Original Article

Dietary and nutritional factors associated with hyperuricemia: The seventh Korean National Health and Nutrition Examination Survey

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Background and Objectives: The association of dietary and nutritional factors with hyperuricemia and gout is well-known in Western populations. The present study aimed to examine the association of dietary and nutritional factors with hyperuricemia among Korean adults. **Methods and Study Design:** This cross-sectional study included 10,175 participants from the seventh Korean National Health and Nutrition Examination Survey 2016-2017. Dietary information was collected using a single 24-hour recall method, and nutritional information was derived from the 9th Korean Food Composition Table. The associations between serum uric acid and intake of meat, seafoods, nuts, and legumes, sugar-sweetened products, dairy products, alcohol, sodium, vitamin A, vitamin B1, vitamin C, and dietary fiber were analyzed using linear regression analysis adjusting for confounding variables. The association with hyperuricemia was analyzed using logistic regression analysis. All analyses were weighted by the sampling design. **Results:** Alcohol intake was associated with serum uric acid in both men and women. In men, the highest quartile of alcohol intake was associated with a 1.5-times higher prevalence of hyperuricemia (odds ratio [OR] 1.5, 95% confidence interval [CI] 1.16–1.95), while vitamin C and dietary fiber intakes were found to be inversely associated with hyperuricemia. For vitamin C and dietary fiber intake, the ORs for a quartile increase were 0.93 (95% CI 0.86–0.99) and 0.92 (95% CI 0.85–0.99), respectively. **Conclusions:** The associations between vitamin C, dietary fiber and alcohol intakes and hyperuricemia in men support the Dietary Approach to Stop Hypertension (DASH)-based approach and attention to alcohol intake for managing hyperuricemia in Korean men.

Key Words: hyperuricemia, gout, dietary fiber, vitamin C, alcohol, hypertension

INTRODUCTION

Gout is the most common form of inflammatory arthritis,[1-3] which is caused by high serum levels of the end-product of purine metabolism in humans, uric acid. Gout is a curable disease, which can be treated by lowering serum uric acid (SUA) below the saturation point, resulting in the dissolution of monosodium urate crystals in tissues.[4] Gout is associated with metabolic risk factors such as hypertension and diabetes, and their corresponding morbidity and mortality.[5-10] Evidence for the clinical benefits of urate-lowering therapy is weaker compared with evidence for the benefits in gouty arthritis.[11]

It is believed that diet has little influence on SUA, although dietary intake is the sole source of purines in human. Dietary modification has been shown to be able to reduce SUA by only 10%–18%; therefore, dietary modification alone is ineffective for achieving SUA targets in patients with gout and hyperuricemia of persistently higher than 7 mg/dL (0.42 mmol/L, in order to convert to mmol/L multiply by 0.0595).[12] Although diet can also have beneficial effects on gout flares independent of the influence on SUA, most patients with gout require medical therapy to prevent gout flares.[4]

Lifestyle modification, including dietary changes, should be considered as part of a holistic approach for treating the metabolic diseases and their sequelae which are highly prevalent in gout, such as hypertension. Studies have shown that the Dietary Approach to Stop Hypertension (DASH) diet can lower and is associated with a lower risk of incident gout SUA.[13,14] Although confirmation through interventional trials is required, it is likely that diet

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modification based on the DASH pattern diet may contribute to the prevention of cardiovascular disease and morality in patients with gout, as well as preventing gout flares.

Numerous studies have focused on food items and nutrients associated with hyperuricemia and gout,[15] but most have included Western subjects. There have been fewer studies on Asian patients,[16-18] whose dietary pattern is characterized by high carbohydrates and high sodium intake. The influence of food items or nutrients on SUA may be dependent on the dietary pattern in which they are consumed. Therefore, we investigated the association of food groups and nutrients with hyperuricemia in Korean adults.

