ORIGINAL ARTICLE

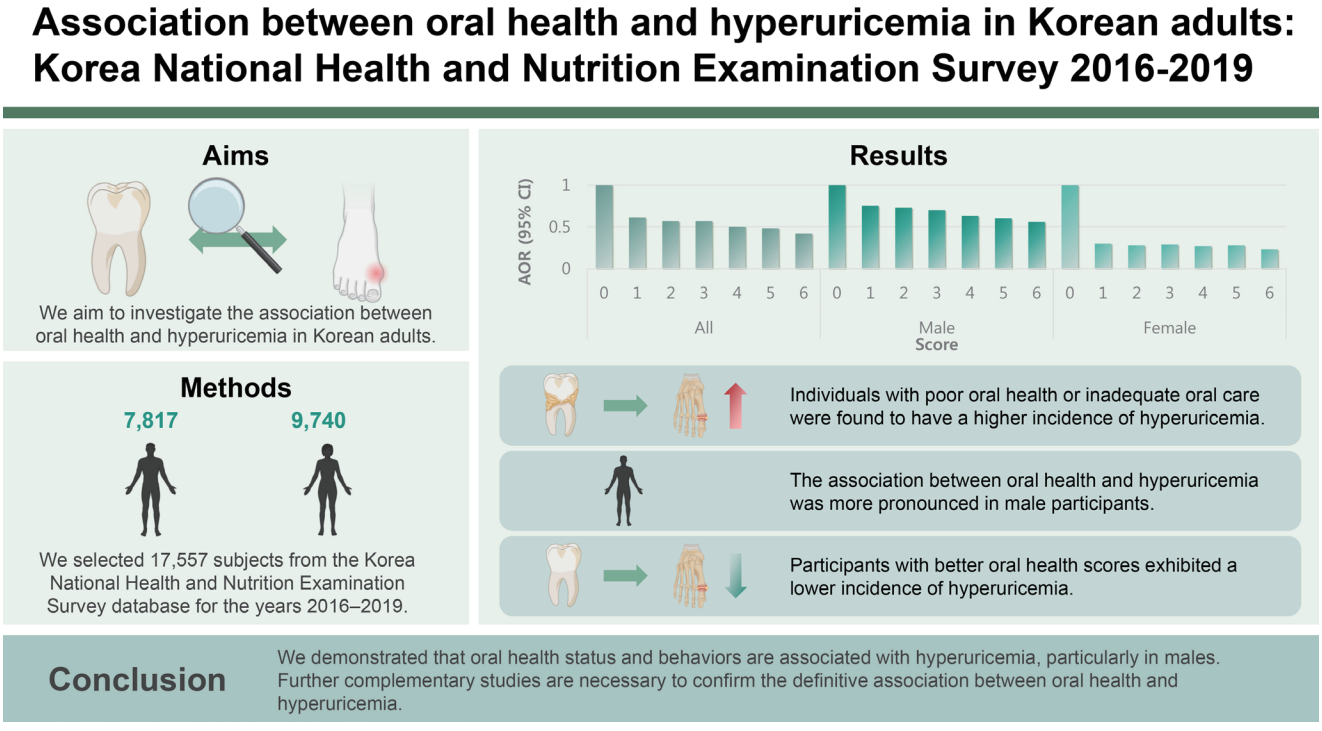
Korean J Intern Med 2024;39:1001-1010
https://doi.org/10.3904/kjim.2023.425

Association between oral health and hyperuricemia in Korean adults: Korea National Health and Nutrition Examination Survey 2016–2019

Junyong Park[1,*], Minkook Son[2,3,*], Sung Won Lee[1], Won Tae Chung[1], and Sang Yeob Lee[1]

[1]Division of Rheumatology, Department of Internal Medicine, Dong-A University College of Medicine, Busan; [2]Department of Physiology, Dong-A University College of Medicine, Busan; [3]Department of Data Sciences Convergence, Dong-A University Interdisciplinary Program, Busan, Korea

*These authors contributed equally to this manuscript.



Background/Aims: Hyperuricemia plays an essential role in the gout. Despite the clinical significance of hyperuricemia, a direct relationship between oral health and hyperuricemia has not been established. We aim to investigate the association between oral health and hyperuricemia.

Methods: We selected 17,557 subjects from the Korea National Health and Nutrition Examination Survey database for the years 2016–2019. Oral health-related variables included the number of dental caries, regular tooth brushing, use of secondary oral products, and regular dental examinations. The odds ratio (OR) and 95% confidence intervals (CIs) for hyperuricemia

pISSN 1226-3303
eISSN 2005-6648
http://www.kjim.org

were calculated using a multivariable-adjusted logistic regression model.
Results: Oral health status with dental caries and oral health behaviors, including tooth brushing, secondary oral products, and regular dental examination, were significantly associated with hyperuricemia in all participants. The adjusted OR and 95% CIs for hyperuricemia comparing more than three dental caries with no dental caries were 1.28 (1.08–1.52). The adjusted OR and 95% CIs for hyperuricemia in regular tooth brushing, use of secondary oral products, and regular dental examination were 0.78 (0.67–0.91), 0.91 (0.83–1.00), and 0.86 (0.78–0.95), respectively. Notably, the association between oral health and hyperuricemia was more prominent in male subjects. In addition, when subjects were grouped by the oral health scoring system, the prevalence of hyperuricemia was lower in groups with better oral health scores.
Conclusions: We demonstrated that oral health status and behaviors are associated with hyperuricemia, particularly in males. Further studies are necessary to confirm the association between oral health and hyperuricemia.

Keywords: Oral health; Hyperuricemia; Cross-sectional study

INTRODUCTION

Hyperuricemia is a metabolic disease in which uric acid levels remain excessively high. Hyperuricemia plays an essential role in the development of gout and is well- known as a prerequisite of gout. In addition, hyperuricemia has important clinical implications because it is considered a risk factor for coronary heart disease, hypertension, insulin resistance, stroke, and death [1-4]. Nevertheless, the prevalence rate of hyperuricemia is 11.4% in Korea and 12.7% in the United States [5,6] and the prevalence of gout is increasing rapidly in Korea [7].

The oral cavity is a complex environment with various microorganisms [8]. Unless appropriately managed, inflammatory conditions, such as dental caries and periodontitis, may occur. Furthermore, oral health is known to be related to pneumonia, cardiovascular diseases, and other oral diseases [9,10]. Oral health is critically affected by oral hygiene and can be improved through regular self-management. Therefore, it would be important to investigate specific diseases related to oral health and prevent them [11].

