.9 (2)		1.774 (1.387, 2.269)
Female	50.7 (2.1)	39.1 (2)		1 (reference)
Smoking			<0.0001[a]	
No	60.4 (2.2)	43.5 (2)		1 (reference)
Ex	21 (1.8)	24.9 (1.8)		1.514 (0.993, 2.31)
Current	18.6 (1.6)	31.6 (2.1)		2.503 (1.67, 3.752)
Drinking			0.0362[a]	
Non-drinker	37.3 (1.9)	30.8 (2)		1 (reference)
Mild to moderate drinker	54 (2.1)	57.1 (2.1)		1.176 (0.9, 1.535)
Heavy drinker	8.7 (1.3)	12.1 (1.4)		1.388 (0.855, 2.255)
Exercise			0.3669	
No	83.9 (1.8)	86.1 (1.8)		1 (reference)
Yes	16.1 (1.8)	13.9 (1.8)		0.832 (0.559, 1.237)
Number of household members			0.0079[a]	
1	10.5 (1.2)	13.6 (1.5)		1 (reference)
2	30.9 (1.8)	36.7 (2.2)		0.793 (0.544, 1.156)
≥3	58.6 (2)	49.7 (2.5)		0.626 (0.414, 0.949)
Education			0.2500	
Middle-school graduate or lower	51.2 (2.2)	54.8 (2.2)		1 (reference)
High-school education or higher	48.8 (2.2)	45.2 (2.2)		0.924 (0.689, 1.24)
Income (the lowest quartile)			0.0157[a]	
No	76.1 (1.7)	69.8 (2.2)		1 (reference)
Yes	23.9 (1.7)	30.2 (2.2)		1.312 (0.979, 1.757)
Self reported health status			0.0122[a]	
Good	17.4 (1.6)	12.3 (1.3)		1 (reference)
Average or bad	82.6 (1.6)	87.7 (1.3)		1.67 (1.19, 2.343)
Body mass index (kg/m^2)			0.2601	
<25	47.8 (2.1)	51.2 (2.1)		1 (reference)
≥25	52.2 (2.1)	48.8 (2.1)		0.939 (0.735, 1.199)
High waist circumference, ≥90 cm in men and ≥80 cm in women			0.0793[a]	
No	44 (2.1)	49 (2.1)		1.091 (0.852, 1.396)
Yes	56 (2.1)	51 (2.1)		1 (reference)
Hypertension			0.1316	
No	47 (2.1)	42.4 (2.2)		1 (reference)
Yes	53 (2.1)	57.6 (2.2)		1.052 (0.809, 1.367)
Hypercholesterolemia			0.8652	
No	69.2 (1.9)	69.7 (1.9)		1 (reference)
Yes	30.8 (1.9)	30.3 (1.9)		1.04 (0.79, 1.37)
Estimated glomerular filtration rate (ml/min/1.73 m^2)			0.7636	
≥60	91.7 (1.1)	92.1 (1)		1.197 (0.796, 1.801)
<60	8.3 (1.1)	7.9 (1)		1 (reference)
Cardiovascular disease			0.9456	
No	90.9 (1.1)	90.8 (1.1)		1 (reference)
Yes	9.1 (1.1)	9.2 (1.1)		0.912 (0.615, 1.352)
Diabetes (recognition)			0.3699	
No	37.6 (2.2)	40.2 (2.2)		1 (reference)
Yes	62.4 (2.2)	59.8 (2.2)		0.785 (0.611, 1.008)

Table I. Continued.

