



Nut intake and hyperuricemia risk in young adults

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Abstract

Objective: The relationship between dietary nut intake and hyperuricemia risk remains unclear. The aim of this study was to investigate the relationship between different nut intake and hyperuricemia risk with a cross-sectional study.

Design: A semi-quantitative FFQ was adopted to collect dietary information. Biochemical and anthropometric parameters were measured by standard methods. Multivariate-adjusted logistic regression models were implemented to analyse the relationship between individual nut intake and hyperuricemia risk.

Setting: Qingdao University in Shandong Province, China.

Participants: During 2018–2019, a total of 14 056 undergraduates (6862 males and 7194 females) aged 15–25 years participated in the study.

Results: After adjusting for multiple confounding factors, compared with the lowest quartile, the highest quartile intakes of pine nut (95 % CI (0.51, 0.98)) was significantly associated with 29 % reduction in hyperuricemia risk, the highest quartile intake of walnut (OR = 0.78; 95 % CI (0.58, 1.05)) was marginally negatively associated with hyperuricemia risk.

Conclusions: The present study showed that the relationships between intakes of different nuts and hyperuricemia risk were different. Increased dietary intakes of walnut and pine nut are negatively associated with the hyperuricemia.

Keywords

Nut

Hyperuricemia

Young adult

Cross-sectional study

Hyperuricemia is caused by the excessive secretion of uric acid in the liver, and/or by the decrease of uric acid excretion in the kidney or intestine, resulting in accumulation of uric acid in the body⁽¹⁾. Approximately a quarter of patients with hyperuricemia will develop gout⁽²⁾, which is a common rheumatic disease characterised by the deposition of sodium urate crystals around the joints⁽³⁾, affecting patient's activities and daily life. Besides, an increasing body of evidence have demonstrated that hyperuricemia is a risk factor associated with chronic diseases, such as hypertension, diabetes, metabolic syndrome, CHD and chronic kidney disease^(4,5). Thus, it is urgent and necessary to identify the protective factors in the prevention of hyperuricemia. Plenty of factors have been reported to be associated with the initiation and progression of hyperuricemia, such as gene, gender, age, lifestyle, dietary habits, drug treatment and economic development. Regarding the changeable factors, dietary factors play a pivot role in the prevention of hyperuricemia. Several diets are associated with elevated levels of blood uric acid and might trigger hyperuricemia, such as excessive intakes of meat, meat

broth, seafood, beer and sweets, while moderate intakes of vegetable and fruit, dietary fibre, and vitamin C have been reported to be negatively associated with hyperuricemia risk^(6–9).

Nuts are rich in essential fatty acids, high-quality protein, various vitamins and trace elements. Different types of nuts have different nutrient contents, which might provide differential effects in the prevention of hyperuricemia. So what is the effect of nut intake on serum uric acid? A randomised controlled trial (RCT) found that supplemental Pakistani almond and American almond had a reduced effect on serum uric acid levels in patients with CHD⁽¹⁰⁾. Conversely, another randomised controlled trial demonstrated that supplemental walnut and salt-free cashew nut had no significant effect on serum uric acid concentration and other biochemical parameters in patients with metabolic syndrome⁽¹¹⁾. To date, no study has assessed the relationship between different types of nut intake and hyperuricemia risk. Therefore, by using the data from the Health Check Program of Undergraduates (HCPU), the present study comprehensively investigated the relationship between different nut intake and hyperuricemia risk with a cross-sectional study.

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Methods

Study population and design

We conducted a cross-sectional study of undergraduates who participated in the HCPU at Qingdao University from August 2018 to October 2019 to evaluate whether dietary intake, lifestyle and other factors are associated with the risk factors of chronic disease. A total of 16 211 undergraduates who took part in health check programme were recruited. Undergraduates who voluntarily completed the semi-quantitative FFQ were included in the cross-sectional study. Participants who did not complete the FFQ, with a history of malignancy, liver, CVD and metabolic diseases were excluded. Finally, 14 056 participants were included in the statistical analysis. This study was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University (Qingdao University, China). All undergraduate participants signed written informed consent forms. This study was conducted in accordance with the criteria set out in the Declaration of Helsinki.