METHODS

Study design and participants

This study was a cross-sectional study that analyzed data obtained from participants of the seventh Korean National Health and Nutrition Examination Survey (KNHANES) conducted from January 2016 to December 2017. The KNHANES is a South Korean nationwide health and nutrition survey of children, adolescents, and adults, for which participants were selected by systematic sampling. Overall participation rates were 75.4% in 2016 and 77.9% in 2017. In the seventh KNHANES, blood tests including SUA were indicated for participants older than 10 years old. Exclusion criteria for the blood tests were hemophilia, anticoagulation therapy, chemotherapy in a month, poor vascular access, and age of 80 years or older. We included all adults aged 19 or older who underwent SUA measurement and participated in the nutritional survey in the present study. All participants provided written informed consent both for participation in the survey and for use of their data for research purposes. The survey was approved by the institutional review board of the Korean Centers for Disease Control and Prevention and the Statistics Korea (approval number: 117002).

Nutritional survey and derivation of nutritional information

Dietary information was collected using a single 24-hour dietary recall method. Trained interviewers conducted face-to-face interviews at the participants' home at 7–12 days after the health interview and examination, so that the nutritional survey was not all conducted on a specific day. Interviewers used supplementary materials such as two-dimensional models of dishes, bowls (69 different kinds in ten categories) and foods, measuring cups, measuring spoons, and rulers. The serving size of each food was recorded by volume and converted to weight using a database which includes 785 conversion factors. Nutritional information of each dietary item such as energy (kcal), water content (g), and vitamin content (mg) was obtained from a database containing information on 5,120 dietary items based on the Food Composition Table, 9th edition, published by the National Agricultural Science Institute in 2017.[19] The energy density (percentage) of each food group was calculated by dividing the energy from the food group by daily energy intake. We collected information on the following food groups and nutrients: meat, seafoods, nuts and legumes, sugar-sweetened products, dairy products, alcohol, sodium, vitamin A, vitamin B1 (thiamine), vitamin C, and dietary fiber.

Health interview and examination

Body mass index (BMI; kg/m^2) was calculated using body weight and height measurements, and was categorized into the following groups: reference body weight (<25 kg/m^2), overweight (25-29.9 kg/m^2), or obese (≥30 kg/m^2).[20] Blood pressure was measured after overnight fasting with participants sitting relaxed for at least 5 minutes with their feet flat on the floor by experienced nurses using a mercury sphygmomanometer (Baumanometer Wall Unit 33[0850]; Baum, Copiague, NY, USA) and stethoscopes (Littmann Cardiology 3; 3M, Maplewood, NJ, USA). Participants' arms were supported with a cushion 4 cm in height to match the center of the cuff to the level of the heart (the fourth intercostal space or middle of the sternum). Systolic and diastolic blood pressure (SBP and DBP, respectively) were measured three times with a minimum of 30-second intervals, and the average value of the last two recordings was used. Hypertension was defined as SBP of ≥140 mmHg or DBP of ≥90 mmHg. Prehypertension was defined as SBP 120-140 mmHg, or DBP 80–90 mmHg. Normal blood pressure was defined as SBP <120 mmHg and DBP <90 mmHg.[21] Additionally, 12-hour fasting blood samples were collected and kept refrigerated at 2–8°C before transferring to a central testing institute for analysis within 24 hours of sampling. Serum fasting glucose, creatinine, and uric acid was measured using a Hitachi Automatic Analyzer 7600-210 (Hitachi, Tokyo, Japan). High sensitivity C-reactive protein (hsCRP) was measured by immunoturbidimetry using Cobas (Roche, Basel, Switzerland). Hyperuricemia was defined as SUA ≥6.0 mg/dL.[22] Diabetes was defined as fasting blood glucose (FBG) of ≥126 mg/dL. Impaired fasting glucose was defined as FBG 100–126 mg/dL.[23] Normal FBG was defined as <100 mg/dL. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation, and CKD was defined as eGFR of <60 mL/min.[24] Elevated hsCRP was defined as hsCRP ≥1.0 mg/dL.

Statistical analysis

Food groups were analyzed by energy density (percentage) of meats, seafoods, nuts, and legumes, sugar-sweetened products, dairy products, and alcohol. Nutrients were analyzed by absolute amounts. Data on food groups and nutrients were grouped into quartiles. For dairy and alcohol intake, the following cutoffs were used for quartiles, accounting for the distribution of data and sample sizes of each group: <75th percentile, 75th–89.9th percentile, 90th–94.9th percentile, and ≥95th percentile.