Despite the clinical importance of hyperuricemia, little is known about its prevention. Although several self-managed interventions can improve oral health, a direct relationship between oral health and hyperuricemia has not been established. Therefore, we aim to investigate the association between oral health and hyperuricemia in Korean adults using the nationwide population-based Korea National Health and Nutrition Examination Survey (KNHANES) database.

METHODS

Data source and study population

The KNHANES is a cross-sectional survey and a nationally representative database of the Korean population managed by the Korea Centers for Disease Control and Prevention (KCDC) [12]. The KNHANES database includes physical examinations, blood test results, and health-related interviews, including oral health behaviors. To conduct the KNHANES, trained staff interviewed subjects and applied standardized health examination protocols [13]. This study used data from the KNHANES 2016–2019 because this database contains blood test results for uric acid levels. Informed consent was obtained from all participants, and the KNHANES was approved by the Institutional Review Board of the KCDC. This study used anonymized KNHANES data, and the protocol was approved by the Institutional Review Board of Dong-A University Hospital (DAUHIRB-EXP-21-106).

From 23,335 subjects in the KNHANES 2016–2019 database, we excluded 3,255 subjects without uric acid data. Subjects under the age of 20 (n = 2,063), pregnant (n = 69), or with missing values (n = 391) were also excluded. Finally, this study included 17,557 subjects (7,817 males and 9,740 females). Subsequently, we investigated the association between oral health and uric acid. A flow of the study population is shown in Figure 1.

Definition of oral health-related variables

The oral health examination program comprised oral examinations conducted by trained dentists and self-report questionnaires. The number of dental caries was categorized as

https://doi.org/10.3904/kjim.2023.425

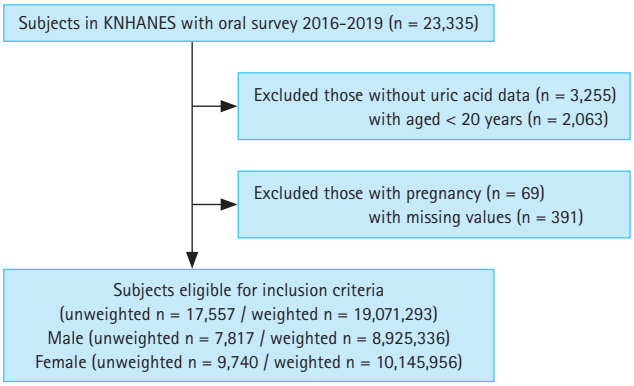


Figure 1. Flow of the study population. KNHANES, Korea National Health and Nutrition Examination Survey.

0, 1–2, or ≥ 3. Oral health-related questionnaires included questions on the time of day when subjects brushed their teeth and used secondary oral products, as well as the presence of regular dental examination as oral health behaviors. The time of day for tooth brushing was classified as before or following breakfast, lunch, and dinner or before bedtime and after snack. We calculated the frequency of daily tooth brushing. The number of tooth brushing was categorized as ≤1, 2, or ≥3. The secondary oral products included the following: dental floss, mouthwash, interdental brushes, electric toothbrushes, irrigation devices, tongue cleaners, end-tufted brushes, and special devices for dentures. The presence of regular dental examinations within a year was also evaluated.

To evaluate the association between oral health and hyperuricemia, we devised and calculated the oral health score by scoring the oral health-related variables available in the database and summing them together. A schematic diagram of the oral health score is presented in Supplementary Table 1. Unlike a few other scoring systems for the evaluation of oral health [14,15], the oral health score in this study comprises the numbers of dental caries and efforts to maintain oral hygiene. Therefore, we hypothesized that the oral health score in this study is related to oral hygiene. For example, A higher oral health score suggests better oral hygiene, and a lower oral health score indicates poor oral hygiene.

Clinical variable measurements and definitions

Body mass index (BMI) was calculated using the formula weight (kg) divided by height squared (m^2). All subjects fasted for at least eight hours before blood sampling. Blood samples were processed and refrigerated immediately for transportation to the Central Testing Institute (NeoDin Medical Institute, Seoul, Korea). Uric acid, fasting glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), and creatinine were measured using a Hitachi Automatic Analyzer 7600-210 (Hitachi, Tokyo, Japan). The estimated glomerular filtration rate (GFR) was calculated using the modification of diet in renal disease equation [16]. Hyperuricemia was defined as a serum uric acid level ≥ 7.0 mg/dL in males and ≥ 6.0 mg/dL in females [17].

Hypertension status was categorized into three groups: (a) hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg, or antihypertensive medication use; (b) prehypertension was defined as 120 mmHg ≤ SBP < 140 mmHg or 80 mmHg ≤ DBP < 90 mmHg; and (c) normal hypertension status was defined as SBP < 120 mmHg and DBP < 80 mmHg [18]. Diabetes status was categorized into three groups: (a) diabetes was defined as fasting blood sugar (FBS) ≥ 126 mg/dL or taking anti-diabetic medication; (b) pre-diabetes was defined as 100 mg/dL ≤ FBS < 126 mg/dL; and (c) normal status was defined as FBS < 100 mg/dL [19]. Using the dyslipidemia criteria for Koreans, dyslipidemia status was categorized into two groups with cutoff values as follows: total cholesterol ≥ 240 mg/dL, triglycerides ≥ 200 mg/dL, and HDL-C ≤ 40 mg/dL [20]. Furthermore, we extracted information on cancer and depression status from the survey.

Income level was divided into four groups according to the standard income quartile of the sample population. The higher the income quartile is, the greater the income. Smoking status was categorized into current smokers, ex-smokers, and non-smokers. Alcohol consumption status was categorized into two groups: (a) non-consumers, with no alcohol consumption in the past year or less than once a month, and (b) consumers, with alcohol consumption more than once a month. Physical exercise status was categorized into two groups: (a) the regular exercise group, in which participants performed moderately hard exercise for at least 150 minutes a week, hard exercise for at least 75 minutes a week, or mixed exercise equivalent to the above level (1 minute of hard exercise equivalent to 2 minutes of moderately hard exercise); and (b) the non-regular exercise group, in which participants performed physical activity less than the above-mentioned level.