Dietary nut intake

The dietary intakes of different nuts were assessed by a semi-quantitative FFQ designed by trained dietitians from the Department of Nutrition, the Affiliated Hospital of Qingdao University. The type, frequency (daily, weekly and monthly) and dose (servings) of nut consumed by participants in the previous months were investigated. We have pre-defined a small handful without shells as one serving, namely 25 g. The dietary intakes of nuts were transformed into g/d. The semi-quantitative FFQ contained the following nut: peanut, melon seed, pine nut, pistachio, cashew, pecan, walnut, almond and daily nut. Among them, daily nut is a packaged food with mixed nuts. The mean intake of total nuts of the subjects is 35.63 ± 60.79 g/d, composed of peanut, melon seed, pine nut, pistachio, cashew, pecan, walnut, almond and daily nut.

Physical examination

Anthropometric information, including systolic blood pressure and diastolic blood pressure (mmHg), height (m) and weight (kg), was measured by well-trained nurses in accordance with standard procedures. BMI (kg/m^2) was calculated by dividing weight in kilograms by height in square metres.

Biochemical measurement

Participants were required to fasting for at least 10 h, and their venous blood was collected in a vacuum sampling vessel for laboratory examination. The serum was obtained by centrifugation (4000 rpm for 10 min at 4°C) for biochemical analysis. The outcome of interest was uric acid, which was determined by enzyme colorimetry and uricase-peroxidase method (Accute TBA-40FR autoanalyser, Toshiba). Male participants with serum uric acid

$\geq 416.0 \mu\text{mol}/\text{l}$ ($7.0 \text{ mg}/\text{dl}$) and female participants with serum uric acid $\geq 357.0 \mu\text{mol}/\text{l}$ ($6.0 \text{ mg}/\text{dl}$) were defined as hyperuricemia⁽¹²⁾. In addition, automatic biochemical analyser was adopted to measure blood glucose and lipid profiles.

Statistical analysis

Shapiro–Wilk test was conducted to check whether the distribution of continuous variables was normal. If the variable was a normal distribution, the data were expressed as the mean and standard deviation. For skewed variables, the data were presented as median (quartile range). The continuous variables were compared by using *t* test, and the categorical variables were analysed with chi-square test (χ^2).

Dietary exposure to different types of nuts (peanut, melon seed, pine nut, pistachio, cashew, pecan, walnut, almond, daily nut and total nut) was classified by quartiles (quartile 1: < 25 th percentile, quartile 2: ≥ 25 th– 50 th percentile, quartile 3: ≥ 50 th– 75 th percentile and quartile 4: ≥ 75 th percentile), and each quartile intake was compared with the lowest category. Logistic regression model was implemented to calculate OR and 95 % CI, by using the lowest category as reference. Multivariable-adjusted models were adopted to assess the association between individual nut intake and hyperuricemia, the model 1 was adjusted for age, gender, BMI, blood pressure, serum concentrations of glucose, total cholesterol, TAG and HDL-cholesterol, model 2, as model 1 added physical activity, dietary intakes of total energy, total carbohydrate, total protein and total fat, dietary intakes of candies, meat (pork, beef and mutton), soup (poultry and cattle broth, fish and shrimp soup) and seafood. Besides, the individual nut items were included in the multivariable-adjusted model and adjusted for each other. The trend test was performed by assigning a median value to each category and modelling the variable as a continuous variable⁽¹³⁾. Subgroup analyses stratified by gender and BMI were conducted to assess potential interaction with this variable. Statistical analyses were conducted with STATA 15.0 (Stata Corp.), and two-tailed *P*-value < 0.05 was considered as statistically significant.

