Associations between the number of natural teeth and renal dysfunction

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Abstract
The purpose of the present study was to investigate the association between the number of natural teeth and measures of kidney dysfunction, such as urinary albumin/creatinine ratio (ACR) and estimated glomerular filtration (eGFR) rate, using nationally representative data.

The data used were from the Korea National Health and Nutrition Examination Survey with cross-sectional design, which was conducted between 2011 and 2012; the sample analyzed in this study consisted of a total of 10,388 respondents, each of whom was 19 years or older and had no missing outcome variables. The association between the number of natural teeth and kidney function was assessed by multiple logistic regression and model was adjusted for age, sex, waist circumference, smoking, drinking, exercise, education, income, frequency of tooth brushing per day, diabetes, metabolic syndrome, urinary ACR, and eGFR.

The mean age, body mass index, and waist circumference were significantly higher among those with lower kidney function (urinary ACR ≥30 mg/g and eGFR <60 mL/min/1.73m²). Urinary ACR and eGFR were associated with loss of natural teeth. As urinary ACR increased, the number of natural teeth decreased accordingly. Conversely, the number of teeth increased with an increase in eGFR.

This study showed that the number of natural teeth is inversely associated with the presence of kidney disease. Severity of tooth loss may be considered an independent risk indicator for kidney disease among Koreans. More epidemiological studies are warranted to investigate the role of tooth loss in kidney disease, to confirm this relationship and to test possible underlying mechanisms.

Abbreviations: ACR = albumin/creatinine ratio, eGFR = estimated glomerular filtration, KNHANES = Korean National Health and Nutrition Examination Survey.

Keywords: albuminuria, dentition, epidemiology, glomerular filtration rate, kidney diseases, oral health, tooth loss

1. Introduction
Observational studies have shown an association between poor oral health and systemic diseases.1,2 Periodontitis and pulp necrosis are important sources of systemic microinflammation in chronic kidney disease patients.3-5 It was suggested that periodontal disease is associated with increased risk of cardiovascular disease.1,2,4 In the previous study, severe periodontitis was associated with compromised glycemic control and periodontal treatment was associated with improvements in glycemic control in diabetic patients.5

Chronic kidney diseases were shown to affect the oral health status of patients by inducing xerostomia, delayed eruption of teeth, calcification of root canals, and gingival hyperplasia.6,7 The incidence of periodontal disease (bleeding and calculus) was significantly higher among people with renal disease than among controls.7,8 Recently, it was reported that periodontitis was associated with increased prevalence of inflammatory markers in end-stage renal disease patients.9 Recent epidemiological studies have suggested that periodontitis is a major risk factor for renal failure.9,10 Within the authors’ knowledge, there is no known report to evaluate the association between the number of natural teeth and eGFR with nationally representative data. Thus, this study was performed to investigate the association between the number of natural teeth and both urinary ACR and eGFR using nationally representative data.

2. Methods
2.1. The design of the study
The data from the Korea National Health and Nutrition Examination Survey (KNHANES), which was performed between 2011 and 2012, were used for the study. KNHANES is conducted to evaluate the health and nutritional status for the Korean people and KNHANES is an ongoing surveillance system in the Republic of Korea that assesses the health and nutritional status of Koreans, monitors trends in health risk factors and the
prevalence of major chronic diseases, and provides data for the development and evaluation of health policies and programs in Korea. The KNHANES uses a stratified and multistage probability-sampling design with a rolling survey-sampling model. The sample weights were used to calculate all the statistics in this survey. A total of 16,576 patients initially participated in the survey. The analysis in this study was confined to a total of 10,388 respondents who were 19 years or older and who had no missing values for the outcome variables (Fig. 1). This survey was reviewed and approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention.

2.2. Evaluation of kidney function

The level of kidney function is usually determined by urinary albumin/creatinine ratio (ACR) and by estimated glomerular filtration rate (eGFR). In this study, urinary ACR and eGFR were used for the categorization and evaluation of the presence of kidney diseases. When urinary ACR was 30 mg/g or greater, the patient was considered to have albuminuria. The level of kidney function was also determined by eGFR using an abbreviated equation: eGFR (mL/min/1.73 m²) = 186.3 × (serum creatinine)⁻¹.ₐ.₁₄ × (age)⁻₀.₂₀₃; this result was then multiplied by the constant 0.742 if the patient was female. The equation was developed from the Modification of Diet in Renal Disease (MDRD) formula. Participants with eGFR < 60 mL/min/1.73 m² were considered to have kidney disease. For this study, chronic kidney disease was ascertained if a patient’s eGFR was < 60 mL/min/1.73 m². The KNHANES 2011-2012 adult participants (n=16,576)

Excluded (n=6,188)
Participants younger than 19 (n=3,987)
Missing values (n=2,201)
Final sample (n=10,388)

Figure 1. Participant flow chart.