Table 1. Baseline characteristics of subjects according to uric acid level

Variable	No hyperuricemia (n =15,196/16,328,652)	Hyperuricemia (n = 2,361/2,742,640)	*p* value
Age (yr)	50.0 ± 0.3	47.0 ± 0.6	< 0.001
Sex			< 0.001
Male	42.8 (0.5)	70.7 (1.3)	
Female	57.2 (0.5)	29.3 (1.3)	
Income (quartile)			0.26
1st	24.0 (0.7)	25.6 (1.3)	
2nd	25.2 (0.6)	23.6 (1.2)	
3rd	25.4 (0.6)	26.6 (1.3)	
4th	25.5 (0.8)	24.2 (1.4)	
BMI (kg/m^2)	23.6 ± 0.0	25.9 ± 0.1	< 0.001
SBP (mmHg)	118.1 ± 0.2	121.7 ± 0.5	< 0.001
DBP (mmHg)	75.3 ± 0.1	78.4 ± 0.3	< 0.001
Uric acid (mg/dL)	4.8 ± 0.0	7.5 ± 0.0	< 0.001
Fasting blood glucose (mg/dL)	100.5 ± 0.3	101.6 ± 0.5	0.05
Total cholesterol (mg/dL)	191.6 ± 0.4	198.4 ± 1.0	< 0.001
Triglyceride (mg/dL)	124.7 ± 1.1	182.1 ± 4.0	< 0.001
HDL-C (mg/dL)	52.9 ± 0.2	47.1 ± 0.4	< 0.001
GFR (mL/min/1.73 m^2)	92.5 ± 0.3	83.5 ± 0.	< 0.001
Hypertension			< 0.001
Normal	46.4 (0.7)	32.3 (1.4)	
Pre-hypertension	25.2 (0.5)	29.7 (1.3)	
Hypertension	28.4 (0.6)	38.1 (1.5)	
Diabetes			< 0.001
Normal	58.0 (0.7)	47.0 (1.3)	
Pre-diabetes	30.2 (0.6)	41.0 (1.2)	
Diabetes	11.9 (0.4)	12.0 (0.8)	
Dyslipidemia	38.4 (0.6)	55.3 (1.5)	< 0.001
Cancer	2.0 (0.1)	1.5 (0.3)	0.17
Depression	2.5 (0.2)	2.4 (0.4)	0.89
Smoking			< 0.001
Non-smoker	61.2 (0.6)	42.9 (1.4)	
Ex-smoker	23.7 (0.5)	34.3 (1.2)	
Current smoker	15.1 (0.4)	22.9 (1.4)	
Alcohol drinking	43.5 (0.5)	57.4 (1.4)	< 0.001
Regular exercise	57.1 (0.6)	53.9 (1.3)	0.02
The number of dental caries			< 0.001
0	74.6 (0.7)	68.3 (1.5)	
1–2	18.8 (0.5)	23.0 (1.4)	
≥ 3	6.5 (0.3)	8.7 (0.8)	

https://doi.org/10.3904/kjim.2023.425

Table 1. Continued

Variable	No hyperuricemia (n =15,196/16,328,652)	Hyperuricemia (n = 2,361/2,742,640)	*p* value
The number of tooth brushing			< 0.001
≤ 1	8.7 (0.4)	12.2 (0.8)	
2	36.7 (0.6)	37.3 (1.4)	
≥ 3	54.6 (0.7)	50.4 (1.5)	
The use of secondary oral products	57.7 (0.6)	53.9 (1.4)	0.007
Regular dental examination	38.6 (0.6)	34.7 (1.4)	0.008

Values are presented as mean ± standard error or percentage (standard error).
The numbers of groups are expressed as unweighted and weighted numbers (unweighted n/weighted n).
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; GFR, glomerular filtration rate.

Statistical analysis

All statistical analyses were performed using a complex sample design in SPSS ver. 22.0 (IBM Corp., Armonk, NY, USA) and R 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria). The characteristics of the subjects were analyzed according to their uric acid levels. Continuous variables are presented as the means and standard deviations, and categorical variables are presented as the number of cases with percentages. Continuous variables are presented as the means with standard errors, and categorical variables are presented as the percentages with standard errors. Logistic regression analysis was performed, and odds ratios (ORs) with 95% confidence intervals (CIs) for hyperuricemia were calculated to investigate the association between oral health and hyperuricemia. The multivariable-adjusted logistic regression analysis was adjusted for age, sex, income level, BMI, GFR, hypertension status, diabetes status, dyslipidemia status, cancer status, depression status, smoking status, alcohol consumption status, and regular exercise status. A p value < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics of the study population

The baseline characteristics of the subjects according to their uric acid levels are presented in Table 1. There were significant differences between the groups with no hyperuricemia and those with hyperuricemia, except for the exercise variable. The mean uric acid levels in each group were 4.8 and 7.5 mg/dL, respectively. The hyperuricemia group included young males. In addition, compared to the no hyperuricemia group, the hyperuricemia group had higher BMI, SBP, DBP, total cholesterol, and triglyceride levels but lower HDL-C and GFR levels. Comorbidities, including hypertension, diabetes, and dyslipidemia, were more common in the hyperuricemia group. A greater number of dental caries and a lower number of tooth brushing were more common in the hyperuricemia group. The use of secondary oral products and regular dental examinations were more frequent in the no hyperuricemia group. The baseline characteristics of the subjects divided into male and female are presented in Supplementary Table 2 and 3.

Association between oral health and hyperuricemia

The associations between oral health and hyperuricemia are presented in Table 2. The multivariable-adjusted logistic regression analyses were performed. Oral health status with dental caries and oral health behaviors, including tooth brushing, the use of secondary oral products, and regular dental examination, were significantly associated with hyperuricemia in all the participants. The adjusted OR and 95% CIs for hyperuricemia comparing more than three dental caries with no dental caries were 1.28 (1.08–1.52). The adjusted OR and 95% CIs for hyperuricemia comparing more than three tooth brushing with under one tooth brushing were 0.78 (0.67–0.91). The adjusted ORs and 95% CIs for hyperuricemia associated with secondary oral products and regular dental examinations were 0.91 (0.83–1.00) and 0.86 (0.78–0.95), respectively. When the

Table 2. ORs with 95% CIs for the association between oral health and hyperuricemia

