Major Dietary Patterns and Risk of Asymptomatic Hyperuricemia in Chinese Adults

Meilin ZHANG1, Hong CHANG1, Yuxia GAO2, Xuan WANG1, Weili XU3, Dongmei Lü4, Guangjing LI5 and Guowei HUANG1,*

1 Department of Nutrition and Food Hygiene, School of Public Health, Tianjin Medical University, Tianjin 300070, China
2 Department of Cardiology, General Hospital of Tianjin Medical University, Tianjin 300152, China
3 Department of Epidemiology, School of Public Health, Tianjin Medical University, Tianjin 300070, China
4 Health Examination Center of Heping District, Tianjin 300070, China
5 Health Bureau of Heping District, Tianjin 300040, China
(Received March 13, 2012)

Summary In this study, we conducted a case-control study to evaluate the association of major dietary patterns and asymptomatic hyperuricemia taking account of blood lipids in Chinese adults. 187 cases with confirmed asymptomatic hyperuricemia and 187 controls were frequency matched on age, gender and area of residence. We conducted factor analysis using dietary information from a validated food frequency questionnaire to derive dietary patterns. The association between major dietary patterns and asymptomatic hyperuricemia was assessed by logistic regression analysis. Three major dietary patterns were found: 1) “animal products and fried food,” 2) “western,” 3) “soybean products and fruit.” In multivariate analyses the “animal products and fried food” pattern score was associated with an odds ratio (OR) of 2.15 (95% CI, 1.22–3.76) compared with the lowest tertile. The OR for the top tertile of score for “soybean products and fruit” pattern was 0.32 (95% CI, 0.19–0.57) compared with the lowest tertile of “soybean products and fruit” pattern score. The significant association of these two patterns and asymptomatic hyperuricemia persisted after further adjusting for blood lipids. On the other hand, the “western” pattern was not associated with asymptomatic hyperuricemia. We observed a positive relationship between the “animal products and fried food” pattern and asymptomatic hyperuricemia, and a negative relationship between the “soybean products and fruit” pattern and asymptomatic hyperuricemia, independent of blood lipids.

Key Words dietary patterns, factor analysis, asymptomatic hyperuricemia, blood lipids

Asymptomatic hyperuricemia is a purine metabolic disorder known as a precursor of gout. The rising incidence of asymptomatic hyperuricemia in parallel with economic development in China indicates that environmental factors including diet might contribute to the risks of asymptomatic hyperuricemia (1–3). Diet in relation to asymptomatic hyperuricemia or gout risk has most often been described based on intakes of individual foods or nutrients (4–6). Since foods and nutrients tend to be correlated, the specific effect of each aspect of diet may be difficult to identify and can be partly confounded by the effect of other dietary components (7). The use of dietary patterns has thus been proposed to analyze the association between diet and asymptomatic hyperuricemia, given their ability to capture the variations in overall food intake (7).

Currently, only one epidemiological study has addressed the role of dietary patterns on the risk of asymptomatic hyperuricemia in Taiwan, which showed that the frequency of consumption of lean meat, soy products and soymilk, milk, eggs, vegetables, carrots, mushrooms, fruit and coffee was negatively associated with hyperuricemia, whereas consumption of organ meats, bamboo shoots, and soft drinks was positively associated with hyperuricemia (8). Furthermore, it has been reported that asymptomatic hyperuricemia is often associated with dyslipidemia (1, 9, 10). To our knowledge, no studies have investigated the association between major dietary patterns and asymptomatic hyperuricemia taking account of blood lipid levels in China. Here, we conducted this case-control study to identify major dietary patterns among Chinese adults residing in Tianjin Province and to examine the relationship between these patterns and asymptomatic hyperuricemia risk.