All analyses incorporated the complex sampling design including strata, cluster, and weights which accounted for the proportion of selection, proportion of response, and post-hoc corrections for age- and sex-specific population structures. Participant characteristics were described in relation to the presence of hyperuricemia. Continuous variables are presented as population mean values and 95% confidence intervals (CI) with statistical significance of mean differences. Categorical variables are presented as proportions (percentage) with 95% CI with tests for independence.

Multiple linear regression modeling for SUA was performed for each dietary and nutrition quartile, adjusting for age, sex, BMI category, blood pressure category, FBG

category, presence of CKD, presence of elevated hsCRP, and energy and water intake. In addition to the main effects of factors and covariates, the interaction between sex and diet or nutrient quartiles was analyzed a priori, based on studies reporting effect modification by sex.[25-27] The estimated marginal means for quartiles are presented for each sex with the statistical significance of the difference between the first and the other quartiles. Nutrients that showed significant association with SUA were additionally adjusted for alcohol intake. In addition, the association between hyperuricemia and dietary and nutritional quartile was examined using survey-weighted multivariable logistic regression analysis, adjusting for the same factors (including interaction between sex and diet/nutrition quartile) and covariates in the multiple linear regression models. Statistical analyses were performed using SPSS 25 software. Statistical significance was set at two-sided type I error probability of <5%.

RESULTS

We identified a total of 12,900 participants aged 19 years or older who participated in the survey as eligible for the present study. Among these, 10,175 (78.9% of eligible participants) underwent both the health examination and nutritional survey and were finally enrolled in this study.

Participant characteristics

The mean age of the total study population was 47 (47–48) years and 48% (47%–49%) were male. The mean SUA was 5.1 (5.1–5.2) mg/dL, and the prevalence of hyperuricemia was 25.6% (24.5%–26.8%). The prevalence of overweight and obesity was found to be 29.4% (28.3%–30.5%) and 5.7% (5.1%–6.3%), respectively, while those of hypertension, diabetes, and chronic kidney disease were 27.0% (25.9%–28.3%), 10.4% (9.7%–11.2%), and 2.9% (2.5%–3.3%). The proportion of participants with elevated hsCRP was 28.9% (27.8%–30.0%) and mean daily energy intake was 1996 (1969–2023) kcal. The energy densities of meat, seafoods, nuts and legumes, sugar-sweetened products, dairy product, and alcohol were 10.3% (10.0%–10.7%), 3.2% (3.1%–3.4%), 1.2% (1.2%–1.3%), 2.0% (1.9%–2.0%), 3.6% (3.5%–3.8%), and 4.4% (4.1%–4.7%). The mean daily intakes of sodium, vitamin A, vitamin B1, vitamin C, and dietary fiber were 3.8 (3.7–3.8) g, 533 (503–563) mcg, 1.7 (1.7–1.7) mg, 83 (79–87) mg, and 24 (23–24) g, respectively.

The mean age was lower, and the proportion of men higher, among participants with hyperuricemia. Metabolic risk factors such as obesity, hypertension, impaired fasting glucose, chronic kidney disease, and elevated hsCRP were associated with hyperuricemia. Intake of meat, alcohol, sodium, vitamin A, and vitamin B1 intake was higher in participants with hyperuricemia, whereas consumption of nuts and legumes, sugar-sweetened products, dairy products, and vitamin C intake was lower in these participants. Characteristics of participant stratified by sex is presented in Table 1.

Association between serum uric acid and dietary and nutritional factors

The estimated marginal mean (EMM) values of SUA across quartiles of food groups and nutrients stratified by sex are presented in Table 2. Alcohol intake was positively associated with SUA in both men and women. The difference in EMM of SUA between the fourth and first quartiles (EMM Q4–Q1) was 0.22 mg/dL (standard error [SE]=0.09, p=0.020) in men and 0.21 mg/dL (SE=0.10, p=0.046) in women. Vitamin B1 was negatively associated with SUA, with EMM Q4–Q1 for SUA being −0.16 mg/dL (SE=0.08, p=0.044) and −0.10 mg/dL (SE=0.05, p=0.049) in men and women, respectively. The intake of seafoods, vitamin C, and dietary fiber was inversely associated with SUA in men. The EMM Q4–Q1 for SUA was −0.12 mg/dL (SE=0.06, p=0.039), −0.18 mg/dL (SE=0.07, p=0.005), and −0.26 mg/dL (SE=0.07, p<0.001) for seafoods, vitamin C, and dietary fiber, respectively. Although the EMM Q4–Q1 for SUA was −0.14 mg/dL (SE=0.06, p=0.019) for sugar intake, the trend was not linear. Intake of meat, nuts and legumes, dairy products, sodium, and vitamin A was not found to be associated with SUA in either sex.

