

Association between periodontal disease and diabetes using propensity score matching

The seventh Korea National Health and Nutrition Examination Survey

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Abstract

The association between periodontitis and diabetes have been assessed by many cross-sectional studies, in which controlling confounding factors is important. Propensity score matching (PSM) may help address this issue. Therefore, we evaluated this relationship in a (PSM) analysis of individuals representing the general Korean population. Periodontitis was significantly associated with diabetes before PSM (odds ratio [OR] = 1.53; 95 % confidence interval (CI) = 1.31–1.80) and after PSM (OR = 1.52; 95 % CI = 1.28–1.80). This study showed the association between periodontitis and diabetes using PSM, suggesting that periodontitis may be positively related with diabetes. We included 9508 adults who were aged ≥ 19 years from the Korea National Health and Nutrition Examination Survey VII (2016–2018) and performed logistic regression analyses before and after PSM. The PSM was based on periodontal disease (yes or no) using a 1:1 match ratio and included 5858 individuals (2929 per group). Confounding variables, such as age, sex, marital status, occupation, education, income, smoking and drinking habits, obesity, hypertension, hypercholesterolemia, and hypertriglyceridemia, were matched and adjusted in the logistic regression analysis.

Abbreviations: CPI = community periodontal index, IRB = institutional review board, KDCA = Korea disease control and prevention agency, KNHANES = Korea national health and nutrition examination survey, OR = odds ratio, PSM = propensity score matching, SMD = standardized mean difference, WHO = World Health Organization.

Keywords: diabetes mellitus, periodontitis, propensity score matching

1. Introduction

The global incidence of diabetes mellitus has rapidly increased due to population growth, aging, and lifestyle changes. The World Health Organization (WHO) estimates that the number of adults with diabetes will grow globally from 171 million in 2000 to 366 million in 2030.^[1] Furthermore, Korea National Health and Nutrition Examination Survey (KNHANES) data indicated that the prevalence of diabetes among Korean adults aged ≥ 30 years increased from 8.9 % in 2001 to 14.4 % in 2016. Furthermore, in Korea, 39.7 % of adults aged ≥ 30 years were estimated to have glycemic control disorders in 2016.^[2] Diabetes mellitus is a group of chronic metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The common symptoms of diabetes mellitus include polydipsia, polyuria, polyphagia, and ketoacidosis. However, numerous and often severe complications are possible, including nephropathy, neuropathy, retinopathy, and cardiovascular, peripheral, vascular, cerebrovascular, and periodontal diseases.^[3,4]

Periodontal diseases are highly prevalent. For example, the 2009 to 2014 National Health and Nutrition Examination Surveys reported that 42.2% of the American population had periodontitis.^[5] In Korea, the prevalence of periodontitis among adults is 73.4% and is continuously increasing.^[6,7] Periodontitis is a chronic inflammatory disease caused by bacterial biofilms (dental plaque) that affect the supporting structures of the teeth (e.g., the gingiva, bone, and periodontal ligament), resulting in their destruction and tooth loss.^[5,8,9]

Several epidemiological studies have reported an association between periodontitis and diabetes, and type 2 diabetes has been confirmed as a major risk factor for periodontal disease.^[10–12] Furthermore, recent research has emphasized the bidirectional relationship between diabetes and periodontitis, suggesting that diabetes influences periodontitis and periodontitis negatively affects glycemic control.^[13–16] Nevertheless, there are still the need for additional epidemiologic studies on the effect of periodontitis on diabetes according to previous studies.^[17]

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

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Some studies have attempted to elucidate this relationship using data of KNHANES, which is a nationally representative survey by Korean government agency. In the cross-sectional study, it is important to compensate for confounding, an important cause of bias although these are limited their ability to discern the causal relationship between the diseases.^[18-21] An emerging approach called propensity score matching (PSM) may help to control confounding variables. PSM reduces confounding factors owing to the nonrandom assignment of the exposure in an observational study or a prospective study where it is difficult to apply a random assignment or adjusts for confounding variables in cross-sectional study to assess the relationship between exposure and outcome variable.^[22] The propensity score is defined as the probability of receiving a specific conditional exposure of the observed covariates. Matching the propensity score can depend on a large set of covariates, resulting in an unbiased estimation of the effects of the independent variable.^[23,24] The most common implementation of PSM is a 1:1 match, forming pairs of case and control individuals.^[25] However, PSM analyses have several limitations: the size of the data set decreases after matching the groups, and inappropriate covariates included in the propensity score model reduce the efficiency; thus, residual confounding may still occur across the exposure and non-exposure groups.^[26] Nevertheless, the consensus is that the propensity score model adequately controls measured residual confounders although it is limited by unmeasured ones and the quality of the PSM model.^[27] Therefore, this study examined the relationship between periodontal disease and diabetes using logistic regression analyses and 1:1 PSM with KNHANES-derived data to clarify this relationship while efficiently addressing confounding factors.

