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Type 2 diabetes as a risk indicator for dental caries in Korean adults: the 2011-2012 Korea national health and nutrition examination survey

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Objectives: The associations between type 2 diabetes (T2D) and untreated dental caries was examined. This study hypothesized that there would be a positive association between T2D and the prevalence of decayed permanent teeth (DT) in representative Korean adults. ***Methods:*** The information was derived from the Korea National Health and Nutrition Examination Survey conducted in 2011-2012. Sociodemographic and lifestyle variables, anthropometric and biochemical status, metabolic health and glucose tolerance status, oral health behaviors, and dental caries index were evaluated. ***Results:*** The number of DT had a positive association with degree of fasting plasma glucose (FPG) level, and glycated hemoglobin (HbA1c) (p-value = 0.045 and 0.007, respectively). The levels of FPG and HbA1c increased with the number of DT (p for trend = 0.009 and 0.004, respectively). The prevalence of untreated caries uncontrolled T2D participants was about 26% higher than those with normal glucose tolerance levels after adjusting for potential confounders including diets and socioeconomic status (OR [95% CI] = 1.26 [1.02, 1.56]). ***Conclusions:*** T2D is an independent risk indicator for untreated caries in Korean adults.

Keywords: *diabetes mellitus, epidemiology, metabolic diseases, nutrition survey, oral health, dental caries*

Introduction

Diabetes mellitus (DM) has been a social and economic burden worldwide. The International Diabetes Federation estimated that about 415 million people, or one in 11 adults worldwide had DM in 2015, and this will rise to 642 million, or one in 10 adults by 2040. The financial burden worldwide reached to $673 billion USD, 12% of the whole global health expenditure in 2015 (IDF, 2015). WHO reported that about 1.5 million deaths were directly caused by DM in 2012, and predicted that it would be the 7th highest cause of mortality in 2030 (Alwan, 2011).

Dental caries is explained as the local breakdown of vulnerable tooth structure by acidic by-products originating from dietary carbohydrates fermented by bacterial species (Selwitz *et al.*, 2007). The process begins within the bacterial biofilm (plaque), and proceeds to cavitation due to physiological imbalance between mineralized tooth portion and oral bacterial films. Dental caries is triggered by endogenous microbial components like Streptococcus mutans or lactobacilli (Selwitz, Ismail *et al.*, 2007). It is a complex condition affected by other factors including a low socioeconomic status (SES), dietary habits, salivary flow rate, and fluoride exposure (Schwendicke *et al.*, 2015) and is reported to be associated with various systemic diseases like cardiovascular and cerebrovascular disease (Taubman and Nash, 2006; Ylöstalo *et al.*, 2006) and metabolic syndrome (Ojima *et al.*, 2015). Over the past decade several reports have tried to explain the relationship between dental caries and DM with contrasting findings of positive (Arheiam and Omar, 2014; Biesbrock *et al.*, 2003; Gæde *et al.*, 2008), neutral (Collin, H.-L. *et al.*, 1998; Collin, H.L. *et al.*, 1998) or negative associations (Gupta *et al.*, 2014).

In this study, we tried to identify a clear association between T2D and dental caries with a representative sample of Korean adults. This study hypothesized that T2D would increase the risk of untreated dental caries.

Methods

Overview of the survey and participants

The data were collected from the 2011-2012 Korea National Health and Nutrition Examination Survey, a cross-sectional nationwide survey supervised by the Ministry of Health and Welfare of South Korea. Specially trained investigators inspected a representative population of South Korean adults with well-designed questionnaires,tions, health interviews, and physical and nutritional examinations.

In this study, 10,439 participants aged≥30 who maintained fasting at least 8 hours before blood sample collection were included. The 290 participants with missing caries and 692 with missing diabetes data were excluded, leaving

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9,457 participants. All participants gave written informed consent. This study was permitted by the Institutional Review Board (IRB) of the Korean Center for Disease Control and Prevention, and was accomplished according to the Ethical Principles for Medical Research Involving Human Subjects based on Helsinki Declaration. This study was confirmed according to the STROBE guidelines, and presented as a flowchart (Fig 1).