MATERIALS AND METHODS

Participants. All individuals aged 20–59 y were recruited from the Health Examination Center of Heping District, Tianjin, China on the basis of a routine health checkup, which was a part of the subjects’ employment scheme from March 2010 to January 2011. Data were collected by trained dietitians during a structured inter-
view, using a questionnaire. A total of 200 of asymptomatic hyperuricemia cases were ascertained according to the criteria of a serum uric acid concentration $>7.0$ mg/dL (416.4 $\mu$mol/L) for males or $>6.0$ mg/dL (356.9 $\mu$mol/L) for females, which is commonly used in clinical laboratories and has been proposed in previously published studies to define hyperuricemia (11, 12). Of the cases, 13 were excluded due to: (1) those with incomplete self-reported hyperuricemia or gout; (2) those who were taking medications for hyperuricemia or gout; (3) those with hypertension, diabetes, renal failure, lymphoproliferative and myeloproliferative diseases. Another 187 nonhyperuricemia subjects (definition for not having the condition) were enrolled as controls matched with cases in terms of age (5-y intervals), gender and area of residence. Thus, a total of 374 subjects were left for the current study. The study protocol was approved by the Ethics Committee of Tianjin Medical University. Written informed consent was obtained from all participants.

Assessment of dietary intake. A validated semiquantitative food frequency questionnaire (FFQ) was used to assess dietary intake over the period of one year prior to the study (13). The FFQ includes 33 food items. For each food item or food group, subjects were asked the frequency of consumption (daily, weekly, monthly, yearly or never) and the amount of consumption in the unit of liang ($1$ liang = $50$ g) per unit of time over the past 12 mo. According to the similarity of nutrient profiles and culinary usage among the foods and the grouping scheme used in other studies, we collapsed the 33 food items into 20 predefined food groups. We classified low-fat, high-fat, free-fat milk, yogurt, cheese and milk powder under the milk products group. Alcohol consumption was calculated based on the drinking frequency and consumption of different types of liquor, which was collected by FFQ also.

Assessment of other variables. Body mass index (BMI) was calculated as weight/height$^2$ (kg/m$^2$). An average systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated from two measurements with the subjects in a sitting position after 5 min rest. Venous blood samples were taken from all participants after an overnight fast (12 h at least) and the samples were stored at $-80^\circ$C until the assessment assayed was performed. Serum triglyceride and cholesterol were measured by routine enzymatic methods. Serum high-density lipoprotein cholesterol (HDL-cholesterol) and low-density lipoprotein cholesterol (LDL-cholesterol) were measured using the colorimetric method. Serum uric acid was determined using the colorimetric enzymatic method. All biochemistry indices were measured with an automatic biochemical analyzer (TBA-40, Tokyo, Japan).

A structured questionnaire was used to elicit detailed information on demographic factors, physical activity, and tobacco and alcohol use. Current smokers were defined as those who smoked at least one cigarette per day and non-smokers were defined as those who were either former smokers or never smoked a cigarette in their lives. Those who had stopped smoking for less than a year were classified as smokers. A participant was classified as a drinker in the case of having drunk beer or any other alcoholic beverage during the last year. Physical activity was recorded as a three-level variable (light, moderate, and heavy), as recommended by the China Nutrition Society (14) to reflect total energy expenditure. Participants responded to standardized questionnaires and the questionnaires were examined by trained investigators.

Statistical methods. Data were analyzed using SPSS software (SPSS Inc., Chicago, IL, Version 16). Factor analysis (principal component) was used to identify dietary patterns based on the 20 food groups from the FFQ. To identify major dietary patterns based on the 33 food items, we used principal component analysis with orthogonal rotation. Factors with Eigenvalues $\geq 1.5$ were defined as major dietary patterns. An orthogonal rotation procedure, the varimax rotation, was then applied to achieve a more simplistic structure with greater interpretability. The derived factors were labeled on the basis of interpretation of the data and the earlier literature. Factor scores for each pattern were calculated as the sum of the products of the factor loading coefficients and the standardized daily intake of each food associated with that pattern. For each factor, participants were grouped into 3 categories according to tertiles of factor scores among the control population. We estimated the odds ratio (OR) and the corresponding 95% confidence interval (CI) for each tertile, using unconditional multiple regression models adjusted for various confounding variables including age, sex (men/women), education level ($\leq 10$ y/$11–14$ y/$\geq 15$ y), physical activity (light, moderate, and heavy), smoking status (never smoked/smoker), drinking status (never drunk/drinker) and BMI (categorical variable). Tests for linear trend were also calculated assigning to each subject the median value of each factor within the tertile class. Since numerous studies have indicated the strong relation between blood lipids and asymptomatic hyperuricemia (9, 10, 12), we further included blood lipids in the model to assess whether the associations between dietary patterns and asymptomatic hyperuricemia were mediated by blood lipids status. $p<0.05$ was considered significant.