Intake of vitamin C and dietary fiber remained inversely associated with SUA in men after adjusting for alcohol intake. The EMM Q4–Q1 for SUA was −0.16 mg/dL (SE=0.07, p=0.016) for vitamin C and −0.23 mg/dL (SE=0.07, p=0.002) for dietary fiber. The EMM values for vitamin B1 quartiles did not differ significantly after adjustment for alcohol intake (Table 3).

Association between hyperuricemia and dietary and nutritional factors

Table 4 presents the odds ratios (ORs) for the association of hyperuricemia with quartiles of food and nutrient groups stratified by sex. In men, alcohol intake was associated with hyperuricemia, while vitamin C, and dietary fiber were inversely associated. The OR for a quartile increase in alcohol intake was 1.15 (95% CI 1.07–1.24), and 0.93 (95% CI 0.86–0.99) for vitamin C and 0.92 (95% CI 0.85–0.99) for dietary fiber.

DISCUSSION

We found that intake of alcohol is associated with SUA and hyperuricemia, which was unsurprising because alcohol intake is the most well-known dietary risk factor for hyperuricemia and gout. Vitamin C and dietary fiber intake was inversely associated with hyperuricemia in men, although there was no significant association of either SUA or hyperuricemia with consumption of meat, nuts and legumes, sugar-sweetened products, and dairy products.

The uricosuric effect of vitamin C and its inverse association with hyperuricemia is well-known, and increasing vitamin C intake has been recommended for the prevention of gout flares.[28] In the present study, we identified an inverse association between vitamin C intake and hyperuricemia in men only. This may be explained by a sex-dependent difference in the effect of vitamin C on SUA, which have been demonstrated in a short-term trial of vitamin C supplementation and is supported by the results of the present study. In the previous trial, SUA decreased following supplementation with 500 mg per day of vitamin C for two months by 0.8 (95% CI 0.5–1.2) mg/dL in men and 0.4 (0.1–0.6) mg/dL in women.[25] Although the statistical significance of the difference was not tested, the results provide suggestive evidence of sex-difference in the effects of vitamin C on hyperuricemia. The total intake of

Table 1. Characteristics of study participants in relation to the presence of hyperuricemia[†]