2. Methods

2.1. Survey and subjects

We used data derived from the KNHANES VII collected from 2016 to 2018.^[28] The KNHANES was conducted by the Korea Disease Control and Prevention Agency (KDCA) and is a nationally representative, stratified, complex, and multistage sample survey. Demographic, social, health, and nutritional data were collected through standardized questionnaires and examinations. For representative and reliable statistics, the survey targets were constructed with approximately 10,000 household members of 20 households extracted by probability samples from 192 survey districts selected annually based on the recent Population and Housing Census. Once the mobile examination center was installed in the survey region, all health examinations were performed by trained medical personnel, and face-to-face interviews were conducted by trained field workers.^[29] In total, 16,489 individuals participated in the KNHANES VII; 6981 individuals were excluded because they were < 19 years old ($n = 3290$) or had missing data ($n = 3691$). Thus, we included 9508 individuals. Finally, we performed 1:1 PSM based on the periodontitis classification, resulting in 5858 individuals in total with 2929 per group (Fig. 1). Informed consent was obtained from all KNHANES VII participants. The KDCA Institutional Review Board approved the KNHANES VII procedure protocol (IRB number: 2018-01-03-P-A). Raw data were obtained publicly through a request procedure for KDCA. Therefore, this study was exempt from the IRB of Kyungpook National University (KNU 2018-01-03-P-A).

2.2. Periodontal assessment

The periodontium was assessed using the Community Periodontal Index (CPI).^[30] Dentists trained on the KNHANES protocol examined the CPI of the following teeth based on the

Federation Dentaire Internationale dental numbering system: 17, 16, 11, 26, 27, 37, 36, 31, 46, and 47. A CPI probing force of approximately 20 g was applied following the WHO guidelines (World Health Organization, 2013). CPI scores were assigned as 0 (healthy periodontal tissue), 1 (bleeding periodontal tissue observed with the eye and dental mirror), 2 (periodontal tissue with plaque), 3 (periodontal tissue forming a shallow periodontal pocket of 4–5 mm), and 4 (periodontal tissue forming a deep periodontal pocket of ≥ 6 mm). The highest CPI score per mouth was the representative value per participant. The participants were classified into 2 groups based on periodontal disease: non-periodontitis (CPI score of 0, 1, or 2; controls) and periodontitis (CPI score of 3 or 4; cases).

2.3. General characteristics

Sociodemographic factors (e.g., age, sex, marital status, occupation, education level, and income) and health-related behavioral factors (e.g., alcohol consumption and smoking) were examined using questionnaires. The participants were classified per factor as follows: age (19–49, 50–59, 60–69, and ≥ 70 years), sex (male or female), marital status (married or unmarried), occupation (employed or unemployed), education level (elementary school, middle school, high school, or university), and income level (4 quartiles). Smoking was classified as yes or no based on the current smoking status and the number of cigarettes smoked throughout life; those who had smoked more than 100 cigarettes in total were classified as yes. Alcohol consumption was categorized as yes or no based on drinking more than once per month over the previous year. Therefore, participants who had previously consumed alcohol but not during the prior year were classified as no.

2.4. Medical assessment

General health-related factors, such as obesity, hypertension, diabetes, hypercholesterolemia, and hypertriglyceridemia, were evaluated using questionnaires, clinical examinations, and laboratory procedures. The participants were grouped based on the following medical assessments: obese (yes or no), hypertensive (yes or no), diabetic (yes or no), hypercholesterolemic (yes or no), and hypertriglyceridemic (yes or no). The participants were classified as obese using the body mass index, calculated by dividing weight by height squared (kg/m^2). Obesity was defined as a body mass index $\geq 25 \text{ kg}/\text{m}^2$ based on the guidelines for obesity management by the Korean Society for the Study of Obesity.^[31] The participants were classified as hypertensive if they had a systolic blood pressure $\geq 140 \text{ mm Hg}$ or a diastolic blood pressure $\geq 90 \text{ mm Hg}$, were previously diagnosed with hypertension, or were on antihypertensive medication. In November 2017, the American College of Cardiology/American Heart Association updated its definition of hypertension from 140/90 mm Hg to 130/80 mm

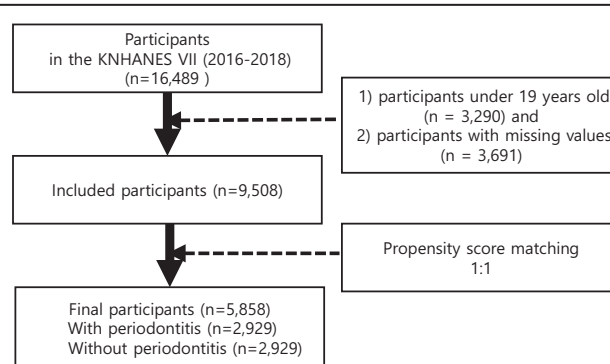


Figure 1. Study flow chart.