RESULTS

The general characteristics of the participants are shown in Table 1. Education level was significantly different between the cases and the controls, whereas there were no significant differences in age or lifestyle factors including smoking status, drinking status and physical activity level between the cases and the controls. The cases had significantly higher serum uric acid levels, education levels. BMI, total cholesterol, triglyceride and LDL-cholesterol than the controls.

Three major dietary patterns were identified by the factor analysis: 1) an animal products and fried food pattern (high in pork, eggs, animal giblets, poultry and fried wheat products while low in vegetables and fruits),
a western pattern (high in beef, lamb, cake, and beverages, including juice and alcoholic beverages) and a soybean products and fruit pattern (high in soybean products, fruits, vegetables and starchy tubers). In total these dietary patterns explained 36.1% of the variations in dietary intake. Loading factors of foods or food groups across these major food patterns are presented in Table 2.

Odds ratios for asymptomatic hyperuricemia across tertiles of major dietary pattern score are presented in Table 3. In multivariate analyses those in the upper tertile of the “animal products and fried food” pattern had greater odds of asymptomatic hyperuricemia (OR = 2.15, 95% CI: 1.22–3.76) and the “soybean products and fruit” pattern was associated with lower odds of asymptomatic hyperuricemia (OR = 0.32, 95% CI: 0.19–0.57) after adjusting for age, sex, education level (continuous), alcohol consumption, physical activity level, smoking status and body mass index. The significant association of these two patterns (“animal products and fried food” pattern and “soybean products and fruit” pattern) and asymptomatic hyperuricemia persisted after further adjusting for blood lipids. All the quoted factors displayed significant p-values for linear trend. Finally, the western pattern was not associated with risk of asymptomatic hyperuricemia.

**DISCUSSION**

In this study, we identified three major dietary patterns and associated them with asymptomatic hyperuricemia taking account of blood lipids among Chinese adults. The “animal products and fried food” dietary pattern might be positively associated with the risk of asymptomatic hyperuricemia, whereas the “soybean products
and fruit pattern” dietary pattern might be negatively associated with the risk of asymptomatic hyperuricemia. The associations were both independent of blood lipids. On the other hand, the western dietary pattern was not associated with asymptomatic hyperuricemia.

The “animal products and fried food” and the “soybean products and fruit pattern” we found related to asymptomatic hyperuricemia are consistent with previous reports (4, 6, 8, 15, 16). The pattern labeled as “animal products and fried food,” which was positively associated with asymptomatic hyperuricemia risk, revealed a clear eating style: these individuals preferred

<table>
<thead>
<tr>
<th>Dietary patterns</th>
<th>Tertiles of factor score</th>
<th>Serum uric acid (mg/dL)</th>
<th>Cases/Controls</th>
<th>Model 1 OR (95% CI)</th>
<th>Model 2 OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Min</td>
<td>Max</td>
<td>Continuous</td>
<td>p-value for trend</td>
</tr>
<tr>
<td>Animal products and fried foods pattern</td>
<td>lower</td>
<td>5.5</td>
<td>2.6</td>
<td>10.6</td>
<td>42/64</td>
</tr>
<tr>
<td></td>
<td>middle</td>
<td>6.5</td>
<td>3.5</td>
<td>12.6</td>
<td>65/61</td>
</tr>
<tr>
<td></td>
<td>upper</td>
<td>6.9</td>
<td>2.6</td>
<td>13.0</td>
<td>80/62</td>
</tr>
<tr>
<td>Western pattern</td>
<td>lower</td>
<td>5.9</td>
<td>3.1</td>
<td>13.0</td>
<td>52/64</td>
</tr>
<tr>
<td></td>
<td>middle</td>
<td>6.3</td>
<td>2.6</td>
<td>10.6</td>
<td>59/60</td>
</tr>
<tr>
<td></td>
<td>upper</td>
<td>6.9</td>
<td>2.6</td>
<td>10.6</td>
<td>76/63</td>
</tr>
<tr>
<td>Soybean products and fruit pattern</td>
<td>lower</td>
<td>7.0</td>
<td>2.6</td>
<td>13.0</td>
<td>101/62</td>
</tr>
<tr>
<td></td>
<td>middle</td>
<td>6.1</td>
<td>2.6</td>
<td>10.6</td>
<td>50/63</td>
</tr>
<tr>
<td></td>
<td>upper</td>
<td>5.6</td>
<td>3.1</td>
<td>10.6</td>
<td>36/62</td>
</tr>
</tbody>
</table>