2.3. Anthropometric measurements

Trained staff members performed anthropometric measurements. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively. The participants wore light indoor clothing without shoes during the anthropometric measurements. Waist circumference was measured at the narrowest point between the iliac crest and the lower border of the rib cage. Body mass was divided by height squared to calculate body mass index.

2.4. Sociodemographic variables

Sociodemographic variables were obtained by the trained interviewers. The self-report questionnaire was used for the smoking status: current smoker or not. Participants were also categorized into 2 groups by the number of drinking episodes (0 vs. 1 or more in the 1-month period before the interview).

Participants were regarded as regular physical exercisers if the participants performed vigorous exercise at least 3 times per week for at least 20 minutes per session or moderate exercise at least 5 times per week for at least 30 minutes per session. If the monthly house income was <$1092.40, it was considered the lowest quartile. The participants were categorized by those with at least a high school degree and those with less education. Sleep duration and stress recognition were self-reported. Daily energy, fat, protein, and calcium intake were calculated based on the survey.

2.5. Biochemical measurements

Blood pressure measurements were performed using a standard mercury sphygmomanometer (Baumanometer; W.A. Baum Co, Inc, Copiague, NY). Systolic and diastolic blood pressures were measured 2 times at intervals of 5 minutes, and the analysis used the average values.

A blood sample was collected from each participant’s antecubital vein after the individual had fasted for >8 hours to measure concentrations of serum-fasting plasma glucose, glycated hemoglobin (HbA1c), total, low-density lipoprotein, high-density lipoprotein cholesterol, triglycerides; white blood cell count, and serum 25-hydroxyvitamin D. The blood samples were analyzed within 24 hours of transportation. Levels of serum-fasting plasma glucose, HbA1c, cholesterol, and triglycerides were measured with the analyzer (Hitachi Automatic Analyzer 7600, Hitachi, Tokyo, Japan) using enzymatic methods and commercially available kits (Daiichi, Tokyo, Japan). A gamma counter (1470 Wizard; PerkinElmer, Wallac, Turku, Finland) and a 25-hydroxyvitamin D125I radioimmunoassay kit (DiaSorin, Stillwater, MN, USA) were utilized to measure serum 25-hydroxyvitamin D levels.

2.6. Description of hypertension, diabetes and metabolic syndrome

If participant had a systolic blood pressure of >160 mmHg, a diastolic blood pressure of >90 mmHg, or currently used systemic antihypertensive drugs, the individuals were considered having hypertension. Diabetes was diagnosed when fasting blood sugar was >126 mg/dL or when the individual was currently using antidiabetic medications. Metabolic syndrome was defined according to the criteria for Asians in the American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Three or more of the following criteria must be met to be diagnosed with metabolic syndrome: waist circumference of at least 90 cm in men or 80 cm in women; fasting triglycerides of at least 150 mg/dL (or use of lipid-lowering medication); high-density lipoprotein cholesterol of <40 mg/dL in men or 50 mg/dL in women (or use of medication); blood pressure of at least 130 mmHg systolic blood pressure and 85 mmHg diastolic pressure (or use of antihypertensive medication); and fasting blood glucose of at least 100 mg/dL (or use of antidiabetic medication).

2.7. Oral health behaviors

The time of day of patients’ tooth brushing was noted as part of their oral health behavior and the frequency of daily tooth brushing was calculated from the oral health behavior.
### Table 1
Baseline characteristics of study individuals according to kidney disease, as categorized by urinary ACR and eGFR.