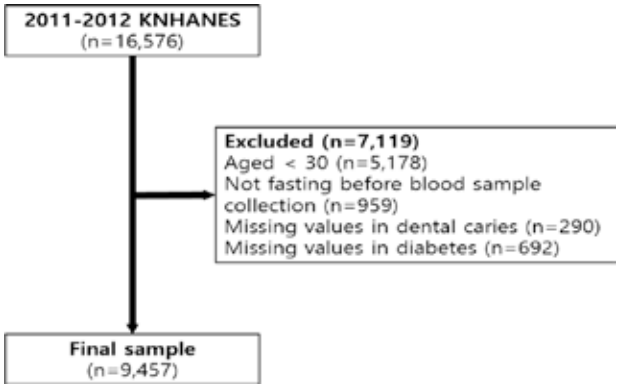

Figure 1. *Flowchart of the study according to STROBE guideline.*

Sociodemographic and lifestyle variables

Sociodemographic and lifestyle data were collected with a self-administered questionnaire enquiring about physical exercise, cigarette smoking, household income, alcohol drinking, and education level. Smokers were categorized as non-smokers, ex-smokers, or current smokers. Alcohol drinking was categorized as heavy drinkers (> 30 g/day), mild to moderate drinkers (1–30 g/day), and non-drinkers. Education level was classified as either having graduated from high school (≥ 13 years) or not. Physical exercise rate was measured based on the International Physical Activity Questionnaire. Participants who do body exercise for 30 minutes/session and at least 5 times/week, or those who do physical exercise actively for 20 minutes/session and at least 3 times/week were demarcated as regular exercisers. Household income was divided into quartiles.

Anthropometric measurements

Qualified trained examiners collected the data. Height was measured to the nearest 0.1 cm, and body weight was recorded using a digital scale to the nearest 0.1 kg in bare feet and lightweight clothing. Waist circumference was estimated to the nearest 0.1 cm at the slenderest midpoint between the costal and the iliac crest margin, with loose clothing at the end of a normal expiration. BMI was measured by dividing body weight (kg) by the square of height (m^2). These measurements were accomplished according to the recommendations of World Health Organization. Hypertension was defined as a systolic and/or a diastolic blood pressure higher than 140/90 mm Hg. Prehypertension was demarcated as elevated blood pressure above normal but below hypertension as follows; a diastolic pressure 80-89 mm Hg or a systolic blood pressure 120-139 mm Hg. Neither hypertension nor prehypertension was designated as normotension.

Biochemical measurements

Trained staff gathered biochemical samples. A standard mercury sphygmomanometer (Baumanometer, W. A. Baum Co., Copiague, NY, USA) was used to measure blood pressure. Gradations of diastolic and systolic blood pressure were read three times at five minute intervals and averaged. Blood was collected from the antecubital vein after fasting for at least eight hours. Samples were stored immediately at a low temperature, then conveyed to a central testing institute (NeoDin Medical Institute, Seoul, South Korea). Low and high-density lipoprotein cholesterol, serum fasting plasma glucose (FPG), total cholesterol, and triglycerides were admeasured by an automated enzymatic analyzer (Hitachi 7600; Hitachi, Ltd., Tokyo, Japan). To evaluate liver function, serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) enzyme levels were admeasured with UV light by the aforementioned chemical analyzer (Hitachi 7600), and were classified as follows; abnormal (ALT≥35 unit/L, AST≥40 unit/L) or normal (ALT<35 unit/L, AST<40 unit/L).

Descriptions of metabolic syndrome and T2D

Data regarding T2D were based on the blood samples. Participants with 100–125 mg/dL FPG were classified as having impaired fasting glucose, and participants with FPG level < 100 mg/dL were defined as normal glucose tolerance. Those previously diagnosed with T2D by a physician, or those who fulfilled the diabetic criteria provided from American Diabetic Association were defined as T2D; FPG ≥ 126 mg/dL (ADVIA® 1650; Siemens, Deerfield, IL, USA) or ≥6.5% glycated hemoglobin (HbA1c) admeasured by liquid chromatography (Bio-Rad Varian™ II, Bio-Rad, Hercules, CA, USA) . Additionally, T2D being under control was defined as having HbA1c levels below 6.5% (48 mmol/mol) among the type 2 diabetic patients.

Metabolic syndrome in Asians was defined according to the criteria of the American Heart Association/National Heart, Lung, and Blood Institute. Participants with at least three of the following 5 criteria were defined as having metabolic syndrome: waist circumference ≥ 80 cm for women and ≥ 90 cm for men, current use of an antihypertensive drug or blood pressure ≥ 130/85 mmHg, use of an anti-diabetic drug or FPG ≥ 100 mg/dL, use of an anti-dyslipidemic drug or fasting triglycerides ≥ 150 mg/dL, and use of an anti-dyslipidemic drug or high-density lipoprotein cholesterol < 50 mg/dL in women and < 40 mg/dL in men.