Hg.^[32] However, we used the KNHANES protocol that stated 140/90 mm Hg. The participants were classified as diabetic if they had a fasting blood glucose level ≥ 126 mg/dL, were previously diagnosed with diabetes, or were on anti-diabetic medication.^[33] Furthermore, hypercholesterolemia was defined as a total blood cholesterol level of ≥ 240 mg/dL or use of lipid-lowering medication.^[34] Hypertriglyceridemia was defined as a total blood triglyceride level ≥ 200 mg/dL or triglyceride-lowering medication.

2.5. Statistical analyses

Based on the KCDC guidelines, we performed clustering, stratification, and weighting of the KNHANES VII raw data with the nation as the population. Next, we performed complex sample analyses and PSM using a 1:1 ratio. In the PSM analysis, we included confounding variables, which have been reported to be associated with the risk of periodontitis and type 2 diabetes.^[16,35] The included variables were age, sex, marital status, occupation, education, income, smoking and drinking habits, obesity, hypertension, hypercholesterolemia, and hypertriglyceridemia.^[16,35] PSM was performed using the Greedy matching technique with a caliper width of 22 % of the observed standard deviation of the logit-transformed propensity score without replacement. Then, we calculated the standardized mean difference (SMD) and C-statistic. SMD is the difference between the case and control group covariates, and the C-statistic is used to evaluate the covariate balance in the propensity score model before and after matching. A complex sample design analysis and McNemar’s

analysis were conducted before and after PSM, respectively. Logistic and conditional logistic regression analyses were also conducted before and after PSM to determine associations between diabetes and periodontitis. All statistical analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC). A *P* value of $< .05$ was statistically significant.

3. Results

3.1. Participant demographics before and after PSM for periodontal disease

Before PSM, the individuals with periodontitis were older, less educated, and had a lower income than those without periodontitis. Furthermore, more individuals with periodontitis were men, married, and did not smoke than those without periodontitis. Finally, more participants with periodontitis were obese, hypertensive, diabetic, hypercholesterolemic, and hypertriglyceridemic than those without periodontitis (Table 1). The mean age difference between the 2 groups was 12.2 years. The SMD for most variables ranged from 7% to 32%, except for occupation and drinking, for which the SMD was 0% (Table 1). After PSM, more participants with periodontitis were male, diabetic, and did not smoke than those without periodontitis (Table 2). The mean age difference was 1.3 year. The SMD for all variables was less than 7% (Table 2). The ideal SMD was a value of 0% for all covariates. However, values $<10\%$ indicated that the covariate was similarly distributed between the case and control groups.^[36] In

Table 1
Characteristics of participants according to periodontitis before PSM.

Variables	Group	Periodontitis (N = 2982)		No periodontitis (N = 6526)		P	SDM
		n	Weighted %	n	Weighted %		
Age	Mean (SD)	59.2 (36.6)		47.0 (33.0)		<.0001	0.31
	19 ≤ age ≤ 49	722	23.1	3766	57.2	<.0001	0.32
	50 ≤ age ≤ 59	735	25.8	1089	17.6		
	60 ≤ age ≤ 69	794	26.5	898	13.7		
Sex	70 ≤ age	731	24.5	773	11.6		
	Male	1543	50.1	2479	36.7	<.0001	0.12
Marital status	Female	1439	49.9	4047	63.3		
	Married	2821	94.5	5078	77.4	<.0001	0.20
Occupation	Not married	161	5.5	1448	22.6		
	Employed	1778	58.5	3918	58.5	.99	0.00
Education	Not employed	1204	41.5	2608	41.5		
	Elementary school	927	30.5	930	13.7	<.0001	0.25
	Middle school	409	14.4	506	7.8		
	High school	871	29.6	2173	34.0		
Income	University	775	25.5	2917	44.5		
	First quartile	778	26.0	984	14.7	<.0001	0.15
	Second quartile	810	26.8	1509	22.9		
	Third quartile	727	24.4	1958	29.7		
Smoking	Fourth quartile	667	22.8	2075	32.7		
	Current	2291	77.5	5641	86.8	<.0001	0.11
Drinking	None/Ex-smoker	691	22.5	885	13.2		
	No	1387	47.0	3021	46.4	.67	0.00
Obesity	Yes	1595	53.0	3505	53.6		
	No	1749	59.6	4496	69.6	<.0001	0.09
Hypertension	Yes	1233	40.4	2030	30.4		
	No	1640	55.5	4880	75.5	<.0001	0.20
Diabetes	Yes	1342	44.5	1646	24.5		
	No	2384	80.3	5963	91.9	<.0001	0.16
Hypercholesterolemia	Yes	598	19.7	563	8.1		
	No	2172	72.5	5192	79.4	<.0001	0.07
Hypertriglyceridemia	Yes	810	27.5	1334	20.6		
	No	2407	80.6	5721	88.1	<.0001	0.09
	Yes	575	19.4	805	11.9		