Variable	Hyperuricemia (uric acid > 7.0 mg/dL in male, > 6.0 mg/dL in female)					
	Crude OR	95% CI	*p* value	Adjusted OR[a)]	95% CI	*p* value
All subjects (n = 17,557/19,071,293)						
The number of dental caries						
0	1			1		
1–2	1.33	1.20–1.48	< 0.001	1.14	1.01–1.28	0.03
≥ 3	1.51	1.30–1.76	< 0.001	1.28	1.08–1.52	0.004
The number of tooth brushing						
≤ 1	1			1		
2	0.74	0.65–0.85	< 0.001	0.84	0.72–0.98	0.02
≥ 3	0.63	0.55–0.72	< 0.001	0.78	0.67–0.91	0.002
The use of secondary oral products						
No	1			1		
Yes	0.85	0.78–0.92	< 0.001	0.91	0.83–1.00	0.05
Regular dental examination						
No	1			1		
Yes	0.85	0.78–0.93	< 0.001	0.86	0.78–0.95	0.004
Male subjects (n = 7,817/8,925,336)						
The number of dental caries						
0	1			1		
1–2	1.18	1.04–1.35	0.01	1.10	0.96–1.27	0.17
≥ 3	1.29	1.07–1.55	0.006	1.28	1.04–1.56	0.02
The number of tooth brushing						
≤ 1	1			1		
2	1.03	0.87–1.22	0.74	0.86	0.71–1.03	0.09
≥ 3	1.03	0.88–1.21	0.71	0.81	0.67–0.97	0.02
The use of secondary oral products						
No	1			1		
Yes	1.15	1.03–1.28	0.02	0.99	0.88–1.11	0.84
Regular dental examination						
No	1			1		
Yes	0.92	0.82–1.03	0.16	0.87	0.77–0.98	0.03
Female subjects (n = 9,740/10,145,956)						
The number of dental caries						
0	1			1		
1–2	1.31	1.09–1.58	0.005	1.15	0.94–1.41	0.18
≥ 3	1.37	1.02–1.83	0.04	1.21	0.88–1.66	0.25
The number of tooth brushing						
≤ 1	1			1		
2	0.55	0.43–0.70	< 0.001	0.77	0.59–1.02	0.07
≥ 3	0.43	0.34–0.55	< 0.001	0.80	0.61–1.06	0.13

https://doi.org/10.3904/kjim.2023.425

Table 2. Continued

Variable	Hyperuricemia (uric acid > 7.0 mg/dL in male, > 6.0 mg/dL in female)					
	Crude OR	95% CI	*p* value	Adjusted OR[a)]	95% CI	*p* value
The use of secondary oral products						
No	1			1		
Yes	0.67	0.58–0.78	< 0.001	0.87	0.73–1.03	0.10
Regular dental examination						
No	1			1		
Yes	0.76	0.65–0.89	< 0.001	0.94	0.79–1.12	0.48

OR, odds ratio; CI, confidence interval.
[a)]Logistic model was adjusted for age, sex, income level, body mass index, glomerular filtration rate, hypertension, diabetes, dyslipidemia, cancer, depression, smoking, alcohol consumption, and exercise status.

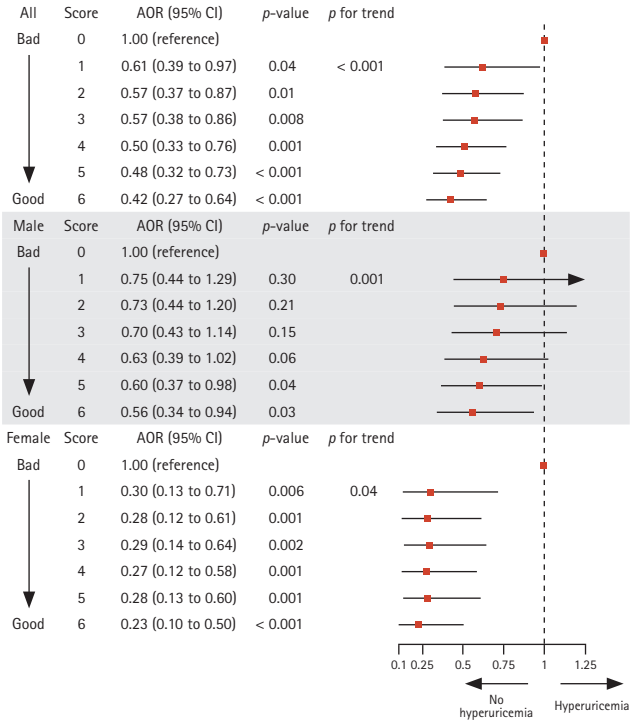


Figure 2. ORs with 95% CIs for the association between oral health score and hyperuricemia. AOR, adjusted odds ratio; CI, confidence interval.

study was expanded to include sex stratification, the male group exhibited a significant association with oral health and hyperuricemia. In addition, subgroup analysis according to pre- and post-menopausal women can be found in Supplementary Table 4. There was no consistent correlation between oral health and hyperuricemia depending on pre- and post-menopausal women.

Association between the oral health score and hyperuricemia

We calculated the oral health score using oral health status and behaviors. The association between the oral health score and hyperuricemia incidence is presented in Figure 2. There was a significant tendency between the oral health score and hyperuricemia regardless of the study population (*p* for trend < 0.05). Specifically, the adjusted OR and 95% CIs for hyperuricemia comparing score 6 with score 0 were 0.42 (0.27–0.64) for all subjects, 0.56 (0.34–0.94) for male subjects, and 0.23 (0.10–0.50) for female subjects. The subgroup analysis between pre- and post-menopausal women for the association between the oral health score and hyperuricemia incidence is described in Supplementary Table 5. When the female population was divided into pre- and post-menopausal states, the adjusted OR and 95% CIs for hyperuricemia comparing score 6 with score 0 were 0.20 (0.05–0.81) for premenopausal women and 0.28 (0.11–0.76) for postmenopausal women, respectively. In addition, the subgroup analysis based on age is described in Supplementary Table 6. When the study population was divided by age (over 65 yr), the adjusted OR and 95% CI for hyperuricemia comparing score 6 with score 0 were 0.55 (0.31–0.98) for those under 65 years of age and 0.40 (0.18–0.86) for those above 65 years of age.

DISCUSSION

This study investigated the association between oral hygiene and hyperuricemia using a large-scale, cross-sectional study with KNHANES data. The number of dental caries was asso-

ciated with hyperuricemia, and oral hygiene behaviors, such as regular tooth brushing, the use of secondary oral products, and regular dental examination, were also related to hyperuricemia in all subjects. Furthermore, we applied the oral health score by grading oral health-related variables and summing them together. As a result, a significant association between the oral health score and hyperuricemia was also confirmed. According to the sex-based subgroup analysis, a higher oral health score was associated with a lower incidence of hyperuricemia regardless of sex. In detail, a statistically significant relationship between higher oral health scores and a lower incidence of hyperuricemia was observed in the male subgroup. However, in the female group, only a small difference between oral health score groups 1~6 was observed, and the group with an oral health score of 0had a remarkably greater incidence of hyperuricemia. There were no significant differences in trend between the premenopausal and postmenopausal subgroup analyses. According to the age-based subgroup analysis, a similar correlation between the oral health score and hyperuricemia was maintained in both groups, but this correlation was statistically valid only in the elderly group (aged 65 to 80 yr).