Oral health behaviors and dental caries index

Participants reported the times of day when they brushed their teeth from the choices before bedtime, after snacks, and before or after breakfast, lunch, and dinner. Use of secondary oral products such as dental mouthrinse, dental floss, interdental brushes, and electric toothbrushes was recorded. The frequency of toothbrushing was defined as number of toothbrushings per day. The number of dental visits within a year was also determined. Self-reported oral health was categorized as “very good,” “good,” “normal,” “bad,” or “very bad” with the “very good” and “good” categories aggregated to denote “positive oral health”.

Dental caries and treatment experience was measured according to WHO criteria. As the DMFT index includes decayed, missing and filled teeth we analysed only the presence and number of decayed teeth in the permanent dentition.

Statistical analyses

The data are described as percentages (standard error) for categorical and mean ± standard error for continuous variables. Rao–Scott chi-square tests for categorical variables and Student's t-tests for continuous variables were used to missing with decayed teeth. Multiple linear regression analyses of the number of DT and biochemical parameters were performed after adjustment for covariates including age and sex. We explored whether parameters of metabolic health status including FPG and HbA1c differed with the number of DT. In addition, multiple logistic regressions were conducted to determine the odd ratios for experience of untreated caries according to the diabetic status (normal glucose tolerance, impaired fasting glucose, or T2D). Model 1 made no adjustment. Model 2 was adjusted for sex and age, model 3 for components of Model 2 and smoking, drinking, and physical activity, education status, and household income and model 4 was adjusted for the components of model 3 plus hypertension, metabolic syndrome, BMI, and number of daily toothbrushings. The SAS statistical software version 9.3 (SAS institute, Cary, NC, USA) was used for the analysis. All relationships were deemed significant at $p< 0.05$.

Results

Table 1 displays the general features of participants with and without untreated caries. The prevalence was significantly higher in men, heavy drinkers, present smokers, people who did not exercise regularly, and participants with household income in the lowest quartile. Individuals with annual dental visits, positive oral health, and no mastication problems had fewer DT (all p-value < 0.05). Caries was more prevalent with greater age, weight, height, or waist circumference (all p-value < 0.05).

Table 2 shows the associations between the number of DT and biochemical / anthropometric parameters in multiple linear regression analysis. More DT was associated with higher FPG and HbA1c (p-value = 0.045 and 0.007, respectively) following adjustment for age and sex. Other variables did not show significance.

The patterns of glucose intolerance by the number of DT are shown in Fig 2. The levels of FPG and HbA1c increased with the number of DT (p for trend = 0.009 and 0.004, respectively).

The prevalence of untreated caries was about 26% higher among uncontrolled T2D participants than those with normal glucose tolerance levels after adjustment for diet and SES (OR [95% CI] = 1.26 [1.02, 1.56]), and this prevalence was higher than controlled T2D (1.2 [0.84, 1.72]) (Table 3).

Discussion

This study revealed that untreated tooth decay is positively associated with T2D. The number of DT was significantly correlated with FPG and HbA1c levels. The prevalence of caries was much higher in T2D participants than those of normal and participants with impaired fasting glucose. T2D diagnostic parameters (FPG and HbA1c) increased with the number of DT.

A link between dental caries and diabetes has been sought in several animal studies (Kodama *et al.*, 2011; Selwitz, Ismail *et al.*, 2007). The occurrence of dental caries increased in diabetic compared to healthy rats, and insulin-mediated glycemic control decreased the caries-related periodontal infection and progression of dental caries (Nakahara *et al.*, 2013). Diabetes was also closely associated with numerous infectious diseases, supported by the fact that diabetic animals were prone to fungal and bacterial infection (Nakahara *et al.*, 2013). The present study demonstrated that odds ratio for the prevalence of caries slightly decreased in controlled compared to uncontrolled T2D. Because caries is caused by oral cariogenic bacteria (Kleinberg, 2002), diabetic control might reduce the incidence of tooth decay.

Clinical studies of dental caries and diabetes, still present contrasting results. Some reports showed no difference between non-diabetic and T2D individuals (Cherry-Peppers and Ship, 1993; Collin, H.L., Uusitupa, M. *et al.*, 1998). However, caries was more prevalent in type 1 (Miko *et al.*, 2010; Siudikiene *et al.*, 2006), and type 2 diabetic patients (Biesbrock *et al.*, 2003). The current cross-sectional study also found caries to be more prevalent among T2D patients.