PSM = propensity score matching, SD = standard deviation, SMD = standardized mean difference. *P* values are results of Chi-squared test using complex sample design.

Table 2
Characteristics of participants according to periodontitis after PSM.

Variables	Group	Periodontitis (N = 2929)		No periodontitis (N = 2929)		P	SMD	
		n	Weighted%	n	Weighted %			
Age	Mean (SD)	59.1 (37.1)		57.8(39.0)		<.001	0.03	
	19 ≤ age ≤ 49	722	23.5	755	25.1			.54
	50 ≤ age ≤ 59	718	25.6	710	26.0			
	60 ≤ age ≤ 69	775	26.5	746	25.1			
70 ≤ age	714	24.4	718	23.8				
Sex	Male	1493	49.4	1384	46.0	.03	0.03	
	Female	1436	50.6	1545	54.0			
Marital status	Married	2768	94.4	2796	95.5	.10	0.02	
	Not married	161	5.6	133	4.5			
Occupation	Employed	1741	58.3	1759	58.6	.84	0.00	
	Not employed	1188	41.7	1170	41.4			
Education	Elementary school	899	30.1	855	27.9	.46	0.02	
	Middle school	394	14.2	401	13.9			
	High school	861	29.8	869	30.8			
	University	775	25.9	804	27.3			
Income	First quartile	760	25.8	740	24.4	.76	0.01	
	Second quartile	787	26.7	787	26.6			
	Third quartile	721	24.6	719	25.1			
	Fourth quartile	661	22.9	683	23.9			
Smoking	Current	2284	78.6	2389	82.2	<.001	0.04	
	None/Ex-smoker	645	21.4	540	17.8			
Drinking	No	1374	47.5	1460	49.7	.18	0.02	
	Yes	1555	52.5	1469	50.3			
Obesity	No	1720	59.7	1743	60.4	.68	0.00	
	Yes	1209	40.3	1186	39.6			
Hypertension	No	1621	56.0	1627	56.8	.64	0.00	
	Yes	1308	44.0	1302	43.2			
Diabetes	No	2341	80.4	2482	86.1	<.001	0.07	
	Yes	588	19.6	447	13.9			
Hypercholesterolemia	No	2133	72.5	2093	71.4	.38	0.01	
	Yes	796	27.5	836	28.6			
Hypertriglyceridemia	No	2378	81.0	2392	82.5	.21	0.01	
	Yes	551	19.0	537	17.5			

PSM = propensity score matching, SD = standard deviation, SMD = standardized mean difference. P values are results of Chi-squared test using complex sample design.

this study, the SMDs were > 10% in case of 8 covariates among a total of 12 covariates before matching. However, after matching, the SMDs of all covariates were <10%, which means similar distribution of all covariates between groups. C-statistic was 0.81 and 0.73 before and after PSM, respectively, indicating an improved covariate balance after PSM.

3.2. Associations with diabetes before and after PSM for periodontal disease

Logistic regression analysis with a complex sample design identified a significant association between periodontitis and diabetes (odds ratio [OR] = 1.53; 95 % confidence interval (CI) = 1.31–1.80) after adjusting for confounding variables, such as age, sex, marital status, occupation, education, income, smoking and drinking habits, obesity, hypertension, hypercholesterolemia, and hypertriglyceridemia (Table 3). In addition, significant association between periodontitis and diabetes was still observed in the conditional logistic regression analysis after matching on propensity scores which were derived from the model including age, sex, marital status, occupation, education, income, smoking and drinking habits, obesity, hypertension, hypercholesterolemia, and hypertriglyceridemia (OR = 1.52; 95 % CI = 1.28–1.80; Table 3).