Although several previous studies exist, the association between oral disease and hyperuricemia has remained controversial. Recently, Byun et al. [21] analyzed the relationship between periodontitis and hyperuricemia in a large population and reported that the two diseases were not significantly correlated. On the other hand, Banu et al. [22] reported that blood uric acid levels in patients with periodontitis were greater than those in normal subjects. The former study may have had data reliability issues because it used data acquired over an extended period (from 2004 to 2016). In the latter study, there may have been problems with including a limited number of patients as samples. In this study, we used data from the KNHANES 2016–2019 database with the same protocol within a relatively short period. We secured a sufficient number of subjects for statistical analysis, which could be a strength of this study.

Although a clear mechanism underlying the relationship between oral hygiene and hyperuricemia is unknown, several perspectives can be derived from previous studies. First, the change in the oral microbiota caused by poor oral hygiene can be mentioned, as the oral microbiota is known for its association with various diseases [23]. In a previous study, *Prevotella intermedia*, which is known as one of the causative bacteria of tooth decay and periodontitis, was found to be abundant in the oral microbiota of gout patients [24]. In addition, the color of the root of the tongue, which may be related to oral health and oral microbiota, is indicative of hyperuricemia [25]. Furthermore, it has been reported that abnormal findings of the oral microbiota are also associated with severe asthma, cardiovascular disease, diabetes, and rheumatoid arthritis [26-32]. Most importantly, Sheng et al. [33] recently reported that hyperuricemia is associated with changes in the gut microbiota. As the composition of the oral microbiota is known to affect the composition of the gut microbiota [34], poor oral hygiene may cause changes in the oral microbiota, which may explain the association between oral hygiene and hyperuricemia [35]. Second, oral disease itself is known to be associated with metabolic disorders. Consistent with the results of this study, a previous meta-analysis study also revealed an association between periodontitis and hypertension [36]. In addition, Kobayashi et al. [37] reported that oral hygiene is associated with metabolic syndrome. According to a recent randomized controlled trial, the risk of metabolic syndrome was lower in the group with oral hygiene intervention than in the group without intervention [38]. Taken together, these findings suggest that oral hygiene may be related to hyperuricemia and metabolic disorders.

This study has several limitations. First, the oral health-related variables did not include the presence of periodontitis, a common clinical manifestation of an individual's oral hygiene. However, in patients with periodontitis, dental examinations and radiological examinations are necessary. Furthermore, since the severity of periodontitis may vary from patient to patient, we quantitatively evaluated the patient's oral health status by counting the number of dental caries. Second, oral health status and behaviors were investigated using a self-report questionnaire. Third, there is a possibility that unadjusted covariates were not analyzed in this study. Fourth, as our categories of the oral health score comprise efforts to prevent oral diseases, there is a possibility that individuals in the low oral health score group have lower concerns about their health status, resulting in hyperuricemia. Finally, this cross-sectional study aimed to determine the association between oral hygiene and hyperuricemia but could not establish a cause-and-effect relationship. We expect that a future study will be able to identify the predecessor relationship between oral hygiene and hyperuricemia.

In conclusion, we demonstrated that oral health status and behaviors are associated with hyperuricemia, especial-

https://doi.org/10.3904/kjim.2023.425

ly in males. In addition, when subjects are grouped by the oral health scoring system, the prevalence of hyperuricemia is lower in groups with better oral health scores. Further complementary studies are needed to confirm a definitive association between oral health and hyperuricemia.

KEY MESSAGE

1. We demonstrated that oral health status and behaviors are associated with hyperuricemia, especially in males.
2. When subjects are grouped by the oral health scoring system, the prevalence of hyperuricemia is lower in groups with better oral health scores.

REFERENCES

1. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and coronary heart disease: a systematic review and meta-analysis. Arthritis Care Res (Hoboken) 2010;62:170-180.
2. Grayson PC, Kim SY, LaValley M, Choi HK. Hyperuricemia and incident hypertension: a systematic review and meta-analysis. Arthritis Care Res (Hoboken) 2011;63:102-110.
3. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and risk of stroke: a systematic review and meta-analysis. Arthritis Rheum 2009;61:885-892.
4. Carnethon MR, Fortmann SP, Palaniappan L, Duncan BB, Schmidt MI, Chambless LE. Risk factors for progression to incident hyperinsulinemia: the Atherosclerosis Risk in Communities Study, 1987-1998. Am J Epidemiol 2003;158:1058-1067.
5. Kim Y, Kang J, Kim GT. Prevalence of hyperuricemia and its associated factors in the general Korean population: an analysis of a population-based nationally representative sample. Clin Rheumatol 2018;37:2529-2538.
6. Krishnan E. Interaction of inflammation, hyperuricemia, and the prevalence of hypertension among adults free of metabolic syndrome: NHANES 2009-2010. J Am Heart Assoc 2014;3:e000157.
7. Park JS, Kang M, Song JS, Lim HS, Lee CH. Trends of gout prevalence in South Korea based on medical utilization: a National Health Insurance Service Database (2002~2015). J Rheum Dis 2020;27:174-181.
8. Loesche WJ. Association of the oral flora with important medical diseases. Curr Opin Periodontol 1997;4:21-28.
9. Yoneyama T, Yoshida M, Matsui T, Sasaki H. Oral care and pneumonia. Oral Care Working Group. Lancet 1999;354:515.
10. Park SY, Kim SH, Kang SH, et al. Improved oral hygiene care attenuates the cardiovascular risk of oral health disease: a population-based study from Korea. Eur Heart J 2019;40:1138-1145.
11. Jepsen S, Blanco J, Buchalla W, et al. Prevention and control of dental caries and periodontal diseases at individual and population level: consensus report of group 3 of joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases. J Clin Periodontol 2017;44 Suppl 18:S85-S93.
12. Korea Centers for Disease Control and Prevention. Korea National Health and Nutrition Examination Survey [Internet]. Osong: Korea Centers for Disease Control and Prevention, c2023 [cited 2023 Oct 8]. Available from: https://knhanes.kdca.go.kr/knhanes/eng/index.do.
13. Kweon S, Kim Y, Jang MJ, et al. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int J Epidemiol 2014;43:69-77.
14. Kragh Ekstam A, Andersson P. Oral health status using the revised oral assessment guide and mortality in older orthopaedic patients: a cross-sectional study. Clin Interv Aging 2023;18:1103-1113.
15. Busby M, Chapple L, Matthews R, Burke FJ, Chapple I. Continuing development of an oral health score for clinical audit. Br Dent J 2014;216:E20.
16. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461-470.
17. Bardin T, Richette P. Definition of hyperuricemia and gouty conditions. Curr Opin Rheumatol 2014;26:186-191.
18. Lee HY, Shin J, Kim GH, et al. 2018 Korean Society of Hypertension Guidelines for the management of hypertension: part II-diagnosis and treatment of hypertension. Clin Hypertens 2019;25:20.
19. Kim MK, Ko SH, Kim BY, et al. 2019 Clinical Practice Guidelines for type 2 diabetes mellitus in Korea. Diabetes Metab J 2019;43:398-406.
20. Rhee EJ, Kim HC, Kim JH, et al. 2018 Guidelines for the management of dyslipidemia. Korean J Intern Med 2019;34:723-771.
21. Byun SH, Yoo DM, Lee JW, Choi HG. Analyzing the association between hyperuricemia and periodontitis: a cross-sec-