Results

Baseline characteristics of the participants are shown in Table 1. A total of 16 211 undergraduates at Qingdao University participated in the HCPU. Among them, 14 056 participants (6862 males and 7194 females) aged 15–25 years completed the semi-quantitative FFQ and were included for data analysis. Among them, 5767 participants were identified as hyperuricemia (41 %). The prevalence of male participants (53.4 %) was significantly higher than that of female participants (29.3 %) ($P < 0.001$). The BMI and fasting blood glucose levels of hyperuricemia participants

Table 1. The baseline characteristics of the participants

Characteristics	Hyperuricemia (total)						Hyperuricemia (male)						Hyperuricemia (female)					
	Yes			No			Yes			No			Yes			No		
	Mean	SD	P-value	Mean	SD	P-value	Mean	SD	P-value	Mean	SD	P-value	Mean	SD	P-value	Mean	SD	P-value
Number of participants	5767	8289		3662	3200		2105	5089		2105	5089		2105	5089		2105	5089	
<i>n</i>	41.0 %	59.0 %		53.4 %	46.6 %		29.3 %	70.7 %		29.3 %	70.7 %		29.3 %	70.7 %		29.3 %	70.7 %	
Age, year	18.22	0.84	0.83	18.26	0.85	0.762	18.15	0.77	0.078	18.15	0.77	0.078	18.15	0.77	0.078	18.18	0.78	0.145
BMI, kg/m ²	22.77	4.20	2.88	23.26	4.38	<0.001	20.74	3.26	<0.001	20.74	3.26	<0.001	21.93	3.73	<0.001	20.14	2.58	<0.001
TAG, mmol/l	0.83	0.34	0.27	0.85	0.35	<0.001	0.76	0.30	<0.001	0.76	0.30	<0.001	0.81	0.31	<0.001	0.74	0.25	<0.001
Total cholesterol, mmol/l	3.99	0.74	0.66	3.94	0.73	<0.001	3.61	0.63	<0.001	3.61	0.63	<0.001	4.07	0.76	<0.001	3.83	0.66	<0.001
HDL-cholesterol, mmol/l	1.38	0.31	0.29	1.31	0.27	<0.001	1.36	0.26	<0.001	1.36	0.26	<0.001	1.50	0.34	<0.001	1.55	0.29	<0.001
Glucose, mmol/l	4.51	0.64	0.60	4.52	0.65	<0.001	4.19	0.60	<0.001	4.19	0.60	<0.001	4.48	0.62	<0.001	4.29	0.61	<0.001
Uric acid, μmol/l	473.35	84.24	56.05	507.60	78.44	<0.001	355.09	44.15	<0.001	355.09	44.15	<0.001	413.76	56.11	<0.001	284.97	44.64	<0.001

P for difference between genders was conducted by chi-square test, and the other parameters were analysed with *t* test.

were significantly higher than those of normal subjects. Participants with hyperuricemia had higher levels of TAG and total cholesterol and lower levels of HDL-cholesterol than normal participants ($P < 0.001$). There was no significant difference in age between the participants ($P < 0.001$).

In crude logistic regression model, compared with the lowest quartile, the highest quartile intakes of peanut (OR = 1.18; 95 % CI (1.07, 1.29); $P_{\text{for trend}} < 0.001$), melon seed (OR = 1.17; 95 % CI (1.07, 1.28); $P_{\text{for trend}} < 0.001$), cashew (OR = 1.11; 95 % CI (1.01, 1.22); $P_{\text{for trend}} = 0.001$) and total nut (OR = 1.10; 95 % CI (1.00, 1.21); $P_{\text{for trend}} = 0.011$) were positively associated with the hyperuricemia risk (see online Supplemental Figs. 1–3 and 8). Non-significant association was found for other nuts (Figs. 1–2 and Supplemental Figs. 4–7) in the crude model. The positive association between hyperuricemia risk and peanut, melon seed, cashew, and total nut were disappeared in model 1, adjusting for age, gender, BMI, blood pressure, serum concentrations of glucose, total cholesterol, TAG, HDL-cholesterol and individual nut intake, but walnut (OR = 0.77; 95 % CI (0.57, 1.03); $P_{\text{for trend}} = 0.039$) intake was marginally negatively associated with the hyperuricemia risk (Fig. 2). After further adjustment for dietary information (intakes of energy, carbohydrate, protein, fat, candies, meat, soup and seafood) and physical activity in model 2, the highest quartile of pine nut (OR = 0.71; 95 % CI (0.51, 0.98); $P_{\text{for trend}} = 0.061$) intake, compared with the lowest quartile, was inversely associated with the risk of hyperuricemia (Fig. 1). Walnut (OR = 0.78; 95 % CI (0.58, 1.05); $P_{\text{for trend}} = 0.047$) intake remained the marginally negatively association with hyperuricemia risk in model 2 (Fig. 2).