	Men				Women			
	N	Normouricemia	Hyperuricemia[‡]	*p*-value	N	Normouricemia	Hyperuricemia[‡]	*p*-value
Age (years)	4300	49 (48–50)	44 (43–44)	***	5875	48 (47–48)	54 (52–56)	***
BMI (%)	4296			***	5868			***
Normal	2558	65.0 (62.6–67.4)	50.4 (47.8–53.1)		4063	73.2 (71.7 – 74.7)	41.1 (35.6–47.0)	
Overweight	1512	31.7 (29.5–34.0)	39.9 (37.4–42.5)		1488	22.4 (21.1–23.8)	42.1 (36.6–47.8)	
Obesity	226	3.3 (2.5–4.3)	9.6 (8.1–11.5)		317	4.4 (3.8–5.1)	16.8 (12.5–22.1)	
Blood pressure (%)	4289				5869			***
Normal	1422	39.5 (36.9–42.1)	33.4 (30.9–36.1)	**	2989	58.5 (56.7–60.2)	35.5 (29.7–41.9)	
Prehypertension	1298	30.4 (28.2–32.7)	34.5 (32.2–36.9)		1176	19.7 (18.5–21.0)	17.7 (13.8–22.5)	
Hypertension	1569	30.1 (27.8–32.4)	32.0 (29.7–34.4)		1704	21.8 (20.4–23.3)	46.7 (40.7–52.8)	
Fasting blood glucose (%)	4181			***	5726			***
Normal	2311	59.0 (56.5–61.4)	62.3 (59.6–65.0)		3956	74.4 (73.0–75.9)	48.5 (42.4–54.7)	
Impaired fasting glucose	1230	25.8 (23.8–27.9)	30.1 (27.6–32.7)		1128	16.9 (15.8–18.2)	32.3 (27.2–37.8)	
Diabetes	640	15.2 (13.6–17.0)	7.6 (6.4–9.0)		642	8.6 (7.7–9.6)	19.2 (15.1–24.1)	
Chronic kidney disease (%)	4300	2.0 (1.5–2.6)	3.6 (3.0–4.4)	***	5875	1.8 (1.4–2.2)	21.4 (17.1–26.3)	***
Elevated hsCRP (%)	4256	29.0 (26.8–31.2)	35.8 (33.2–38.5)	***	5804	24.4 (23.2–25.8)	46.5 (40.7–52.4)	***
Energy intake (kcal/day)	4300	2321 (2272–2370)	2360 (2302–2418)		5875	1655 (1468–1679)	1564 (1469–1659)	
Water intake (g/day)	4300	1258 (1218–1297)	1310 (1269–1351)	*	5875	1003 (982–1024)	931 (866–996)	*
Meat (%)	4300	10.9 (10.3–11.5)	12.4 (11.6–13.1)	*	5875	9.1 (8.7–9.4)	9.1 (7.8–10.4)	
Seafoods (%)	4300	3.4 (3.2–3.7)	3.4 (3.1–3.6)		5875	3.1 (2.9–3.2)	3.2 (2.6–8.4)	
Nuts and legumes (%)	4300	1.1 (1.0–1.3)	0.9 (0.8–1.1)	*	5875	1.4 (1.3–1.5)	1.6 (1.2–2.0)	
Sugar–sweetened products (%)	4300	1.9 (1.8–2.1)	1.7 (1.5–1.8)	*	5875	2.1 (2.0 – 2.3)	2.0 (1.5–2.4)	
Dairy products (%)	4300	2.8 (2.5–3.0)	3.2 (2.9–3.5)	*	5875	4.3 (4.1–4.6)	4.1 (3.3–4.9)	
Alcohol (%)	4300	6.0 (5.4–6.6)	7.5 (6.8–8.2)	*	5875	2.0 (1.8–2.3)	2.0 (1.1–3.0)	
Sodium (mg/day)	4300	4443 (4316–4569)	4485 (4342–4628)		5875	3052 (2984–3121)	2886 (2656–3116)	
Vitamin A (mcg)	4300	593 (552–634)	554 (519–589)		5875	492 (452–532)	481 (402–561)	
Vitamin B1 (mg/day)	4300	2.0 (1.9–2.0)	2.0 (1.9–2.0)		5875	1.4 (1.4–1.5)	1.4 (1.3–1.5)	
Vitamin C (mg/day)	4300	84 (79–89)	79 (73–84)		5875	84 (80–89)	82 (70–95)	
Dietary fiber (g/day)	4300	27 (26–27)	25 (24–25)	***	5875	22 (22–23)	21 (20–22)	

BMI: body mass index; hsCRP: high sensitivity C-reactive protein

[†]Data presents population and mean and 95% confidence interval for continuous variables and population proportion (percentage) and 95% confidence interval for categorical variables.

[‡]Hyperuricemia was defined as serum uric acid of ≥6.0 mg/dL.

[*]$p<0.05$, [**]$p<0.01$, [***]$p<0.001$.

Table 2. Estimated marginal mean values of serum uric acid in relation to dietary and nutritional intake according to multiple linear regression analysis (n=9,769)[†]

