Original Article

Relationship between dietary patterns and serum uric acid concentrations among ethnic Chinese adults in Taiwan

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The evidence for a relationship between dietary patterns and uric acid concentrations is scanty. Here, we used a validated food frequency questionnaire for an ethnic Chinese population in Taiwan to investigate the relationship between dietary patterns and uric acid concentrations. A cross-sectional study on 266 adults, who were interviewed with a 38-item food frequency questionnaire, was conducted and serum uric acid levels were measured. Three dietary patterns were derived from the questionnaire by exploratory factor analysis. Participants in the higher vegetable and fruit pattern quartiles were more likely to have a lower uric acid concentration (6.5 for the first, 5.7 for the second, 6.0 for the third, and 6.0 mg/dL for the fourth quartile, p = 0.030). For uric acid-prone patterns, as the quartiles increased, the adjusted mean uric acid concentrations increased significantly (5.88, 5.93, 5.99 and 6.38 mg/dL for each quartile, respectively, p = 0.04). However, the significance level was attenuated after adjusting for additional confounding factors. In conclusion, three dietary patterns were identified for ethnic Chinese in Taiwan, and the relationship between these dietary patterns and uric acid was not significant after adjustment.

Key Words: uric acid, dietary pattern, exploratory factor analysis, food frequency questionnaire, validation study

INTRODUCTION

The high prevalence of hyperuricemia and its association with type 2 diabetes and cardiovascular diseases in the general population[1-3] have rendered it crucial to investigate the causes of hyperuricemia. Biological mechanisms for hyperuricemia include uric acid under-excretion, overproduction or combinations of both pathways. With regards to the overproduction pathway, dietary intake of high purine content foods, such as meat, seafood, sugar-sweetened drinks and alcohol are related to high uric acid levels in plasma.[4-6] Conversely, dietary fiber, dairy and coffee intake are inversely associated with the risk of hyperuricemia.[7-9]

However, evidence about the relationship between specific food intake and hyperuricemia is limited and inconsistent due to the following reasons. Firstly, people consume various types of food in combination, instead of only specific items. Secondly, it has been reported that the interaction between multiple nutrients and food items, in contrast to a single nutrient or food approach, may be more relevant to studies on disease association.[10] In addition, chance findings may be induced due to multiple testing for the association between food and disease. Therefore, another approach, namely dietary pattern identification, has become widely used to investigate the associations between multiple food items/nutrients and health outcomes, rather than looking at associations in isolation.[11] Two strategies for dietary patterns have been proposed in the literature. The first is the biology-driven dietary pattern approach,[11-14] and the second is data-

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driven dietary pattern identification from validated questionnaires, which has been a useful way to investigate the association of nutrition and disease in population studies.[11,15] Previous studies on identifying dietary patterns have been undertaken for chronic diseases, such as obesity,[16] type 2 diabetes,[17] cancers[18,19] and mortality[20] in Caucasians;[21,22] however, the evidence for uric acid concentrations among ethnic Chinese is scanty. As the prevalence of hyperuricemia in ethnic Chinese in Taiwan is high,[23,24] it is crucial to understand the associations between dietary patterns and hyperuricemia. The aim of this study was to use a validated questionnaire for ethnic Chinese in Taiwan to investigate the relationships between dietary patterns and uric acid concentrations in a Taiwanese population.

MATERIALS AND METHODS

Participants

We conducted a cross-sectional study during 2009, and recruited participants from three settings: patients from the outpatient clinic and health examination centre of National Taiwan University Hospital in Taipei City, and a local hospital in Chin-Shan community in Taipei County. A total of 304 individuals in a stable clinical situation and taking medication regularly were recruited. Baseline information including: socio-demographic characteristics, alcohol intake, tea intake, tobacco use, regular exercise, and personal histories of diseases was collected using questionnaires. We estimated total energy intake from the questionnaires and excluded extreme values.[25] Subjects were excluded from the analysis if their total energy intake was outside the range of 800 to 3245 kcal/day for men and 500 to 2842 kcal/day for women, or if their energy intake was beyond mean +/- 3 standard deviations. As a result, 266 participants were included into this study. As their clinical, anthropoimetric and biochemical measurement characteristics were similar, all participants from the three different settings were grouped together for further analysis. Written informed consent was obtained from all participants, and the protocol was approved by the Institutional Research Board of National Taiwan University Hospital