The associations between hyperuricemia and dietary individual and total nut in stratified analyses by gender are shown in Supplemental Table 1. Only pine nut intake (OR = 0.63; 95 % CI (0.39, 1.03); $P_{\text{for trend}} = 0.087$) showed a marginally inversely association with hyperuricemia risk in model 2 stratified by female. No significant associations were found between hyperuricemia risk and other dietary nut intake in crude and adjusted model stratified by gender.

The associations between hyperuricemia and dietary individual and total nut in stratified analyses by BMI are shown in Supplemental Table 2. For participants with BMI ≤ 24 , the highest quartile of peanut (OR = 1.23; 95 % CI (1.11, 1.37); $P_{\text{for trend}} = 0.001$), melon seed (OR = 1.21; 95 % CI (1.09, 1.34); $P_{\text{for trend}} < 0.001$), pistachio (OR = 1.13; 95 % CI (1.02, 1.26); $P_{\text{for trend}} = 0.004$), cashew (OR = 1.18; 95 % CI (1.06, 1.32); $P_{\text{for trend}} = 0.001$), almond (OR = 1.12; 95 % CI (1.01, 1.24); $P_{\text{for trend}} = 0.029$), daily nut (OR = 1.16; 95 % CI (1.04, 1.29); $P_{\text{for trend}} = 0.010$) and total nut (OR = 1.17; 95 % CI (1.05, 1.31); $P_{\text{for trend}} = 0.012$) intake, compared with the lowest quartile, were positively associated with hyperuricemia risk in crude model. After further adjustment in model 1 and model 2, the positive

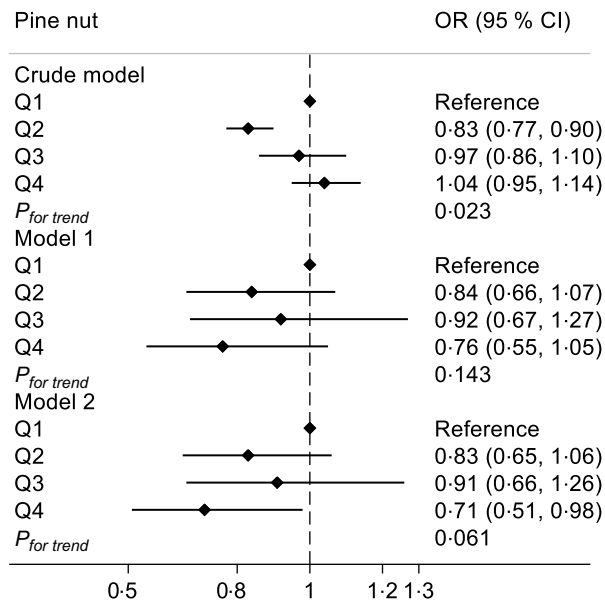


Fig. 1. Association of pine nut intake with hyperuricemia risk. Number of participants in each quartile: Q1, 4401; Q2, 4827; Q3, 1437; Q4, 3391

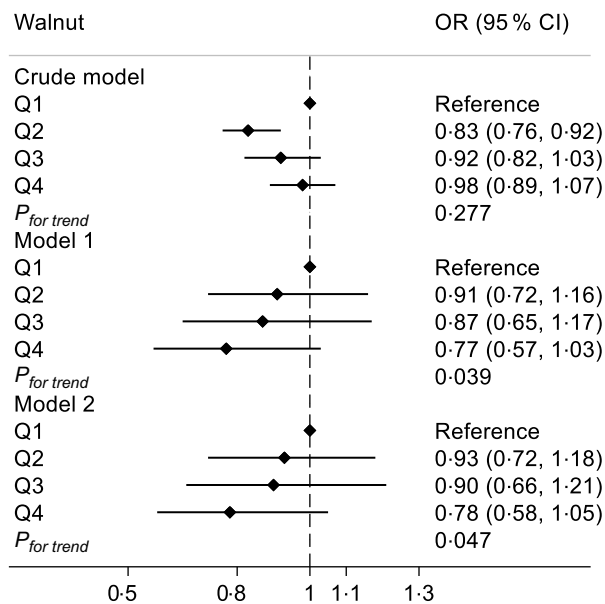


Fig. 2. Association of walnut intake with hyperuricemia risk. Number of participants in each quartile: Q1, 3573; Q2, 4926; Q3, 1631; Q4, 3926