tional study using KoGES HEXA data. Int J Environ Res Public Health 2020;17:4777.
22. Banu S, Jabir NR, Mohan R, et al. Correlation of Toll-like receptor 4, interleukin-18, transaminases, and uric acid in patients with chronic periodontitis and healthy adults. J Periodontol 2015;86:431-439.
23. Sampaio-Maia B, Caldas IM, Pereira ML, Pérez-Mongiovi D, Araujo R. The oral microbiome in health and its implication in oral and systemic diseases. Adv Appl Microbiol 2016;97:171-210.
24. Liu J, Cui L, Yan X, et al. Analysis of oral microbiota revealed high abundance of prevotella intermedia in gout patients. Cell Physiol Biochem 2018;49:1804-1812.
25. Cui Y, Liao S, Wang H, Liu H, Wang W, Yin L. Relationship between hyperuricemia and haar-like features on tongue images. Biomed Res Int 2015;2015:363216.
26. Lopes MP, Cruz ÁA, Xavier MT, et al. Prevotella intermedia and periodontitis are associated with severe asthma. J Periodontol 2020;91:46-54.
27. Jia G, Zhi A, Lai PFH, et al. The oral microbiota - a mechanistic role for systemic diseases. Br Dent J 2018;224:447-455.
28. Eberhard J, Stumpp N, Winkel A, et al. *Streptococcus mitis* and *Gemella haemolysans* were simultaneously found in atherosclerotic and oral plaques of elderly without periodontitis-a pilot study. Clin Oral Investig 2017;21:447-452.
29. Huck O, Saadi-Thiers K, Tenenbaum H, et al. Evaluating periodontal risk for patients at risk of or suffering from atherosclerosis: recent biological hypotheses and therapeutic consequences. Arch Cardiovasc Dis 2011;104:352-358.
30. Ebersole JL, Holt SC, Hansard R, Novak MJ. Microbiologic and immunologic characteristics of periodontal disease in Hispanic americans with type 2 diabetes. J Periodontol 2008;79:637-646.
31. Agbaje HO, Kolawole KA, Folayan MO, et al. Digit sucking, age, sex, and socioeconomic status as determinants of oral hygiene status and gingival health of children in suburban Nigeria. J Periodontol 2016;87:1047-1056.
32. Zhang X, Zhang D, Jia H, et al. The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment. Nat Med 2015;21:895-905.
33. Sheng S, Chen J, Zhang Y, et al. Structural and functional alterations of gut microbiota in males with hyperuricemia and high levels of liver enzymes. Front Med (Lausanne) 2021;8:779994.
34. Singhal S, Dian D, Keshavarzian A, Fogg L, Fields JZ, Farhadi A. The role of oral hygiene in inflammatory bowel disease. Dig Dis Sci 2011;56:170-175.
35. Barboza-Solís C, Acuña-Amador LA. The oral microbiota: a literature review for updating professionals in dentistry. Part I. Odovtos Int J Dent Sci 2020;22:59-68.
36. Muñoz Aguilera E, Suvan J, Buti J, et al. Periodontitis is associated with hypertension: a systematic review and meta-analysis. Cardiovasc Res 2020;116:28-39.
37. Kobayashi Y, Niu K, Guan L, et al. Oral health behavior and metabolic syndrome and its components in adults. J Dent Res 2012;91:479-484.
38. Doke M, Komagamine Y, Kanazawa M, et al. Effect of dental intervention on improvements in metabolic syndrome patients: a randomized controlled clinical trial. BMC Oral Health 2021;21:4.

Received : October 8, 2023
Revised : April 25, 2024
Accepted : June 10, 2024

Correspondence to
Sang Yeob Lee, M.D., PH.D.
Department of Rheumatology, Dong-A University College of Medicine, 32 Daesingongwon-ro, Seo-gu, Busan 49201, Korea
Tel: +82-51-240-5034, Fax: +82-51-240-5852
E-mail: happydragon22@naver.com
https://orcid.org/0000-0002-3180-6758

CRedit authorship contributions
Junyong Park: validation, writing - original draft, project administration, funding acquisition; Minkook Son: resources, investigation, formal analysis, visualization; Sung Won Lee: resources, validation, writing - review & editing, supervision; Won Tae Chung: software, writing - review & editing, visualization, supervision; Sang Yeob Lee: conceptualization, writing - review & editing, funding acquisition

Conflicts of interest
The authors disclose no conflicts.

Funding
This study was supported by the Dong-A University research fund.