Assessment of dietary intake

A 38-item, Chinese language, validated semi-quantitative food frequency questionnaire (FFQ) was administered by one interviewer (YTT) to estimate dietary intake over the preceding year; the questionnaire was a shortened version of a validated FFQ for the Taiwanese.[26,27] Each participant was asked the frequency with which he/she ate a certain amount of each specific food item. Photographs of food items, showing different portion sizes, were used to facilitate quantification of intake. Food items were arranged into sections of the major food groups: dairy, eggs, meat, poultry, fish, seafood, organ meat, soybean products, vegetables, fruits, staples, sugary drinks, pickles, sodium containing condiments, cooking methods, cooking oils, and use of supplements. The frequency response section included 10 categories; 'over 6 times per year', '1 to 3 times per month', 'once per week', '2 to 4 times per week', '5 to 6 times per week', 'once per day', '2 times per day', '3 times per day', '4 to 5 times per day' and 'over 6 times per day'. The intraclass correlation (ICC) for the reliability of two responses to the FFQ from the same participants one month apart ranged between 0.4 and 0.8.[27] In addition, the validity of the FFQ was acceptable, with the correlation coefficients between the unadjusted and energy-adjusted nutrient intakes measured by dietary record and by the FFQ (which collected data on diet during the six months encompassing the diet records) were 0.40 and 0.35, respectively. [27]

Dietary intake estimates for foods were derived from the FFQ by summing the amount of nutrient contents in each food item derived from a previously established nutrient database,[28,29] portion size, and frequency of consumption. The food-composition database used to calculate nutrient values was based primarily on the Taiwan Food Composition Data Base[30-32] and other published data resources.[33-35.]

A total of 38 food items were derived from the FFQ after deleting information on vitamins and tea intake.[7] Eight items for alcohol intake were grouped as one variable, and 30 other items were aggregated into 13 food groups according to similar macronutrient intakes and eating habits in Taiwan (Table 1).

Clinical examinations

Blood pressure was recorded by trained medical assistants in the resting position. Body mass index was calculated as weight (in kilograms)/height (in meters)^2. Medical histo-

Table 1. Contents of the 13 FFQ food groups

Variables	Contents
Milk and dairy	Milk, dairy
Eggs	Eggs
Meat	Red meat, poultry
Fish	Fish from deep sea, freshwater
Seafood	Seafood
Organ meat	Viscera, liver
Soy products	Soy products, soy milk
White vegetables	White vegetables
Dark vegetables	Dark green vegetables, carrots, tomatoes, cauliflower
Fruit	Citrus, papaya, other fruit
Staples	Bread, instant noodles, root, rice, cereal (25%, 50%, 75%, 100%)
Beverages	Beverages
Fried food	Fried food

FFQ: Food Frequency Questionnaire

ries, such as hypertension, hyperlipidemia, diabetes, gout and medication lists were recorded from hospital chart reviews.

Laboratory examinations

Blood samples were sent to the core laboratory of the Department of Internal Medicine, National Taiwan University Hospital for analysis according to the protocol reported in a previous paper.[24] Plasma uric acid concentration was assayed in an Eppendorf 5060 autoanalyzer (Eppendorf) by means of a commercial method (Merck) based on the uricase and peroxidase principle.[36]

Statistical analysis

Basic demographic and clinical variables were presented as mean ± standard deviation if the data were continuous, and presented in contingency tables if the data were binary or categorical.

Exploratory factor analysis (EFA) was employed to identify dietary patterns based on the data collected from the FFQ, after adjusting for total energy intake. In addition, the maximum likelihood method was used to determine the number of different dietary patterns (factors).[37] The factor loadings and coefficients of various foods related to dietary patterns were represented, and we selected a loading value of more than 0.35 as the cut-off point.[38] Factor scores of each dietary pattern were also computed for each subject. Quartiles based on factor scores were then determined for each dietary pattern. Within each dietary pattern, subjects were classified into four groups according to whether their factor score was below the first quartile (Q1), between the first quartile and median quartile (Q2), between the median and the third quartile (Q3), or above Q3. Analysis of variance (for continuous variables) or the Cochran-Armitage trend test (for categorical data)[39] was used to examine linear trend in the quartiles of dietary patterns with respect to demographic and clinical characteristics. General linear regression models were used to investigate the association between the dietary patterns and the uric acid concentration after controlling for demographic variables such as age, gender and body mass index and additional clinical characteristics such as sites, systolic and diastolic blood pressure, smoking status, physical activity intensity, medications for lowering uric acid, total energy and alcohol intake. In addition, discriminant analysis was used to investigate the prediction ability of the resulting dietary patterns for hyperuricemia occurrence.[37]

RESULTS

Factor analysis results

Table 2 shows the food components arranged into three dietary factors. The first factor, the uric acid-prone pattern, composes of meat, seafood, organ meat, eggs and beverages. The second factor, the fish and fried food pattern, composes of fried foods and fish; and the third pattern, the vegetable and fruit pattern, composes of soy products, white vegetables, dark vegetables and fruit.