correlations between hyperuricemia risk and peanut, melon seed, pistachio, cashew, almond, daily nut and total nut were disappeared. In model 2, dietary intakes of pine nut (OR = 0.71; 95% CI (0.49, 1.03); *P*_{for trend} = 0.081) and walnut (OR = 0.73; 95% CI (0.52, 1.03); *P*_{for trend} = 0.047) were marginally inversely associated with the hyperuricemia risk. No significant associations were found between hyperuricemia risk and dietary individual and total nut

intake in crude and adjusted model for participants with BMI ≤ 24.

Discussion

To the best of our knowledge, this study was the first to comprehensively investigate the relationship between individual nut intake and hyperuricemia risk with a cross-sectional study. The results showed that dietary higher intakes of pine nut and walnut were negatively associated with hyperuricemia risk.

The prevalence of hyperuricemia varies greatly in different geographic regions, which is associated with local eating habits. Previously, a national cross-sectional survey of 13 provinces in Chinese, including rural and urban areas, demonstrated that the prevalence of hyperuricemia was 8.4% from 2009 to 2010⁽¹⁴⁾, while another study conducted in a rural area of Henan Province showed that the prevalence of hyperuricemia in adults was 12.6% from 2015 to 2017⁽¹⁵⁾. In the present study, the prevalence of hyperuricemia was as high as 41%, which was significantly higher than previous studies. It could be explained by the following reasons. First, Qingdao is a coastal city, rich in all kinds of seafood. Second, Qingdao's specialty, Tsingtao Beer is well known, and both foods are rich in purines. Therefore, diet composition is an important variable factor contributing to hyperuricemia. Different kinds of nuts contain differential fatty acids, vitamins and trace elements. Therefore, it may have differential effects in preventing hyperuricemia.

In the present study, higher intakes of walnut and pine nut were negatively associated with hyperuricemia risk. Also both walnut and pine nut are nutritious foods, but each has its own unique ingredients. Generally speaking, these nuts are rich in MUFA and PUFA, protein, dietary fibre, vitamins, minerals, polyphenols and antioxidants^(16,17). The specific nutrient composition and content are shown in Table 2. It is generally accepted that nuts are high energy density food, because their fat content is as high as 42–76 g per 100 g. However, diet rich in nuts does not appear to be obesity but was associated with reduced risk of obesity^(18,19), which might be due to the low content of SFA and high content of MUFA and PUFA in nuts⁽²⁰⁾, as shown in Table 2, walnut and pine nut contain more PUFA than other nuts. In the renal tubules of the human kidney, the urate in the crude urine is mainly reabsorbed into the blood through the pathway mediated by urate transporter 1 (URAT1). It has been reported that unsaturated fatty acids, especially long-chain unsaturated fatty acids, can inhibit the uric acid reabsorption role of URAT1⁽²¹⁾. Additionally, several studies have found that minerals in nut, such as Mg, are negatively correlated with hyperuricemia, and its mechanism might be related to inflammation⁽²²⁾. Mg deficiency was related to acute inflammatory response

Table 2. Average nutrient composition of nut (per 100 g)

Nut	Energy (kJ)	Fat (g)	SFA (g)	MUFA (g)	PUFA (g)	LA (g)	ALA (g)	Protein (g)	Fibre (g)	Folate (µg)	Ca (mg)	Mg (mg)	Na (mg)	K (mg)	P (mg)
Peanut	2373	49.2	6.3	24.4	15.6	15.6	0.00	25.8	8.5	240	92	168	18	705	376
Pine nut (dried)	2817	68.4	4.9	18.8	34.1	33.2	0.16	13.7	3.7	34	16	251	2	597	575
Pistachio	2344	45.3	5.9	23.3	14.4	14.1	0.29	20.2	10.6	51	105	121	1	1025	490
Cashew nut	2315	43.9	7.8	23.8	7.8	7.8	0.06	18.2	3.3	25	37	292	12	660	593
Pecan	2892	72.0	6.2	40.8	21.6	20.6	0.99	9.2	9.6	22	70	121	0	410	277
Walnut	2737	65.2	6.1	8.9	47.2	38.1	9.08	15.2	6.7	98	98	158	2	441	346
Almond	2424	49.9	3.8	31.6	12.3	12.3	0.00	21.2	12.5	44	269	270	1	733	481

LA, linoleic acid; ALA, α -linolenic acid.