	Men				Women			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Meat	6.63 (6.48–6.79)	6.67 (6.51–6.82)	6.66 (6.52–6.81)	6.68 (6.54–6.82)	5.31 (5.19–5.43)	5.25 (5.13–5.38)	5.22 (5.10–5.35)	5.27 (5.15–5.40)
Seafoods	6.73 (6.60–6.86)	6.69 (6.54–6.85)	6.62 (6.49–6.76)	6.61 (6.46–6.75)*	5.30 (5.18–5.42)	5.25 (5.12–5.37)	5.21 (5.08–5.33)*	5.30 (5.17–5.42)
Nuts and legumes	6.69 (6.55–6.83)	6.67 (6.52–6.81)	6.67 (6.52–6.81)	6.62 (6.48–6.77)	5.29 (5.17–5.42)	5.22 (5.09–5.34)	5.23 (5.10–5.36)	5.31 (5.20–5.43)
Sugar-sweetened products	6.74 (6.59–6.88)	6.62 (6.47–6.77)	6.70 (6.56–6.84)	6.60 (6.46–6.74)*	5.32 (5.20–5.45)	5.21 (5.08–5.34)*	5.27 (5.14–5.40)	5.26 (5.14–5.38)
Dairy products	6.65 (6.52–6.77)	6.68 (6.53–6.84)	6.81 (6.57–7.04)	6.77 (6.54–7.00)	5.26 (5.15–5.38)	5.23 (5.10–5.36)	5.34 (5.18–5.50)	5.29 (5.14–5.44)
Alcohol	6.63 (6.50–6.75)	6.74 (6.59–6.89)*	6.68 (6.50–6.87)	6.84 (6.63–7.05)*	5.25 (5.14–5.37)	5.29 (5.16–5.42)	5.10 (4.89–5.31)	5.46 (5.23–5.69)*
Sodium	6.73 (6.55–6.91)	6.71 (6.56–6.86)	6.64 (6.50–6.78)	6.62 (6.48–6.76)	5.31 (5.19–5.43)	5.27 (5.14–5.40)	5.25 (5.12–5.37)	5.23 (5.11–5.36)
Vitamin A	6.71 (6.56–6.87)	6.69 (6.55–6.84)	6.65 (6.51–6.80)	6.61 (6.46–6.75)	5.31 (5.19–5.44)	5.26 (5.13–5.39)	5.28 (5.15–5.40)	5.23 (5.11–5.35)
Vitamin B1	6.75 (6.58–6.92)	6.75 (6.60–6.90)	6.62 (6.48–6.76)	6.59 (6.45–6.74)*	5.33 (5.20–5.45)	5.29 (5.16–5.41)	5.25 (5.12–5.37)	5.23 (5.10–5.35)*
Vitamin C	6.74 (6.60–6.87)	6.72 (6.57–6.86)	6.64 (6.49–6.79)	6.55 (6.41–6.69)**	5.28 (5.15–5.41)	5.26 (5.14–5.39)	5.31 (5.18–5.43)	5.23 (5.11–5.35)
Dietary fiber	6.80 (6.65–6.96)	6.65 (6.51–6.80)*	6.67 (6.53–6.81)	6.54 (6.40–6.69)***	5.27 (5.14–5.40)	5.27 (5.15–5.39)	5.24 (5.12–5.37)	5.31 (5.18–5.43)

[†]Data are presented as serum uric acid (mg/dL) and 95% confidence intervals. The models were adjusted for age, sex, obesity, hypertension, chronic kidney disease, elevated high sensitivity C-reactive protein level, and intake of energy and water. Statistical significance of the estimated marginal mean difference with the first quartile is presented for the second, third, and fourth quartiles. $^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$. Q1, Q2, Q3, and Q4 represent the first, second, third, and fourth quartiles, respectively.

Table 3. Estimated marginal mean values of serum uric acid in relation to dietary and nutritional intake from multiple linear regression analysis adjusted for alcohol intake (n=9,769)[†]