|                           | <30 | ≥30 | P'   | ≥60 | <60 | P'   |
|---------------------------|-----|-----|------|-----|-----|------|
| Unweighted, n             | 9528| 860 | <0.0001 | 10,053 | 335 | <0.0001 |
| Age, y                    | 45.4±0.3 | 58.1±0.8 | <0.0001 | 45.4±0.3 | 69.4±0.8 | <0.0001 |
| Sex (male)                | 53.1(0.5) | 44.7(2.0) | <0.0001 | 52.6(0.5) | 49.8(3.3) | 0.4055 |
| Height, m                 | 164.7±0.1 | 160.0±0.4 | <0.0001 | 164.5±0.1 | 158.3±0.6 | <0.0001 |
| Weight, kg                | 64.6±0.2 | 64.4±0.6 | 0.7809 | 64.7±0.2 | 62.1±0.8 | 0.0011 |
| Body mass index, kg/m²    | 23.7±0.1 | 25±0.2 | <0.0001 | 23.8±0.1 | 24.7±0.2 | <0.0001 |
| Waist circumference, cm   | 81.2±0.2 | 85.9±0.5 | <0.0001 | 81.4±0.2 | 85.4±0.6 | <0.0001 |
| White blood cell count (×10³ cells/µL) | 5.86 (5.61–5.92) | 6.17 (6.02–6.31) | <0.0001 | 5.87 (5.62–5.92) | 6.38 (6.16–6.6) | <0.0001 |
| Energy intake, kcal/day   | 2071.0±16.4 | 1826.3±39.2 | <0.0001 | 2066±16.4 | 1547±43.2 | 0.0001 |
| Fat intake, g/day         | 18.9±0.2 | 14.7±0.4 | <0.0001 | 18.7±0.2 | 12.2±0.4 | <0.0001 |
| Protein intake, g/day     | 14.8±0.1 | 13.8±0.2 | <0.0001 | 14.8±0.1 | 12.6±0.2 | <0.0001 |
| Calcium intake, mg/day    | 517.3±5.5 | 460.4±15.9 | 0.0004 | 516.7±5.5 | 369.4±19.3 | <0.0001 |
| Systolic blood pressure   | 117.1±0.2 | 131±9.9 | <0.0001 | 117.8±0.3 | 129.3±1.5 | <0.0001 |
| Diastolic blood pressure  | 76±0.2 | 79.3±0.6 | <0.0001 | 76.3±0.2 | 73.9±1.0 | 0.015 |
| Glucose                   | 95.5±0.3 | 112.4±1.6 | <0.0001 | 96.7±0.3 | 109.1±2.2 | <0.0001 |
| Hemoglobin (HbA1c)        | 5.7±0.01 | 6.3±0.1 | <0.0001 | 5.7±0.01 | 6.3±0.1 | <0.0001 |
| Serum 25-hydroxyvitamin D | 17.1±0.1 | 17.5±0.3 | 0.1637 | 17.1±0.1 | 18.6±0.5 | 0.0008 |
| Cholesterol               | 189.1±0.5 | 195±1.5 | 0.0002 | 189.6±0.5 | 184.4±2.9 | 0.0784 |
| Low-density lipoprotein   | 111.1±0.4 | 112.5±1.4 | 0.3559 | 111.3±0.4 | 107.3±2.5 | 0.115 |
| High-density lipoprotein  | 52.4±0.2 | 50.2±0.5 | <0.0001 | 52.4±0.2 | 46.1±0.9 | <0.0001 |
| Triglyceride              | 109.3 (107.6–111.1) | 139.1 (131.9–146.7) | <0.0001 | 110.7 (108.9–112.5) | 131.1 (121.6–141.2) | <0.0001 |
| Smoking (current)         | 24.9±0 (06) | 19.6±1.9 | 0.0135 | 24.8±0.6 | 14.4±2.8 | 0.0032 |
| Alcohol within 1 month    | 59.4±0.7 | 49.9±2.4 | <0.0001 | 59.3±0.7 | 34.1±6.4 | <0.0001 |
| Exercise (yes)            | 18.9±0.6 | 18±1.7 | 0.6140 | 19±0.5 | 11.3±2.2 | 0.0044 |
| Income (lowest quartile)  | 14±0.6 | 30.9±2 | <0.0001 | 14.6±0.6 | 42.3±0.3 | <0.0001 |
| Education (high-school graduate or higher) | 72.9±0.7 | 46.3±2.4 | <0.0001 | 72±0.8 | 32.4±3.4 | <0.0001 |
| Hour of sleep             | 7.6±0.2 | 8.0±0.5 | 0.4526 | 7.7±0.2 | 7.6±0.7 | 0.9701 |
| Stress                    | 27.3±0.8 | 20.6±1.7 | 0.0005 | 27±0.8 | 17.3±2.9 | 0.0007 |
| Hypertension              | 24.4±0.6 | 64.8±2.4 | <0.0001 | 26±0.7 | 76.9±2.7 | <0.0001 |
| Diabetes                  | 7.2±0.3 | 30.5±2.1 | <0.0001 | 8.2±0.4 | 36.4±5.7 | <0.0001 |
| Metabolic syndrome        | 24.7±0.6 | 58.6±2.3 | <0.0001 | 26.2±0.6 | 64.6±3.3 | <0.0001 |
| Frequency of tooth brushing per day | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