Characteristic	No periodontitis, n=838, % (SEM)	Periodontitis, n=792, % (SEM)	P-value	Odds ratio (95% CI)
Diabetes (treated)			0.1644	
No	43.4 (2.2)	47.7 (2.2)		1 (reference)
Yes	56.6 (2.2)	52.3 (2.2)		0.732 (0.567, 0.944)
Diabetes (controlled)			0.9387	
No	78.2 (1.9)	78 (1.9)		1 (reference)
Yes	21.8 (1.9)	22 (1.9)		0.993 (0.728, 1.353)
Insulin injection			0.4330	
No	94.8 (0.8)	93.8 (1)		1 (reference)
Yes	5.2 (0.8)	6.2 (1)		1.150 (0.663, 1.994)
Diabetic medication			0.234	
No	45 (2.2)	48.6 (2.2)		1 (reference)
Yes	55 (2.2)	51.4 (2.2)		0.758 (0.59, 0.973)
Glucose level			0.9500	
<100	9.8 (1.1)	9.4 (1.2)		1 (reference)
100≤x<120	22.5 (1.7)	22.2 (1.9)		1.095 (0.725, 1.655)
120≤x<140	33.9 (2.1)	32.6 (2.1)		1.079 (0.721, 1.615)
140≤x<160	15.6 (1.6)	15.9 (1.4)		1.146 (0.724, 1.812)
≥160	18.2 (1.7)	19.9 (1.7)		1.326 (0.852, 2.065)
Glycated hemoglobin			0.4800	
<6	5.8 (1.1)	7.8 (1.1)		1 (reference)
6≤x<6.5	16 (1.6)	14.2 (1.6)		0.701 (0.4, 1.231)
6.5≤x<7	27.6 (1.9)	28.6 (2.1)		0.805 (0.468, 1.386)
7≤x<7.9	31.1 (1.9)	28.1 (1.9)		0.699 (0.418, 1.168)
≥8	19.5 (1.7)	21.3 (1.7)		0.91 (0.526, 1.577)
Dental checkup within a year			0.2490	
No	76.7 (1.7)	73.8 (1.9)		1 (reference)
Yes	23.3 (1.7)	26.2 (1.9)		1.184 (0.887, 1.579)
Self-reported oral status			<0.0001[a]	
Favorable	14.9 (1.6)	9.9 (1.2)		1 (reference)
Average	36.6 (2.1)	26.5 (1.7)		1.179 (0.772, 1.801)
Problematic	48.6 (2.2)	63.6 (1.9)		2.019 (1.346, 3.027)
Tooth pain			<0.0001[a]	
No	65.4 (2)	47.6 (2.1)		1 (reference)
Yes	34.6 (2)	52.4 (2.1)		2.086 (1.653, 2.632)
Chewing discomfort			<0.0001[a]	
No	69.7 (2)	56.9 (2.1)		1 (reference)
Yes	30.3 (2)	43.1 (2.1)		1.642 (1.271, 2.12)
Speech discomfort			0.0339[a]	
No	85.5 (1.4)	81.1 (1.6)		1 (reference)
Yes	14.5 (1.4)	18.9 (1.6)		1.277 (0.946, 1.724)
Frequency of tooth brushing per day			0.0019[a]	
≤1	12.5 (1.4)	18.5 (1.7)		1 (reference)
2	42.6 (2.2)	46.1 (2)		0.773 (0.534, 1.119)
≥3	44.9 (2.2)	35.4 (2)		0.583 (0.393, 0.865)
Use of secondary oral products			0.0020[a]	
No	54.1 (2.2)	63.6 (2.1)		1 (reference)
Yes	45.9 (2.2)	36.4 (2.1)		0.757 (0.583, 0.981)

Data are presented as percentages (standard error of the mean) of the study participants. [a]P<0.05. CI, confidence interval. SEM, standard error of the mean.
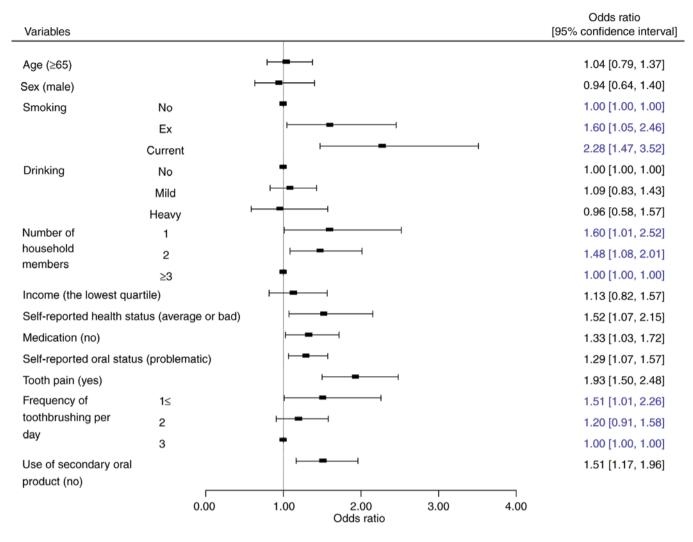
Figure 2. The odds ratio and their 95% confidence intervals for moderate and severe periodontitis categorized by different variables. Blue text indicates values that were significant.

that the glycated hemoglobin levels were not significantly correlated with periodontal values in diabetic participants (28), which was similar to trends observed in the present study. The association between the duration of diabetes and periodontitis was evaluated in the present study; however no significant association was observed. The association between the duration of diabetes and periodontitis is controversial as some reports have demonstrated that the two factors were associated, while others have reported no association (19,20,25,27,28). A previous study reported that the number of years since the diagnosis of diabetes was more significant than age for predicting the severity of periodontal disease in diabetic patients (29). A previous study observed that the duration of diabetes mellitus had an association with the prevalence and severity of periodontal disease (1). It should be noted that the number of participants in these previous reports were relatively small, being composed of only 100 patients (46 males and 54 females) (29) and 1,500 patients (751 males and 749 females), respectively (1). However, no correlation was observed between periodontitis in individuals with diabetes and the length of time from the diagnosis of diabetes (19). Several previous studies have reported that the duration of diabetes was not associated with the periodontal condition (20,27,28). A previous report