OR: odds ratio. 95% CI: 95% confidence interval.
Model 1: adjusted for age, sex (men/women), education level (≤10 y/11–14 y/≥15 y), physical activity (light, moderate, and heavy), smoking status (never smoked/smoker), drinking status (never drank/drinker) and BMI (categorical variable).
Model 2: Model 1 plus blood lipids (cholesterol, triglycerides, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol).
pork, eggs, animal giblets, poultry and fried wheat products combined with low intakes of vegetables and fruits. Choi et al. (17) have indicated that higher levels of consumption of animal products (meat and seafood) are associated with an increased risk of gout. The multivariate relative risk in the highest quintile of total meat intake, as compared with those in the lowest quintile, was 1.41 (95% CI, 1.07–1.86; p for trend=0.02), and the corresponding relative risk associated with seafood intake was 1.51 (95% CI, 1.17–1.95; p for trend=0.02) (17). High-protein diets were associated with increased urinary uric acid excretion and may reduce the blood uric acid level (18). It is well known that a high-protein diet lowers triglycerides (19), is satiating (20, 21), promotes weight loss (22) and increasing evidence supports the notion that it may improve insulin sensitivity (23). However, the animal products and fried food pattern involved fat and total calorie intake, in combination with decreased physical activity, leading to overall obesity with centripetal deposition of fat (24). In a study from Taiwan, waist to height ratio, which indicates central obesity, was found to have a significant linear effect on gout occurrence, independent of body mass index (25). Centripetal obesity, in turn, is a powerful stimulus for increased plasma insulin levels and therefore, for hyperuricemia (24). Thus, lowering fat-rich (animal source) foods may decrease the risk of asymptomatic hyperuricemia.

The other protective pattern, labeled as the “soy products and fruit” pattern involved high loadings for total soybean products, fruits, vegetables and starchy tubers. Previous studies (4, 8) demonstrated the association between soybean food and the prevalence of hyperuricemia or gout. Soy protein was demonstrated to increase the serum uric acid concentrations in healthy subjects (26). Soy food is the predominant plant source of protein in China; it contains other nutrient components such as fiber, isolavones and polyunsaturated fats. One study in Japan to examine the effect of tofu on uric acid metabolism in gout and found no significant increase in plasma or urine uric acid concentrations or in uric acid clearance in gout patients with normal uric acid clearance (27). Similarity, another study compared the serum uric acid concentrations in vegetarians who usually consumed a fairly large amount of soy products as protein sources with those in nonvegetarians and found lower serum uric acid concentrations in the vegetarians (28). Soybean products (tofu) are rich in protein, but most of the purines are lost during processing, and ingestion of tofu produces only a small rise of serum uric acid in both healthy individuals and gout sufferers (27). Lyu et al. (25) suggested that purines are not an important risk factor for hyperuricemia and gout, because in their study of Taiwanese vegetarians who eat mainly plant food and soybean products (a diet high in purines), the risk of developing hyperuricemia and gout was lower. They concluded that food sources rich in dietary fiber, folate and vitamin C, such as fruit and vegetables, protect against hyperuricemia and gout. Vitamin C and uric acid are reabsorbed through anion-exchange transport in the proximal tubule (29). Increased vitamin C concentration in the filtrate may competitively inhibit uric acid reabsorption (30). Both human and animal studies have demonstrated that administration of vitamin C increases renal plasma flow and glomerular filtration rate (31, 32) to lower serum uric acid concentration. Vitamin C could reduce oxidative stress and inflammation to lower uric acid synthesis (33). Fiber has been recognized as having a potential role in binding uric acid in the gut for excretion because approximately two-thirds of the uric acid produced each day is excreted in urine and one-third is eliminated directly in intestinal secretions and saliva (34). Therefore, the “soybean products and fruit” pattern has been suggested to protect against hyperuricemia in our study.