The potential confounders that may affect both T2D and dental caries as both diseases share risk factors including diet and SES. Dental caries and T2D may increase in prevalence if excessive carbohydrate consumed. Frequent and/or excessive sugar intake plays a key role in caries propagation, and *streptococcus mutans* has a principle role in demineralizing enamel by metabolizing carbohydrate to lactic acid (Bradshaw and Lynch, 2013). WHO recommend that consumption of free sugar should not exceed 5% of total energy intake to prevent dental caries both in adults and children (Rugg-Gunn, 2013). Similarly, T2D increases with excessive carbohydrate intake. A randomized clinical trial indicated that a very low carbohydrate improved glucose control in T2D (Saslow *et al.*, 2014). The American Diabetes Association recommends a carbohydrate reduction to less than 130g/day to lower postprandial glucose (Khazrai *et al.*, 2014).

A systematic review demonstrated caries prevalence was significantly higher in those with low educational or occupational status or low income. (Schwendicke *et al.*, 2015). Also, low SES may increase cariogenic bacteria and secretion of stress-evoked salivary cortisol, which would increase dental caries susceptibility (Boyce *et al.*, 2010). As for T2D, a systematic review of prospective cohorts showed a close association between T2D and low SES group (Kivimaki *et al.*, 2015). Likewise, both income and education level were inversely associated with risk of T2D in a female cohort. Several cross-sectional studies revealed low income and education level to be independent risk factors for T2D (Asadi-Lari *et al.*, 2016; Bird *et al.*, 2015; Hwang and Shon, 2014).

Table 1. Characteristics of participants with and without decay

	Presence of Untreated Decayed Permanent Teeth		
	No	Yes	
	n =6,786 % (standard error)	n = 2,671 % (standard error)	*p* (Chi sq.)
Male	46.8 (0.6)	54.2(1.1)	<0.001
Present smoker (yes)	20.2 (0.6)	29.4(1.1)	<0.001
Heavy drinker (yes)	9.6 (0.5)	12.5(0.8)	0.001
Regular exerciser (yes)	18.8 (0.7)	16 (0.9)	0.01
Income (lowest quartile, yes)	15.2 (0.7)	17.3(1)	0.04
Education level (≥ 13 years)	65.8 (1)	67 (1.3)	0.39
DT (n)			
0	100 (0)	.	
1	.	47.8(1.3)	
2	.	23.2(1)	
3	.	12.3(0.8)	
4 or more	.	16.8(0.9)	
Annual dental visits (yes)	27.9 (0.8)	22.3(1.1)	<0.001
Positive SROH (yes)	15.3 (0.7)	8.3(0.7)	<0.001
Mastication problem (yes)	23 (0.7)	33.6(1.2)	<0.001
Speech problem (yes)	8 (0.4)	8.5(0.7)	0.54
Daily toothbrushing (n)			0.001
1	11.2 (0.6)	13.6(0.8)	
2	43.9 (0.9)	46.3(1.2)	
3 or more	44.8 (0.9)	40.1(1.2)	
T2D MED (yes)	6.7 (0.4)	6.8(0.5)	0.83
MetS (yes)	31.5 (0.8)	30.2(1.1)	0.34
Hypertension (yes)			0.63
Normotension	43 (0.9)	41.7(1.3)	
Prehypertension	26.4 (0.7)	27.4(1.1)	
Hypertension	30.6 (0.8)	30.9(1.2)	
	mean±standard error	mean ± standard error	*p* (*t test*)
Age (year)	50.9±0.3	48.7±0.4	<0.001
Height (cm)	162.8±0.1	163.8±0.2	<0.001
Weight (kg)	63.6±0.2	64.9±0.3	<0.001
WC (cm)	82±0.2	82.7±0.3	0.02
BMI (kg/m^2)	23.9±0.1	24.1±0.1	0.01

Positive self-reported oral health includes "very good" and "good". Hypertension was defined as >140/90 mmHg, prehypertension as 120-133 mm Hg of a systolic blood pressure, or 80-89 mm Hg of a diastolic pressure. Neither hypertension nor prehypertension was designated as normotension. Abbreviation: DR; decayed permanent teeth individual, SROR; self-reported oral health, MetS; metabolic syndrome, WC; waist circumference; T2D MED: present taking T2D medication or insulin injection.