	Men				Women			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Seafoods	6.79 (6.65–6.93)	6.75 (6.60–6.91)	6.68 (6.53–6.83)	6.66 (6.51–6.81)*	5.30 (5.17–5.44)	5.26 (5.12–5.40)	5.22 (5.08–5.36)*	5.31 (5.17–5.45)
Sugar-sweetened products	6.80 (6.65–6.95)	6.67 (6.52–6.83)	6.75 (6.61–6.90)	6.60 (6.51–6.81)*	5.34 (5.20–5.47)	5.22 (5.08–5.36)*	5.28 (5.14–5.42)	5.28 (5.14–5.41)
Vitamin A	6.77 (6.61–6.93)	6.75 (6.60–6.90)	6.70 (6.55–6.85)	6.67 (6.51–6.82)	5.31 (5.17–5.45)	5.26 (5.12–5.40)	5.28 (5.15–5.42)	5.25 (5.12–5.38)
Vitamin B1	6.80 (6.62–6.97)	6.80 (6.64–6.95)	6.67 (6.52–6.82)	6.66 (6.51–6.81)	5.32 (5.18–5.45)	5.28 (5.14–5.43)	5.25 (5.11–5.39)	5.24 (5.10–5.38)
Vitamin C	6.77 (6.63–6.82)	6.76 (6.60–6.91)	6.69 (6.53–6.85)	6.61 (6.46–6.77)*	5.27 (5.13–5.41)	5.26 (5.12–5.41)	5.31 (5.18–5.45)	5.24 (5.10–5.38)
Dietary fiber	6.84 (6.68–7.00)	6.70 (6.55–6.86)	6.72 (6.57–6.87)	6.61 (6.45–6.77)**	5.27 (5.13–5.41)	5.27 (5.14–5.40)	5.25 (5.11–5.40)	5.33 (5.19–4.48)

[†]Data represent serum uric acid (mg/dL) and 95% confidence intervals. The models were adjusted for age; sex; obesity; hypertension; chronic kidney disease; elevated high sensitivity C-reactive protein level; and intake of energy, water, and alcohol. The statistical significance of the estimated marginal mean difference with the first quartile is presented for second, third and, fourth quartiles.
*p<0.05, **p<0.01, ***p<0.001. Q1, Q2, Q3, and Q4 represent the first, second, third, and fourth quartile, respectively.

Table 4. Association between hyperuricemia and dietary and nutritional intake analyzed by multivariable logistic regression (n=9,769)[†]

	Men				Women			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Seafoods	Reference	1.00 (0.82–1.22)	0.92 (0.76–1.13)	0.99 (0.81–1.20)	Reference	0.88 (0.64–1.20)	0.86 (0.61–1.21)	1.11 (0.77–1.59)
Sugar-sweetened products	Reference	0.85 (0.69–1.06)	0.97 (0.77–1.23)	0.82 (0.66–1.02)	Reference	0.86 (0.61–1.22)	0.85 (0.61–1.17)	0.74 (0.51–1.06)
Alcohol	Reference	1.29 (1.07–1.56)	1.31 (1.01–1.70)	1.50 (1.16–1.95)	Reference	0.87 (0.59–1.27)	0.17 (0.04–0.70)	0.96 (0.44–2.10)
Vitamin A	Reference	0.90 (0.71–1.14)	1.06 (0.83–1.34)	0.87 (0.68–1.12)	Reference	0.77 (0.54–1.12)	0.98 (0.68–1.41)	0.92 (0.64–1.32)
Vitamin B1	Reference	0.94 (0.72–1.21)	0.90 (0.68–1.18)	0.86 (0.65–1.14)	Reference	1.02 (0.74–1.41)	1.02 (0.70–1.47)	0.84 (0.56–1.25)
Vitamin C	Reference	0.96 (0.77–1.20)	0.90 (0.72–1.12)	0.79 (0.63–0.99)	Reference	1.15 (0.81–1.64)	1.05 (0.73–1.53)	1.04 (0.73–1.48)
Dietary fiber	Reference	0.84 (0.66–1.08)	0.86 (0.68–1.09)	0.75 (0.58–0.97)	Reference	0.80 (0.57–1.12)	0.74 (0.50–1.08)	1.04 (0.73–1.48)

[†]Hyperuricemia was defined as serum uric acid ≥6.0 mg/dL. Data are presented as odds ratios and 95% confidence intervals. The models were adjusted for age, sex, obesity, hypertension, chronic kidney disease, elevated high sensitivity C-reactive protein level, and intake of energy and water. Q1, Q2, Q3, and Q4 represent the first, second, third, and fourth quartile, respectively.

vitamin C was low among the population of the present study, which may further explain the lack of an observed association between vitamin C intake and hyperuricemia in women. In a prospective study on vitamin C intake and gout flares in men, the lowest intake that was significantly associated with a lower risk of gout flare was 500–999 mg per day.[28] In the present study, the median intake of vitamin C in the highest quartile was 191 mg. The effects of vitamin C supplementation in Asian populations, especially in women, merits further investigation.