General characteristics of subjects by factors

The demographic and clinical characteristics of the study participants, according to quartiles of the derived dietary patterns, are presented in Table 3. With regards to the uric acid-prone pattern, the participants in higher quartiles were more likely to be men, younger, to have a higher total energy intake, and less likely to exercise, compared with those in the lowest quartile. The uric acid concentration increased progressively as the quartiles increased; however, it did not reach a significant levels. For the vegetable and fruit pattern, participants in higher quartiles were more likely to have a lower uric acid concentration (mg/dL) (6.5 for the first, 5.7 for the second, 6.0 for the third, and 6.0 for the fourth quartile, p= 0.030). The higher the vegetable and fruit quartile, the higher the total energy intake (p = 0.030).

Dietary patterns and uric acid concentrations

Table 4 lists the adjusted means of serum uric acid levels in the study participants according to the quartiles of the three dietary patterns, simultaneously in the model. For the uric acid-prone patterns, as the quartiles increased, the adjusted mean uric acid concentrations increased significantly (5.88, 5.93, 5.99 and 6.38 mg/dL for each quartile, respectively, p = 0.04). However, the significance level was attenuated after adjusting for additional confounding factors. The other two dietary factors were not related to uric acid levels in the participants.

Table 2. The factor loadings and coefficients for three dietary patterns estimated from factor analysis

	Uric acid-prone pattern	Fish and fried food pattern	Vegetable and fruit pattern
Variable	Loading	Loading	Loading
Seafood	**0.54**	0.24	0.21
Meat	**0.51**	0.07	0.06
Beverages	**0.46**	-0.05	0.03
Organ meat	**0.45**	0.27	-0.08
Fried food	0.30	**0.36**	0.04
Fish	-0.05	**0.96**	0.07
Dark vegetables	-0.11	-0.01	**0.73**
White vegetables	-0.13	-0.01	**0.51**
Soy products	0.19	0.06	**0.36**
Fruit	0.09	0.02	**0.35**
Eggs	0.34	0.15	-0.01
Milk and dairy	-0.07	0.03	0.07
Staples	0.26	-0.06	-0.07

Bold numbers represent the contents of dietary pattern as greater than 0.35, the cut-off point for factor loading.

Table 3. Demographic and clinical characteristics of the study participants, specified by the quartiles of the derived two dietary pattern scores

Quartiles	Q1		Q2		Q3		Q4		*p*-value
Uric acid-prone pattern									
Number of subjects	66		67		67		66		
Gender (n, %)									<.001
Women	43	65.2	32	47.8	27	40.3	17	25.8	
Men	23	34.9	35	52.2	40	59.7	49	74.2	
Smoking status (n, %)									0.002
Never	52	78.8	47	70.2	45	67.2	37	56.1	
Quit	3	4.6	4	6.0	11	16.4	18	27.3	
Current	11	16.7	16	23.9	11	16.4	11	16.7	
Diuretic (n, %)	1	1.5	0	0.0	0	0.0	0	0.0	0.390
Medications for uric acid lowering (n, %)	4	6.1	3	4.5	2	3.0	6	9.1	0.470
Exercise (n, %)									0.030
No	17	25.8	17	25.4	23	34	32	48.5	
< 4 hours/week	8	12.1	12	17.9	12	18	12	18.2	
≥ 4 hours/week	41	62.1	38	56.7	32	48	22	33.3	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (years)	66.1	10.9	64.1	11.1	59.3	11.6	52.7	11.7	<.001
BMI (kg/m^2)	24.7	3.5	24.9	3.8	24.5	3.1	25.8	4.1	0.180
SBP (mm Hg)	124	15.7	124	18.4	119	13.0	120	14.6	0.130
DBP (mm Hg)	73.5	10.2	74.7	13.4	72.9	11.0	75.9	12.0	0.440
Total energy (kcal)	1234	345	1330	366	1518	316	1825	459	<.001
Alcohol (g/day)	5.2	19.9	5.3	18.3	1.8	5.8	7.7	18.5	0.230
Uric acid (mg/dl)	5.9	1.5	5.9	1.4	6.0	1.2	6.4	1.8	0.210
Vegetable and fruit pattern									
Numbers of subjects	67		66		66		67		
Gender (n, %)									0.760
Women	31	46.3	28	42.4	27	40.9	33	49.3	
Men	36	53.7	38	57.6	39	59.1	34	50.8	
Smoking status (n, %)									<.001
Never	41	61.2	43	65.2	43	65.2	54	80.6	
Quit	18	26.9	12	18.2	4	6.1	2	3.0	
Current	8	11.9	11	16.7	19	28.8	11	16.4	
Diuretic (n, %)	1	1.5	0	0.0	0	0.0	0	0.0	0.390
Medications for uric acid lowering (n, %)	5	7.5	3	4.6	2	3.0	5	7.5	0.610
Exercise (n, %)									0.140
No	27	40.3	26	39.4	22	33.3	14	20.9	
< 4 hours/week	7	10.5	11	16.7	14	21.2	12	17.9	
≥ 4 hours/week	33	49.3	29	43.9	30	45.5	41	61.2	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (years)	61.8	14.8	59.0	11.9	60.8	11.1	60.6	11.6	0.650
BMI (kg/m^2)	25.8	3.5	24.3	3.4	24.7	3.5	25.2	4.1	0.120
SBP (mm Hg)	124	16.8	119	13.0	123	18.6	121	13.4	0.260
DBP (mm Hg)	77.1	13.0	73.0	9.5	74.5	13.4	72.4	10.0	0.090
Total energy (kcal)	1400	444	1416	385	1483	387	1605	496	0.030
Alcohol (g/day)	9.1	22.2	1.8	8.6	4.9	19.0	4.1	12.7	0.080
Uric acid (mg/dl)	6.5	1.6	5.7	1.2	6.0	1.4	6.0	1.6	0.030