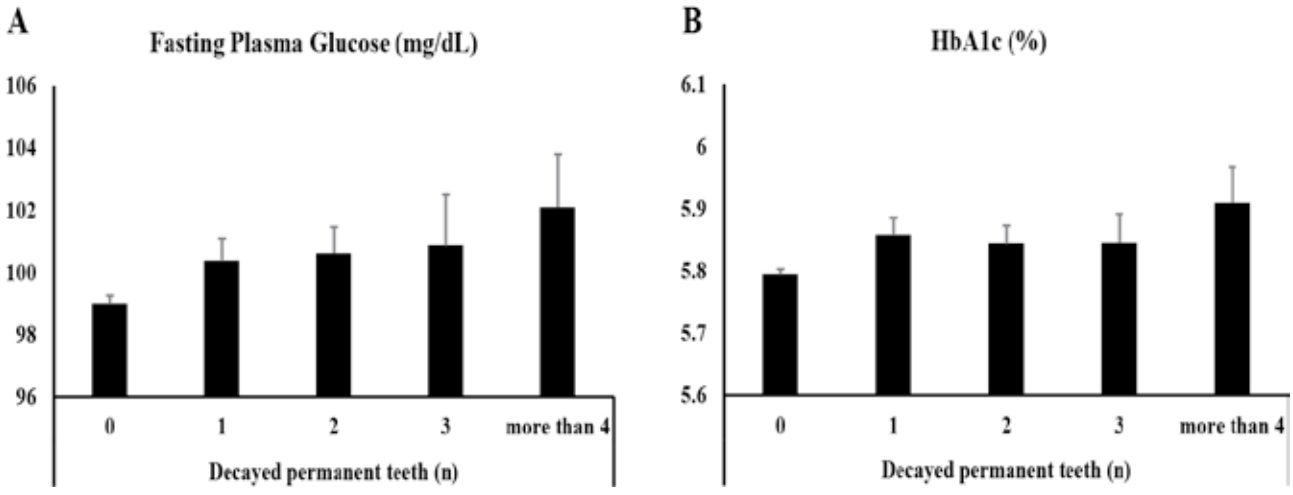

Figure 2. *Glucose intolerance by number of decayed permanent teeth (DT).*

p for trend = 0.009
p for trend = 0.004

Accordingly, the risk of both T2D and dental caries increases with excessive consumption of carbohydrate and/or low SES. However, this study clearly showed that dental caries is an independent risk indicator for T2D after adjusting the effect of diet as and SES. The exact casual factors remain unclear.

Whilst this study attempted to account for a number of behavioural factors, it is likely that residual confounding arises from imprecise control of these factors. Most notably, dental visiting behaviour is an obvious risk factor for untreated dental caries, but was only dichotimised (+/- four or more visits) in this analysis. There is great scope for this behaviour to exert an effect on untreated caries within these categories. Moreover, this variable may also cluster with other risk factors common to untreated caries and diabetes.

Table 2. Multiple regression model for number of decayed permanent teeth by biochemical/ anthropometric parameters

	Individual decayed permanent teeth (n)		
	Beta	SE	*p*-value
WC (cm)	0.0020	0.0029	0.48
BMI (kg/m^2)	0.0039	0.0080	0.63
DBP (mm/Hg)	-0.0016	0.0022	0.46
SBP (mm/Hg)	0.0025	0.0015	0.09
FPG (mg/dL)	0.0028	0.0014	0.05
HbA1c (%, mmol/mol)	0.0923	0.0341	0.01
TC (mg/dL)	0.0001	0.0006	0.88
LDL-C (mg/dL)	0.0000	0.0007	0.98
HDL-C (mg/dL)	-0.0011	0.0017	0.53
TG (mg/dL)	0.0103	0.0328	0.75
ALT (unit/L)	-0.0212	0.0491	0.67
AST (unit/L)	0.0025	0.0651	0.97

Covariates include age and sex.
Abbreviations: Beta; beta coefficient, SE; standard error, WC; waist circumference, BMI; body mass index, DBP; diastolic blood pressure, SBP; systolic blood pressure, FPG; fasting plasma glucose, HbA1c; glycated hemoglobin, TC; total cholesterol, LDL-C; low density lipoprotein cholesterol, HDL-C; high density lipoprotein cholesterol, TG; serum triglyceride, ALT; alanine transaminase, AST; aspartate aminotransferase.