The western pattern involved high loadings for beef, lamb, cake, juice and alcoholic beverages. Although the component is high, this factor was not associated with the risk of asymptomatic hyperuricemia. It differed from previous studies which have suggested that juice and alcoholic beverages increase the risk of hyperuricemia or gout (6, 35).

In our study a higher blood lipid level was often found in individuals with asymptomatic hyperuricemia. The associations of major dietary patterns could be directly linked to the blood lipids or the foods may have an indirect effect on uric acid through improving the lipid profile. We evaluated the associations of major dietary patterns and asymptomatic hyperuricemia after further adjusting for blood lipids. Finally, we observed two major dietary patterns (“animal products and fried food” pattern and “soybean products and fruit” pattern) remained significant, independent of blood lipids. Although asymptomatic hyperuricemia is the precursor of gout, only 5% of hyperuricemia patients developed clinical symptoms of gout (36, 37). Therefore, most physicians believe that asymptomatic hyperuricemia does not need any treatments. However, since hyperuricemia is considered a risk factor for cardiovascular disease (9, 10, 38), and it has been associated with metabolic syndrome components including obesity, diabetes mellitus, lipid abnormalities, and hypertension in some studies (12, 39–43), prevention should be prioritized.

The current study suggested that it is important to prevent asymptomatic hyperuricemia through dietary pattern modifications to reduce the risk of related diseases or serious consequences such as cardiovascular disease and metabolic syndrome.

Potential limitations of our study should not be overlooked. Because of our use of a case-control study, we cannot formally draw conclusions about causality. But it should be noted that when dietary patterns are investigated, it is unlikely that reverse causality has played a role. Furthermore, data on dietary intake were collected by questionnaires referring to a period of 1 y, and dietary habits may change over a lifetime. These changes may have an additional impact on asymptomatic hyperuricemia. However, these problems are mitigated by the exclusion of patients who were known to have asymptomatic hyperuricemia and dyslipidemia prior to the
survey from the analyses. In addition, lack of detailed information on foods (e.g., types of vegetables and fruits) also made it difficult to characterize dietary patterns in more detail. Although we have adjusted for major socio-demographic characteristics and lifestyle factors simultaneously, residual confounding by unknown or unmeasured factors may be present. Conversely, given the magnitude of many of the risk estimates and consistency of our results with prior controlled trials and cohort studies of some dietary patterns, it is improbable that all of the observed risk differences should be attributed to the results of residual confounding.

In conclusion, major dietary patterns (“animal products and fried food” pattern and “soybean products and fruit” pattern) identified by factor analysis significantly associated with asymptomatic hyperuricemia among Chinese adults, independent of blood lipids. Further prospective studies are needed to prove these relationships, and to provide sound evidence for specific diet intervention strategies for individuals with different dietary patterns.

Acknowledgments
The authors wish to thank all who participated in the study and the staff at the Medical Check-up Centre of Heping District, Tianjin, who assisted the study. This study is supported by a grant from Tianjin Natural Science Foundation (No. 10JCZDJC18700) and by the combined support of the Innovation Funding for graduating students of Tianjin Medical University, third phase of the 211 Project for Higher Education (No. 2009GSI05). None of authors had a financial interest or professional affiliation that compromised the scientific integrity of this work.

REFERENCES
23) Reaven GM. 1997. Do high carbohydrate diets prevent the development or attenuate the manifestations (or both) of syndrome X? A viewpoint strongly against. Curr Opin Lipidol 8: 23–27.