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation

Discriminative analysis

With regards to discriminant analysis, we set gender and body mass index as the base model, and we tested if the dietary patterns improved the performance measures significantly. Table 5 shows the sensitivity and specificity of the different models. After adding the uric acid-prone pattern, the sensitivity and specificity of hyperuricemia were 66.2% and 68.7%, respectively, similar to the base model. In addition, we found that specificity after adding the vegetable and fruit pattern increased to 70.2%, higher than the base model.

DISCUSSION

In this cross-sectional study on ethnic Chinese adults and patients on stable medications in Taiwan, we demonstrated that three dietary patterns were derived from a validated FFQ; and the uric acid-prone pattern and the vegetable and fruit pattern were not significantly associated with serum uric acid concentrations after adjustments.

Association between dietary patterns and hyperuricemia

There are plenty of studies on the relationship between dietary factors and uric acid as well as gout,[40-42] however the findings have been inconsistent. Our study did not demonstrate an association between seafood and meat intake, and an increase in uric acid levels, as shown in a large prospective study of 47,000 men.[40] However, our data did support an association between uric acid-prone patterns, including eggs, meat, seafood, organ meat and beverages, and uric acid concentrations.

Table 4. The adjusted means (standard errors) of serum uric acid concentrations according to the quartiles of three dietary patterns

	Q1		Q2		Q3		Q4		p for trend
Dietary patterns	Mean	SE	Mean	SE	Mean	SE	Mean	SE	
Uric acid-prone pattern									
Uric acid (mg/dL) †	5.88	0.18	5.93	0.18	5.99	0.18	6.38	0.18	0.04
Uric acid (mg/dL) ‡	6.12	0.19	6.01	0.17	6.05	0.17	6.00	0.20	0.75
Fish and fried food pattern									
Uric acid (mg/dL) †	6.03	0.18	6.05	0.18	5.95	0.18	6.16	0.18	0.61
Uric acid (mg/dL) ‡	6.16	0.17	6.06	0.17	5.96	0.17	6.00	0.17	0.53
Vegetable and fruit pattern									
Uric acid (mg/dl) †	6.47	0.18	5.72	0.18	6.00	0.18	5.98	0.18	0.15
Uric acid (mg/dL) ‡	6.34	0.17	5.77	0.17	6.00	0.17	6.06	0.17	0.48

†Adjusted for age, gender and body mass index
‡ Adjusted for age, gender, body mass index, sites, systolic and diastolic blood pressure, smoking status, medication for uric acid lowering, exercise, total energy and alcohol
Abbreviation: SE, standard error

Table 5. Sensitivity and specificity of hyperuricemia and normal uric acid by patterns, body mass index and gender

	Hyperuricemia		Normal uric acid	
	Sensitivity		Specificity	
	N	%	N	%
Original	65	100	201	100
Base model	43	66.2	138	68.7
Additional uric acid-prone pattern	43	66.2	137	68.2
Additional fish and fried food pattern	43	66.2	139	69.2
Additional vegetable and fruit pattern	43	66.2	141	70.2

Base model: gender and body mass index

Clinical situations, such as obesity, physical activity intensity and medication history, such as diuretics and uric acid lowering drugs, are related to uric acid concentrations and confound the association between dietary habits and uric acid.[43] Our two models support this argument, as after controlling for clinical variables, the uric acid-prone patterns were not significantly related to uric acid concentrations.