Data availability
The data are available from the Korea National Health and Nutrition Examination Survey (KNHANES), which was performed by the Korea Centers for Disease Control and Prevention (KCDCP), and are freely available from the website (https://knhanes.kdca.go.kr/knhanes/eng/index.do).

https://doi.org/10.3904/kjim.2023.425

Supplementary Table 1. The schematic table for oral health score

Oral health-related variable	Score
The number of dental caries	
0	2
1–2	1
≥ 3	0
The number of tooth brushing	
≤ 1	0
2	1
≥ 3	2
The use of secondary oral products	
No	0
Yes	1
Regular dental examination	
No	0
Yes	1
Oral health score	
Total	6

Supplementary Table 2. Baseline characteristics of male subjects according to uric acid level

Variable	No hyperuricemia (n = 6,207/6,986,441)	Hyperuricemia (n = 1,610/1,938,895)	*p* value
Age (yr)	50.0 ± 0.4	44.0 ± 0.6	< 0.001
Income (quartile)			0.15
1st	23.3 (0.9)	25.4 (1.6)	
2nd	25.9 (0.8)	23.8 (1.5)	
3rd	25.4 (0.8)	27.5 (1.5)	
4th	25.4 (1.0)	23.2 (1.6)	
BMI (kg/m^2)	24.2 ± 0.1	26.0 ± 0.1	< 0.001
SBP (mmHg)	120.2 ± 0.3	121.7 ± 0.5	0.004
DBP (mmHg)	77.2 ± 0.2	79.8 ± 0.4	< 0.001
Uric acid (mg/dL)	5.5 ± 0.0	7.8 ± 0.0	< 0.001
Fasting blood glucose (mg/dL)	103.9 ± 0.5	100.6 ± 0.5	< 0.001
Total cholesterol (mg/dL)	189.0 ± 0.6	198.7 ± 1.3	< 0.001
Triglyceride (mg/dL)	145.6 ± 1.9	192.1 ± 5.0	< 0.001
HDL-C (mg/dL)	48.7 ± 0.2	45.9 ± 0.4	< 0.001
GFR (mL/min/1.73 m^2)	90.1 ± 0.3	84.9 ± 0.6	< 0.001
Hypertension			0.003
Normal	38.0 (0.9)	31.6 (1.7)	
Pre-hypertension	30.4 (0.7)	33.3 (1.7)	
Hypertension	31.6 (0.8)	35.2 (1.7)	
Diabetes			< 0.001
Normal	51.2 (1.0)	49.5 (1.7)	
Pre-diabetes	34.1 (0.9)	41.1 (1.5)	
Diabetes	14.7 (0.6)	9.4 (0.8)	
Dyslipidemia	44.7 (0.8)	55.7 (1.8)	< 0.001
Cancer	1.3 (0.1)	1.4 (0.4)	0.72
Depression	1.6 (0.2)	1.3 (0.4)	0.54
Smoking			0.99
Non-smoker	25.2 (0.9)	25.4 (1.5)	
Ex-smoker	44.9 (0.9)	44.9 (1.7)	
Current smoker	29.8 (0.8)	29.7 (1.8)	
Alcohol drinking	59.5 (0.9)	68.3 (1.6)	< 0.001
Regular exercise	53.7 (0.9)	49.6 (1.6)	0.02
The number of dental caries			0.07
0	70.3 (0.9)	66.0 (1.9)	
1–2	21.7 (0.7)	24.4 (1.7)	
≥ 3	8.0 (0.5)	9.6 (1.0)	
The number of tooth brushing			0.66
≤ 1	13.0 (0.6)	12.5 (1.0)	
2	39.2 (0.8)	38.1 (1.7)	
≥ 3	47.8 (0.9)	49.4 (1.7)	
The use of secondary oral products	51.2 (0.9)	52.9 (1.6)	0.35
Regular dental examination	37.4 (0.9)	35.5 (1.8)	0.32

Values are presented as mean ± standard error or percentage (standard error).
The numbers of groups are expressed as unweighted and weighted numbers (unweighted n/weighted n).
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; GFR, glomerular filtration rate.

https://doi.org/10.3904/kjim.2023.425

Supplementary Table 3. Baseline characteristics of female subjects according to uric acid level

Variable	No hyperuricemia (n = 8,989/9,342,211)	Hyperuricemia (n = 751/803,745)	*p* value
Age (yr)	50.0 ± 0.3	54.2 ± 0.9	< 0.001
Income (quartile)			0.72
1st	24.5 (0.7)	26.2 (1.9)	
2nd	24.6 (0.7)	23.0 (2.0)	
3rd	25.4 (0.7)	24.3 (2.0)	
4th	25.5 (0.9)	26.6 (2.5)	
BMI (kg/m^2)	23.2 ± 0.1	25.7 ± 0.2	< 0.001
SBP (mmHg)	116.5 ± 0.3	121.7 ± 0.9	< 0.001
DBP (mmHg)	73.9 ± 0.2	75.2 ± 0.5	0.01
Uric acid (mg/dL)	4.3 ± 0.0	6.7 ± 0.0	< 0.001
Fasting blood glucose (mg/dL)	98.0 ± 0.3	103.9 ± 0.9	< 0.001
Total cholesterol (mg/dL)	193.5 ± 0.4	197.8 ± 1.7	0.02
Triglyceride (mg/dL)	109.0 ± 1.0	157.9 ± 5.4	< 0.001
HDL-C (mg/dL)	56.0 ± 0.2	49.8 ± 0.7	< 0.001
GFR (mL/min/1.73 m^2)	94.3 ± 0.3	80.2 ± 1.2	< 0.001
Hypertension			< 0.001
Normal	52.8 (0.8)	34.0 (2.2)	
Pre-hypertension	21.3 (0.6)	20.9 (2.0)	
Hypertension	25.9 (0.7)	45.1 (2.3)	
Diabetes			< 0.001
Normal	63.1 (0.8)	40.9 (2.4)	
Pre-diabetes	27.2 (0.6)	40.7 (2.3)	
Diabetes	9.7 (0.4)	18.4 (1.6)	
Dyslipidemia	33.6 (0.7)	54.5 (2.4)	< 0.001
Cancer	2.6 (0.2)	1.6 (0.5)	0.13
Depression	3.2 (0.2)	5.3 (1.0)	0.02
Smoking			0.03
Non-smoker	88.1 (0.5)	84.9 (1.5)	
Ex-smoker	7.8 (0.4)	8.7 (1.2)	
Current smoker	4.1 (0.3)	6.4 (1.2)	
Alcohol drinking	31.6 (0.7)	31.2 (2.5)	0.89
Regular exercise	59.7 (0.7)	64.1 (2.0)	0.04
The number of dental caries			0.15
0	77.9 (0.8)	73.8 (2.3)	
1–2	16.7 (0.6)	19.7 (2.0)	
≥ 3	5.4 (0.4)	6.5 (1.2)	
The number of tooth brushing			< 0.001
≤ 1	5.5 (0.3)	11.5 (1.4)	
2	34.8 (0.7)	35.4 (2.3)	
≥ 3	59.7 (0.8)	53.0 (2.5)	
The use of secondary oral products	62.5 (0.7)	56.3 (2.4)	0.008
Regular dental examination	39.5 (0.7)	32.9 (2.3)	0.007

Values are presented as mean ± standard error or percentage (standard error).
The numbers of groups are expressed as unweighted and weighted numbers (unweighted n/weighted n).
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; GFR, glomerular filtration rate.