Salivary dysfunction may also explain the association. Saliva has a protective role against caries through its unique components of pH, calcium, phosphate, fluoride, and its rinsing effect (Stookey, 2008). The elevation of mineral contents in saliva inhibited caries incidence (Pearce *et al.*, 2002), and saturation of saliva with calcium and phosphate reduced decay by continuous ion exchange (Ten Cate, 2008). As such, an altered salivary function in T2D is suggested as the mechanism of caries susceptibility. One study reported that high blood glucose led to a high glucose content in saliva (Tenovuo *et al.*, 1986). Also, decreased pH and salivary flow, and altered protein composition were suggested as causes for caries susceptibility in diabetic individuals (Sampaio *et al.*, 2011). One comparative clinical study found higher DMFT scores among T2D participants where salivary flow and fluoride, phosphate, and calcium concentrations were significantly lower (Jawed *et al.*, 2011). Similarly, lack of salivary flow with acidic change could aggravate the tooth decay (Chu *et al.*, 2008), whereas participants with controlled diabetes had lower DT, better salivary flow rate, and pH (Kumar and Clark, 2002). Collectively, these results indicated that salivary dysfunction caused by T2D may lead to the onset and/or propagation of dental caries.

A previous large population-based longitudinal study revealed that HbA1c was associated with diabetic risk as well as FPG, and was more powerfully related to the mortality (Selvin *et al.*, 2010). The 2015 ADA suggested that HbA1c of 5.7 to 6.4% (39-46 mmol/mol) was suitable as a gauge for pre-diabetes, and that of > 6.0% (42 mmol/mol) should be of concern for a "very high" risk of diabetes (ADA, 2015). Similarly, other reports have shown that adults with HbA1c >13% (119 mmol/mol) had significantly higher DMFT than those with HbA1c <10% (86 mmol/mol) (Gæde, Lund-Andersen *et al.*, 2008). Another study reported that individuals with HbA1c >8.5% (69 mmol/mol) was significantly associated with greater DMFT than individuals with HbA1c <8.5% (69 mmol/mol) (Syrjala *et al.*, 2003). The present study found that the whole set of surveyed participants had an HbA1c of 5.7% (39 mmol/mol) or more, and this value reached up to almost 6.0% (42 mmol/mol) in those who had more than 4 DT. These results emphasized that participants with more untreated DT are at "very high" risk of diabetes.

Table 3. Logistic regression model for presence of untreated caries by fasting plasma glucose and T2D control

	Prevalence of caries experience			
	MODEL1	MODEL2	MODEL3	MODEL4
Glucose tolerance status				
Normal	1	1	1	1
IFG	1.00(0.88,1.13)	1.1(0.97,1.25)	1.08(0.95,1.23)	1.03(0.89,1.19)
T2D	1.24(1.04,1.47)	1.49(1.22,1.81)	1.42(1.17,1.73)	1.26(1.02,1.56)
T2D control (yes)	1.17(0.82,1.67)	1.23(0.86,1.76)	1.19(0.84,1.7)	1.2(0.84,1.72)

Abbreviations: T2D; T2D. IFG; impaired fasting glucose, FPG; fasting plasma glucose level for at least 8 h of fasting. Data are designated as odds ratio (95% confidence intervals). Control of T2D was defined by glycated hemoglobin (HbA1c), as below 6.5% (48 mmol/mol) was controlled T2D among diabetic patients.
MODEL1 was non-adjusted,
MODEL2 was adjusted for sex and age.
MODEL3 was adjusted for covariates of Model 2 plus drinking, smoking, household income, physical exercise, place of residence, and education level.
MODEL4 was adjusted for covariates of Model 3 plus BMI, number of daily toothbrushings, hypertension, total energy intake, and carbohydrate intake (%).

There were some limitations in this study. First, we have already mentioned the risk of residual confounding due to imprecise control of covariates. Secondly, its cross-sectional design didn't elucidate causal relationships. A longitudinal cohort would be required to reveal the role of caries risk in T2D. Third, this study didn't address some influencing factors such as changes in salivary protein composition or flow rate, bacterial/yeast components on saliva or plaque, and outcome variables including root caries incidence. Forthly, this study couldn't differentiate between type 1 and 2 participants, because records from KNHANES didn't include the diagnostic age which is a criterion differentiating the two, although most participants would have T2D. However, this study has key strengths. First, it showed a close association between T2D and dental caries in adults. Most previous studies have focused on caries in only young individuals. Second, it showed that control of T2D was related to low caries risk. Second, this study showed that untreated caries to be an independent risk indicator of T2D after adjustment of both diet and SES.

Conclusion

T2D is an independent risk indicator for dental caries in Korean adults. These findings suggest diabetes control may prevent dental caries and maintain oral health.

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Disclaimer

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