Data for raw nuts, except where specified.

Source: US Department of Agriculture Nutrient Data Base at: <https://fdc.nal.usda.gov/fdc-app/fdc/#/?query=nut> (accessed November 2020).

mediated by Ca, N-methyl-D-aspartate, IL-6, and TNF- α , and that C-reactive protein as biomarkers of inflammation⁽²³⁾. Hyperuricemia was positively correlated with C-reactive protein, while dietary Mg intake was negatively correlated with C-reactive protein content. Therefore, we inferred that Mg intake was negatively correlated with hyperuricemia, and circulating uric acid played an important role in inflammation^(24–26). In addition, walnut can inhibit the activity of xanthine oxidase and oxidative stress, which is rich in the polyphenols and antioxidants, also reduce the production of uric acid and accelerate the excretion of uric acid^(17,27). Besides, dietary fibre in nut might also contribute to prevent hyperuricemia⁽⁸⁾ and the reasons have been summarised as follows: (1) the viscosity and water-holding capacity of dietary fibre are consistent with the absorption of purine or adenine by digestive system^(28,29) and (2) dietary fibre could promote intestinal emptying and have the potential role of binding intestinal uric acid excretion⁽²²⁾. From what has been mentioned, the synergistic effect provided by nuts could confer a lower risk of hyperuricemia. In addition, walnut and pine nut also contain bioactive components such as tocopherols, phytosterols and sphingolipids. These components might influence the production of uric acid by different pathways, but there are few studies on the relationship between bioactive components in nuts and hyperuricemia⁽³⁰⁾. Besides, elevated serum uric acid is positive correlation with obesity⁽³¹⁾. With the increase in BMI, the level of uric acid would be increased⁽³²⁾. Stratified analysis showed that BMI was a factor influencing the relationships between nuts and hyperuricemia risk. Therefore, it is necessary to control the intakes of nuts to avoid excessive energy intake, and the recommended nut intake is less than 25 g/d⁽³³⁾. Although the intake of pine nut and walnut is negatively correlated with hyperuricemia risk, due to the high oil content of nuts, people with hyperuricemia should correspondingly reduce the intake of fat from other foods to reduce complications.

The present study has several advantages worth mentioning. As far as we know, this study was the first to systematically evaluate the relationship between different nut intake and hyperuricemia risk, which showed that special nuts are beneficial for the prevention of hyperuricemia. The semi-quantitative FFQ was designed by professional dietitians in Affiliated Hospital of Qingdao University, and it has been used for more than three decades and proved to be reliable. Simultaneously, the present study had some shortcomings that needed to be addressed. First, the participants were undergraduates about 18 years of age, and the results were not representative of the general Chinese population. Second, due to the cross-sectional design of this study, it cannot reveal the causal and temporal relationship between nut intake and hyperuricemia risk. Therefore, further prospective cohort studies or intervention trials are warranted to explore these causal relationship. Third, since the nuts consumption by volunteers was not weight each time, semi-quantitative FFQ was not



accurate in estimating nuts intake. In addition, misclassification was unavoidable when using FFQ to assess dietary information. Fourth, there was no design about liquor and alcoholic beverages intake in the questionnaire. Thus, alcohol intake could not be adjusted in the multivariate adjustment model, and that might influence the final results.

Conclusion

The present study indicated that the relationships between different intakes of nuts and hyperuricemia risk are different. Increasing intakes of pine nut and walnut were negatively associated with the hyperuricemia. Further prospective studies and intervention studies are warranted to confirm the findings of the present study.

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Supplementary material

For supplementary material accompanying this, paper visit <https://doi.org/10.1017/S1368980021002998>

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