The inverse association between dietary fiber intake and hyperuricemia has been reported in previous studies involving different ethnic groups including Koreans. An early study on healthy individuals from the Unites States involving a single 24-hour recall revealed the highest quartile of dietary fiber intake to be associated with a reduction of up to 7.5% in SUA, and 50% reduced risk of hyperuricemia compared with the lowest quartile.[29] Another study conducted in the early 2000s on a Caucasian Australian population involving systemic sampling and a food frequency questionnaire reported there to be a ~20% difference in SUA between the highest and lowest quartile groups for fiber intake.[30] Among Korean people, a single-center study which assessed 3-day food records reported the intake of fiber to be significantly lower among subjects with hyperuricemia.[31] A recent study by Sun et al. involving adults from the United States examined sources of dietary fiber (vegetables, fruits, and cereals) and found total fiber and cereal intakes to be inversely associated with hyperuricemia in men.[26] Regarding the mechanism underlying this inverse association, feeding studies on animals have suggested that reduced digestion and absorption of purine-containing compounds in the gut may contribute to this inverse association.[32] In the present study, we detected a significant interaction between sex and dietary fiber intake (data not shown), which was only significant in men, consistent with the study reported by Sun et al. As yet, there is no clear explanation for the difference between sexes, and further research into this issue is warranted.

Meat is one of the primary high-purine components of the human diet, and the identification of an association between meat intake and hyperuricemia and gout can be considered to indicate the quality of our data. In the present study, we did not identify a significant association between meat intake and SUA or hyperuricemia. However, a previous study which included Korean subjects also found no significant difference in meat intake between subjects with hyperuricemia and those without.[31] This may be because the overall consumption of meat is low in Korea. In typical Western (American) diets, the energy density of protein from red or processed meat has been reported to be around 15%[33]; in the present study, this value was around 10%. This suggests that meat intake may not contribute significantly to SUA or hyperuricemia among the Korean population, in which diet patterns are characterized by a high proportion of carbohydrate as the primary energy source.

The present study had some limitations which should be acknowledged. First, this study used dietary data derived from one 24-hour recall; therefore, statistical methods adjusting for day-to-day variation in diet intake based on multiple recalls could not be used.[34] Within-person random error can reduce the statistical power and cause overestimation of tail probabilities and attenuation of relationships. The lack of association between meat, sugar-sweetened products, or dairy products and hyperuricemia may be explained by the lack of statistical power originating from the single 24-hour recall. In addition, the unexpected inverse association that we found between seafood consumption and SUA may be due to bias. Therefore, these issues should be addressed in studies with proper methodology such as two or more recalls. Second, we could not investigate the association between diet and gout, one of the important clinical outcomes of hyperuricemia. Although hyperuricemia is the most significant risk factor for gout, many people with hyperuricemia remain free of gout for years,[35,36] and the relationship is known to be attenuated in women.[27] Therefore, more data are required to be able to generalize the results of the present study to gout and gout-related co-morbidities including dementia in Koreans.[37] Third, the cross-sectional design of this study means that the observed association may be in either direction regarding actual causality. Therefore, the results of this study should be validated in prospective studies or trials. Lastly, the study provided limited information on specific Korean dietary pattern associated with lower risk of hyperuricemia. Although the dietary pattern rich in dietary fiber and fruits is conceptually consistent with the DASH dietary pattern,[38] the blood pressure lowering effect of the dietary pattern has not been validated in Asian diets. Specific dietary pattern associated with lower risk of hyperuricemia and health benefits merits further study. The strengths of this study were the systematically selected sampling, which generates a population representative of the Korean national population, and the weighting of all analyses for this sampling scheme. In addition, we included most of the potential confounding variables for diet and hyperuricemia in the analysis, thus reducing the influence of these variables on the results.

Conclusions

We demonstrate that alcohol intake is the most important dietary factor influencing the development hyperuricemia among Korean individuals, especially in men. Intake of vitamin C and dietary fiber intake are inversely associated with hyperuricemia in men. The results of this study support the DASH-diet-based approach, along with attention to alcohol intake, for managing hyperuricemia for Korean men, which stresses the importance of a diet rich in fruits, vegetables, and whole grains.

AUTHOR DISCLOSURES

The authors declare that they have no competing interests.

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