4. Discussion and conclusions

This study used KNHANES VII data, PSM, and logistic regression analyses to evaluate the association between periodontitis

Table 3
Logistic regression analyses for periodontitis and diabetes associations.

Variables	Group	Before PSM (n = 9508)			After PSM (n = 5858)		
		OR*	(95 % CI)		OR†	(95 % CI)	
Periodontitis	Yes (ref = No)	1.53	1.31	1.80	1.52	1.28	1.80

CI = confidence interval, OR = odds ratio, PSM = propensity score matching.
 *OR from logistic regression analysis with complex sample design after adjusting for age, sex, marital status, occupation, education, income, smoking and drinking habits, obesity, hypertension, hypercholesterolemia, and hypertriglyceridemia.
 †Crude OR from conditional logistic regression analysis after matching on propensity scores which were derived from a model including age, sex, marital status, occupation, education, income, smoking and drinking habits, obesity, hypertension, hypercholesterolemia, and hypertriglyceridemia. All P values < .001.

and diabetes. As anticipated, the complex sample logistic regression analysis identified a significant association between diabetes and periodontitis. Furthermore, more individuals with periodontitis had diabetes than those without (OR = 1.53; 95 % CI = 1.31–1.80; Table 3). After PSM, the conditional logistic regression analysis confirmed a significant association between diabetes and periodontitis (OR = 1.52; 95 % CI = 1.28–1.80; Table 3). These results suggest that periodontitis may be positively associated with diabetes.

Periodontitis is the sixth most common complication of diabetes and is accompanied by microangiopathy, nephropathy,

neuropathy, macrovascular disease, and delayed wound healing.^[37] Therefore, the high prevalence of diabetes in the periodontitis group cannot be discounted because periodontal disease is an early complication of diabetes. Several reviews and epidemiological studies have documented a bidirectional relationship between diabetes and periodontitis.^[16,38–40] However, most of these studies could not exclude the confounding effects of covariates since they were cross-sectional studies. Confounding is a confusion between the exposure and outcome variables of interest. To find appropriate conclusion, control of confounding is necessary through study design or analysis.^[18] Unexpectedly, some longitudinal studies have reported no bidirectional association between periodontitis and type 2 diabetes.^[41–43] In detail, they suggested that periodontitis does not increase the risk of diabetes. Considering these conflicting results of longitudinal studies there is a need to more well-designed studies about association between periodontitis and type 2 diabetes. Because of critical limitation of cross-sectional study, lack of temporal clarity, our study cannot meaningfully be compared to the findings of longitudinal studies. Nevertheless, considering advantage of nationwide representative survey, KNHANES, we adopted PSM to reduce confounding in cross-sectional data analysis.^[44] In this study, we performed 1:1 PSM to randomly select the case and control groups based on the presence of periodontal disease. The variables used for PSM included age, sex, marital status, occupation, education, income, smoking and drinking habits, obesity, hypertension, hypercholesterolemia, and hypertriglyceridemia.

However, this study has several limitations. First, it was still a cross-sectional study. Second, we only focused on the relationship between periodontitis and diabetes. Therefore, a longitudinal study is necessary to investigate the effects of periodontitis duration on the incidence of diabetes. Third, PSM is limited by the quality of the propensity score model, which depends on the selection, definition, and categorization of confounding predictors. Therefore, residual confounding may still be present, and true randomization is impossible. In this study, there were considerable differences in marital status, income, and smoking variables between the periodontal and non-periodontal groups after PSM. This result indicates that there may be important residual confounding factors in our propensity score model. Fourth, according to our definition of diabetes mellitus, most were type 2 diabetes cases. Excluding type 1 diabetes entirely from the KNHANES dataset was impossible because of the survey protocol. However, we selected participants older than 19 years, and the prevalence of type 1 diabetes is extremely low in Korea. Therefore, we can conclude that most were type 2 diabetes cases.^[45]

Nevertheless, to our knowledge, this study is the first to qualitatively examine the association between periodontal disease and diabetes using PSM and large-scale KNHANES data, which represents the national health data. Notably, we identified a significant association between diabetes and periodontitis. Furthermore, these results provide foundational evidence for other studies investigating the relationship between systemic and periodontal diseases.

In conclusion, early awareness is important for patients with type 2 diabetes mellitus to prevent complications, such as kidney failure and peripheral arterial disease.^[46] However, many developing countries have poor diabetes awareness because this chronic disease often has no symptoms for many years after onset.^[47] Our findings suggest that dental healthcare workers could help bring awareness to patients with periodontitis regarding the association between periodontitis and diabetes, which may motivate them to act proactively or receive treatment.

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