revealed that no significant correlation was observed between diabetic duration and gingival bleeding (25). An advantage of the present study is that it was based on a nationally representative sample of Korean patients with diabetes, which allows for an effective investigation into whether age and sex are associated with periodontitis. The sampling units were based on the population and housing census conducted by the National Census Registry in Korea and survey sample weights were adjusted for participation and response rates (30). To the best of our knowledge, the present study is the first to demonstrate the importance of age and sex as risk indicators for the prevalence of periodontitis in individuals with diabetes (31). The present study assessed the effects of various risk indicators by subgroup analysis, including age, sex, control of diabetes and duration of diabetes. However, the present study did have certain limitations. Firstly, as it was a cross-sectional study it was not possible to identify a cause-and-effect association. Secondly, the present study used partial-mouth recording protocols of CPI, which may underestimate the prevalence of periodontal disease. To overcome these limitations a prospective study using full-mouth recording may be designed, however this type of study requires far greater resources to complete.
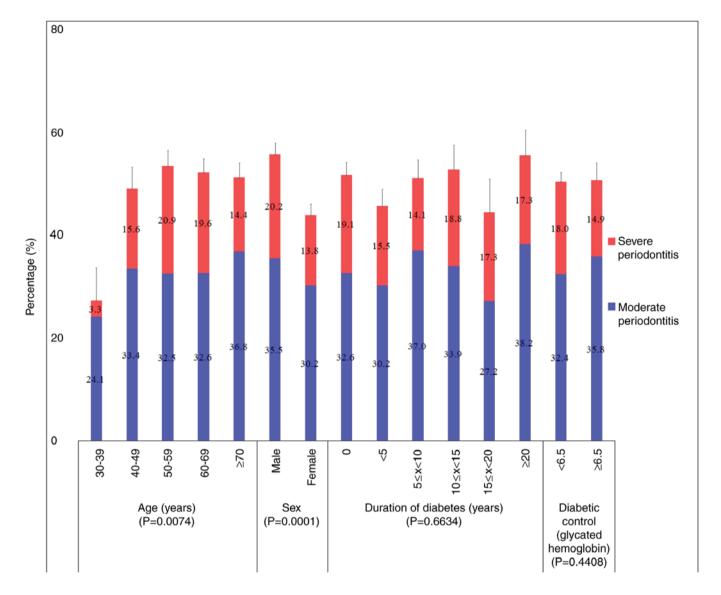
Figure 3. The percentage of the total population of moderate and severe periodontitis categorized by age, sex, duration of diabetes and glycated hemoglobin.

A bidirectional association has been reported between diabetes and periodontitis (3). Patients with diabetes have a higher predisposition to periodontitis (9) and periodontitis is a risk factor in a number of systemic diseases, including diabetes and cardiovascular pathologies (2). In diabetic patients, the elimination of periodontal infections and a reduction in periodontal inflammation produces a noticeable short-term reduction in glycated hemoglobin (32). Individuals with periodontitis had an increased rate of microvascular complications ketoacidosis and of hospitalizations associated with hyperglycemia with odds ratio and 95% confidence intervals of [2.43 (1.74-3.40)], [2.72 (1.53-4.80)] and [2.76 (1.72-4.42)], respectively (33). Treatment of periodontitis reduces the risk of cardiovascular disease in diabetic patients (34). Therefore, periodontitis may stimulate inflammatory changes in adipose tissue and this may create a self-generating cycle of morbidity that links diabetes and periodontal disease (35).

Dental management has a beneficial effect on the health of patients with diabetes (34). Maintaining oral health helps prevent oral chronic diseases and ameliorate the consequences of chronic inflammatory processes (36). Patients with diabetes are likely to visit a physician more frequently than they visit a dentist and it is the physician's responsibility to educate and motivate the patient to seek dental treatment (37).

In conclusion, the results of the present study indicate that age, sex and oral health behavior are risk indicators of periodontitis in Korean adults with diabetes. The present study suggests that that an increased age, being male and engaging in poor oral health behavior increases the risk of periodontitis in participants with diabetes. Further prospective studies involving a larger sample size of diabetic subjects over a longer period of time are required to evaluate the cause-and-effect association. The present study suggests that individuals of a certain age with diabetes should be recommended for regular periodontal evaluation, particularly males.

Acknowledgements

Availability of data and materials

All data generated or analyzed during this study are included in the published article.

Authors' contributions

KH and JP designed the research, analyzed the data and wrote the manuscript. Both authors reviewed the final manuscript.

Ethics approval and consent to participate

The KNHANES was approved by the Institutional Review Board of the Korea Center for Disease Control and all participants provided written informed consent. The Institutional Review Board at the Catholic University of Korea approved the present study (KC14EISI0636).

Consent for publication

Not applicable.

Competing interests

The authors confirm that they have no competing interests.

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