Data are presented as mean±standard error or percentage (standard error). ACR=albumin/creatinine ratio, eGFR=estimated glomerular filtration rate

P' values were obtained using an independent t test for continuous variables or a χ² test for categorical variables.

A log transformation was applied to the value, and the geometric mean (95% confidence interval) is shown.

Geometric mean (95% confidence interval).

The survey also recorded patients’ secondary oral product use, return dental checkup timing (e.g., within a year), and self-reported oral status.

In this study, the natural tooth was considered to be present if the permanent tooth was present or primary tooth was present. The total number of natural teeth was calculated from the examination. Training was provided to each examiner to minimize measurement errors during the examination as part of quality control.

#### 2.8 Statistical analyses

The data were presented as mean±standard error or as a percent (standard error). To achieve normal distribution, a logarithmic transformation was performed when necessary. Either Student t test or a χ² test was used to investigate the differences as categorized by urinary ACR or eGFR. The association between the number of natural teeth and kidney function was assessed by multiple logistic regression. Model 1 was adjusted for age, sex, and waist conference. Model 2 was adjusted for the same variables as Model 1 plus smoking, drinking, exercise, education, income, and frequency of tooth brushing per day. Model 3 was adjusted for the variables in Model 2 plus diabetes, metabolic syndrome, urinary ACR, and eGFR. The survey procedure of a statistical program (SAS version 9.2 for Windows, SAS Institute, Cary, NC) was used for statistical analysis to account for the complex sampling design. Two-sided P values of 0.05 were used for the statistical significance.

### Results

Table 1 describes baseline characteristics of the study individuals according to kidney function, as categorized by urinary ACR and eGFR. Number of natural teeth was significantly lower among...
those with lower kidney function (urinary ACR ≥ 30 mg/g and eGFR < 60 mL/min/1.73 m²). The mean age, body mass index, and waist circumference were significantly higher among those with lower kidney function. Systolic and diastolic blood pressure, glucose, HbA1c, and triglycerides were also statistically higher among those with kidney disease. High-density lipoprotein levels were significantly lower among those with kidney disease.

The percentage of individuals in the lowest-income quartile was higher among those with lower kidney function. The percentage of patients with at least a high school degree was lower among those with kidney disease. The prevalence of hypertension, diabetes, and metabolic syndrome was significantly higher among those with kidney disease. The subgroup analysis (categorized by number natural teeth for urinary ACR ≥ 30 mg/g and eGFR < 60 mL/min/1.73 m²) is shown in Table 2. The number of natural teeth was lower among the participants with body mass index of ≥ 25 (P < 0.01). Similarly, the number of natural teeth was lower among the participants with hypertension, diabetes, or metabolic syndrome (P < 0.01).

Figure 2 shows the percentage and standard error for the participants, categorized by number of natural teeth and kidney status. As urinary ACR increased, the number of natural teeth decreased; conversely, the number of natural teeth increased as eGFR increased.

Table 3 shows the adjusted odds ratios and their 95% confidence intervals from the multiple logistic regression analyses for the individuals with kidney diseases (categorized by urinary ACR ≥ 30 mg/g or eGFR < 60 mL/min/1.73 m²) according to the number of natural teeth. The odds ratios increased in the individuals with urinary ACR ≥ 30 mg/g. The adjusted odds ratios (with 95% confidence intervals) among participants with urinary ACR ≥ 30 mg/g were 1 [reference] for individuals with 28 natural teeth, 1.298 (0.989–1.703) for those with 20 to 27 teeth, and 1.758 (1.302–2.375) among those with ≤ 19 teeth. The adjusted odds ratios (with 95% confidence intervals) for participants with eGFR < 60 mL/min/1.73 m² were 1 [reference] for individuals with 28 natural teeth, 1.329 (0.691–2.557) for those with 20 to 27 teeth, and 1.287 (0.659–2.513) for those with ≤ 19 teeth.