Statistical issues for data-driven dietary pattern construction

Principal component analysis and exploratory factor analysis are the most commonly used statistical methods for investigating dietary patterns.[16,44] Different criteria for factor selection, including eigenvalues larger than 1[18] and variance larger than 0.1,[45] have been proposed. However, these methods are not feasible when the scree plot curve is flat.[44] In our study, the maximum likelihood method was applied to test the model fitness. However, the data-driven dietary pattern methods still depend greatly on the contents of the data collection, and sensitivity analysis and confirmatory factor analysis may be mandatory for further verification of dietary patterns.[11]

Strength of our study and clinical application

The effect of diet on serum uric acid levels has become an urgent issue because of the high prevalence of hyperuricemia worldwide, and its association with atherosclerosis.[46-48] Excess purine intake and endogenous production due to glucose intake elevate uric acid levels. In addition, excess intake of alcohol also stimulates purine increase and depresses uric acid excretion. Clinical variables, including obesity and insulin resistance, are associated with the status of hyperuricemia,[49] which increases the risk of atherosclerotic disease.[50] Our previous studies based on a community cohort also demonstrated that uric acid was associated with type 2 diabetes incidence[24] and cardiovascular risk in ethnic Chinese.[1] Therefore, dietary modification to reduce intake of high purine foods may be mandatory for risk reduction in the general community. In addition, our uric acid-prone dietary pattern, including seafood, meat, and beverages was similar to the national representative data study which showed that hyperuricemia was associated with organ meats, bamboo shoots, and soft drinks intake.[51]

Study limitations

Our study has several limitations. First, the cross-sectional study design may suffer from reverse causation, i.e. participants with hyperuricemia modified their dietary habits to reduce high purine food intake. If true, our results support that dietary patterns are associated with uric acid. Second, the sample size may not be sufficient to test the strength between dietary habits and uric acid. Third, we intentionally reduced the original 38 food items to 13 items, losing detailed information about purine intake. Finally, different distributions for various risk factors from the three sites were found. We still decided to group the dietary patterns together due to the following reasons. Firstly, the uric acid distributions were similar among three sites (p=0.08); and secondly, we collected these participants from different sites to extend the heterogenity of the sample so that the results are applicable to different populations.

In conclusion, three dietary patterns were derived from a validated FFQ; and the uric acid-prone pattern and the vegetable and fruit pattern were marginally associated with serum uric acid concentrations. Further studies on the biological mechanism of dietary patterns and uric acid, and interventional trials on dietary habit modifications are warranted.

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AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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Original Article

Relationship between dietary patterns and serum uric acid concentrations among ethnic Chinese adults in Taiwan

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飲食型態與尿酸濃度在臺灣華人族群之相關性

過去針對飲食型態與尿酸濃度相關的證據仍然缺乏，因此我們利用一具有效度的食物頻率問卷在臺灣華人族群研究飲食型態及尿酸濃度的相關。在一橫斷式研究收集 266 位成年人的 38 項食物頻率問卷及其血液尿酸濃度值，利用探索性因素分析得到三類飲食型態因子。我們發現在較高的蔬菜水果攝食因子四分位的參與者有比較低的尿酸值(分別是第一四分位為 6.5，第二四分位為 5.7，第三四分位為 6.0 及第四四分位為 6.0 mg/dL，*p* 值為 0.030)。而高尿酸食物因子中，隨著四分位值增加，尿酸值呈現有意義的增加(四分位尿酸值分別為 5.88、5.93、5.99 及 6.38 mg/dL，*p* 值為 0.04)。然而，當調整其他干擾因子之後則呈現沒有統計上相關。總結而言，在臺灣華人族群可發現有三類飲食型態因子，然而這些飲食型態因子與尿酸濃度在多變數調整後並無顯著的相關。

關鍵字：尿酸、飲食型態、探索性因素分析、食物頻率問卷、效度研究