Supplementary Table 4. Additional analysis between pre- and post-menopausal women for the association between oral health score and hyperuricemia

Variable	Hyperuricemia (uric acid > 7.0 mg/dL in male, > 6.0 mg/dL in female)					
	Crude OR	95% CI	*p* value	Adjusted OR[a)]	95% CI	*p* value
Pre-menopausal women subjects (n = 4,930/5,581,335)						
The number of dental caries						
0	1			1		
1–2	1.36	1.02–1.82	0.005	1.07	0.78–1.46	0.68
≥ 3	1.87	1.26–2.77	0.04	1.19	0.77–1.85	0.44
The number of tooth brushing						
≤ 1	1			1		
2	0.45	0.27–0.72	< 0.001	0.52	0.30–0.89	0.02
≥ 3	0.47	0.30–0.75	< 0.001	0.68	0.41–1.16	0.16
The use of secondary oral products						
No	1			1		
Yes	0.87	0.68–1.12	0.27	1.02	0.78–1.34	0.88
Regular dental examination						
No	1			1		
Yes	0.85	0.67–1.09	0.20	0.97	0.75–1.27	0.85
Post-menopausal women subjects (n = 4,810/4,564,621)						
The number of dental caries						
0	1			1		
1–2	1.33	1.04–1.70	0.02	1.22	0.93–1.59	0.18
≥ 3	1.08	0.69–1.69	0.73	1.03	0.63–1.67	0.15
The number of tooth brushing						
≤ 1	1			1		
2	0.64	0.48–0.86	0.003	0.94	0.68–1.31	0.32
≥ 3	0.46	0.35–0.62	< 0.001	0.89	0.63–1.26	0.71
The use of secondary oral products						
No	1			1		
Yes	0.64	0.53–0.78	< 0.001	0.86	0.69–1.08	0.20
Regular dental examination						
No	1			1		
Yes	0.75	0.60–0.92	0.007	1.02	0.81–1.30	0.85

OR, odds ratio; CI, confidence interval.

[a)]Logistic model was adjusted for age, sex, income level, body mass index, glomerular filtration rate, hypertension, diabetes, dyslipidemia, cancer, depression, smoking, alcohol consumption, and exercise status.

https://doi.org/10.3904/kjim.2023.425

Suuplementary Table 5. Subgroup analysis between pre- and post-menopausal women for the association between oral health score and hyperuricemia

Variable	Hyperuricemia (> 6.0 mg/dL in female)					
	Crude OR	95% CI	*p* value	Adjusted OR[a)]	95% CI	*p* value
Pre-menopausal women subjects (n = 4,930/5,581,335)						
Oral health score						
0	1			1		
1	0.36	0.10–1.36	0.13	0.21	0.05–1.01	0.05
2	0.22	0.07–0.73	0.01	0.16	0.04–0.69	0.01
3	0.22	0.07–0.71	0.01	0.21	0.05–0.83	0.02
4	0.21	0.07–0.65	0.007	0.22	0.06–0.88	0.03
5	0.17	0.05–0.54	0.003	0.20	0.05–0.81	0.02
6	0.15	0.05–0.48	0.001	0.20	0.05–0.81	0.02
p for trend			0.001			0.80
Post-menopausal women subjects (n = 4,810/4,564,621)						
Oral health score						
0	1			1		
1	0.48	0.19–1.22	0.12	0.36	0.12–1.01	0.05
2	0.37	0.16–0.88	0.01	0.37	0.14–0.98	0.04
3	0.36	0.16–0.83	0.02	0.39	0.15–0.98	0.04
4	0.27	0.12–0.62	0.02	0.33	0.13–0.85	0.02
5	0.25	0.11–0.58	0.002	0.40	0.15–1.02	0.06
6	0.16	0.06–0.37	0.001	0.28	0.11–0.76	0.01
p for trend			< 0.001			0.23

OR, odds ratio; CI, confidence interval.

[a)]Logistic model was adjusted for age, sex, income level, body mass index, glomerular filtration rate, hypertension, diabetes, dyslipidemia, cancer, depression, smoking, alcohol consumption, and exercise status.

Supplementary Table 6. Subgroup analysis based on age (65 years) for the association between oral health score and hyperuricemia

Variable	Hyperuricemia (uric acid > 7.0 mg/dL in male, > 6.0 mg/dL in female)					
	Crude OR	95% CI	*p* value	Adjusted OR[a)]	95% CI	*p* value
Age, < 65 yr (n = 13,055/15,670,683)						
Oral health score						
0	1			1		
1	0.70	0.40–1.21	0.21	0.71	0.38–1.30	0.27
2	0.58	0.35–0.96	0.04	0.66	0.37–1.16	0.15
3	0.52	0.31–0.85	0.01	0.65	0.37–1.14	0.14
4	0.48	0.29–0.79	0.003	0.66	0.38–1.15	0.15
5	0.42	0.26–0.69	< 0.001	0.67	0.38–1.17	0.16
6	0.31	0.19–0.51	< 0.001	0.55	0.31–0.98	0.04
p for trend			< 0.001			0.12
Age 65–80 yr (n = 3,749/3,400,610)[b)]						
Oral health score						
0	1			1		
1	0.52	0.25–1.09	0.08	0.35	0.15–0.79	0.01
2	0.43	0.22–0.83	0.01	0.36	0.17–0.74	0.006
3	0.54	0.29–1.01	0.05	0.44	0.22–0.89	0.02
4	0.33	0.17–0.62	< 0.001	0.31	0.15–0.63	0.001
5	0.29	0.15–0.57	< 0.001	0.27	0.13–0.57	< 0.001
6	0.40	0.20–0.81	< 0.001	0.40	0.18–0.86	0.02
p for trend			< 0.001			0.03

OR, odds ratio; CI, confidence interval.

[a)]Logistic model was adjusted for age, sex, income level, body mass index, glomerular filtration rate, hypertension, diabetes, dyslipidemia, cancer, depression, smoking, alcohol consumption, and exercise status.

[b)]In the subgroup analysis based on age, subjects over 80 years were excluded because their age was coded as 80 for deidentification.

https://doi.org/10.3904/kjim.2023.425