**Table 2**
Subgroup analysis for each group in percentage (standard error).

| The number of natural teeth | Urinary ACR ≥ 30 | eGFR < 60 |
|-----------------------------|------------------|----------|
| Age, y                      | 19–64            | 65+      |
| Sex                         | Male             | Female   |
| Body mass index             | < 25             | ≥ 25     |
| Waist circumference         | Male: < 90 cm, Female: < 80 cm | Male: ≥ 90 cm, Female: ≥ 80 cm |
| Hypertension                | No               | Yes      |
| Diabetes                    | No               | Yes      |
| Metabolic syndrome          | No               | Yes      |

ACR = albumin/creatinine ratio, eGFR = estimated glomerular filtration rate.
The lack of standardization of commercially available accurate GFR estimates in patients with chronic kidney disease showed that the MDRD equation provided reasonably accurate GFR estimates. Another study suggested that the MDRD equation was considered to be problematic, and another study suggested that the MDRD equation was considered to be problematic. However, these studies did not address the role of tooth loss in participants with renal disease.

This study clearly showed that both urinary ACR and eGFR were associated with loss of natural teeth. The urine albumin test is used to evaluate kidney function and to screen people with chronic conditions, such as hypertension and diabetes, which put patients at an increased risk of kidney disease. Albumin is a protein that is present in high concentrations in the blood; it is not usually detected in the urine when the kidneys are functioning properly. Creatinine is a byproduct of muscle metabolism; its level in the urine is usually considered an indication of the urine concentration because it is normally released into the urine at a constant rate. Albuminuria has been shown to be related to periodontal disease. A previous report showed that decreased kidney function (characterized by low eGFR) may be associated with the presence of kidney disease. Another previous report showed that decreased kidney function (characterized by low eGFR) may be associated with the presence of kidney disease. The most important strength of this study is that it is based on a nationally representative sample of Koreans. KNHANES is a nationwide survey of noninstitutionalized civilians; it uses sample participants and sample weights to represent the Korean population and considers survey nonresponse, complex survey design, and poststratification. However, some limitations should be considered regarding this study, as it used a cross-sectional design, which makes it difficult to determine whether there is a direct relationship between the exposure and the outcome. Another limitation of this study is that individuals’ energy intake and oral health behavior were obtained self-reported and were under recall bias. Data regarding the inflammatory markers (such as C-reactive protein, tumor necrosis factor-α, and interleukin-6) were not available, so the study’s explanation of inflammation and kidney disease is limited.

This study showed that the number of natural teeth is inversely associated with the presence of kidney disease. Among those with reduced kidney function (eGFR <60 mL/min/1.73 m²), the adjusted odds ratios for the group with 28 natural teeth were lower than the ratios for those with fewer natural teeth. Tooth loss may be considered an independent risk indicator for kidney disease in Korean people. More epidemiological studies are warranted to investigate the role of tooth loss in participants with kidney disease, to confirm this relationship, and to test possible underlying mechanisms.

### 4. Discussion

This study clearly showed that the odd ratios for having fewer natural teeth tended to increase among the participants with lower kidney function (urinary ACR ≥30 mg/g and eGFR <60 mL/min/1.73 m²).

Kidney function may be determined using various methods. ACR = albumin/creatinine ratio, GFR = estimated glomerular filtration rate. Model 1: adjusted for age, sex, and waist circumference. Model 2: Model 1 adjustments plus smoking, drinking, exercise, education, income, and frequency of tooth brushing per day.

| Number of natural teeth | Model 1 | Model 2 | Model 3 |
|------------------------|---------|---------|---------|
|                       | eGFR <60 |         |         |
| 28                     | 1       | 1       | 1       |
| 20–27                  | 1.130   | 1.238   | 1.329   |
|                        | (0.643–1.989) | (0.675–2.271) | (0.691–2.557) |
| ≤19                    | 1.205   | 1.303   | 1.287   |
|                        | (0.681–2.132) | (0.686–2.476) | (0.659–2.513) |

P for trend

0.5046

0.4406

0.5747

**Table 3** Adjusted odds ratios, 95% confidence intervals, and P values in multivariate logistic regression models based on number of natural teeth and kidney status in mean (95% confidence interval).

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