Original Article

Hyperuricemia as a possible risk factor for abnormal lipid metabolism in the Chinese population: a cross-sectional study

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Background: Previous studies have reported that there may be a close relationship between elevated serum uric acid (UA) levels and metabolic syndrome. However, the association between these two factors has not been explored explicitly. Therefore, we carried out this study to investigate the association between UA and lipid profiles.

Methods: A total of 2,482 subjects participated in this cross-sectional study using a multistage stratified sampling method. Lipid profile, glucose metabolism, and other metabolic factors were measured and classified into UA-stratified and age-stratified groups to investigate the relationship between hyperuricemia and metabolic factors. Pearson correlations and logistic regressions were utilized to further explore the association between UA and lipid profile.

Results: The individuals aged 18 to 29 years presented with high serum UA concentrations. Moreover, the prevalence of hyperuricemia was higher among men than in women. Furthermore, statistically significant positive correlations were found between UA and serum triglycerides (TG), serum total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-c). Conversely, only high-density lipoprotein cholesterol (HDL-c) was negatively correlated. Moreover, TG group status (1.70≤ TG <2.30 mmol/L) was an independent risk factor for hyperuricemia in both univariate and multivariate models.

Conclusions: This study found significant positive associations between TG, TC, LDL, and UA but an inverse relationship with HDL-c. Thus hyperuricemia may be a risk factor for abnormal lipid metabolism.

Keywords: Serum uric acid (UA); dyslipidemia; lipid profile; hyperuricemia; metabolic diseases

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Introduction

Purines are ubiquitous biomolecules that sustain life. Purines are generated by either or both of the two pathways: *de novo* purine biosynthesis or purine salvage (1). Serum uric acid (UA), the inert end-product of purine catabolism, is mainly produced by the liver and mostly excreted by the kidney (2,3). The main causes of hyperuricemia are excessive production and/or decreased UA excretion. In China, the diagnostic criteria for hyperuricemia in both men and women is a serum UA >420 μmol/L (4). A high-quality meta-analysis study, which includes articles published between 2000 and 2014, showed that the pooled prevalence of hyperuricemia in mainland China was 13.3% (95% CI: 11.9–16.4%) (5). According to the latest national cross-sectional study, the prevalence of hyperuricemia was 18.8% in people with adequate iodine status, while people living in iodine excessive areas are less likely to suffer hyperuricemia 13.7%, which indicates that iodine status may have effects on uric acid levels (6). The total prevalence of hyperuricemia in the southwest of China was 20.08% in 2017, with the majority belonging to the 20–29 age group for both men and women (7). The high prevalence of hyperuricemia in this young age group is of concern.

The relationship between serum UA levels and lipid profiles has attracted considerable attention for some time. Hyperuricemia is widely considered a key risk factor for dyslipidemia, as some studies have shown a positive association between serum UA levels and lipid profiles in the adult populations of Bangladesh, Italy and the USA (8-10). Moreover, a high UA level is recognized as an independent risk factor for hypertriglyceridemia (11). However, a recent report does not show that serum UA was associated with metabolic syndrome, which is commonly characterized by dyslipidemia, hypertension, and type 2 diabetes (12). The relationship between serum UA levels and dyslipidemia has not been fully elucidated. Additionally, large-scale based studies on Chinese people to investigate the harm hyperuricemia are still to be confirmed. Therefore, we performed a cross-sectional study including 2482 adult participants and performing in both Jiangsu and Fujian Province to assess the relationship between serum UA and lipid profiles, glucose metabolism, other metabolites, and metabolic parameters in UA-specific and age-stratified groups to identify the risk factors for hyperuricemia. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-2734).

Methods

Study participants and survey protocol

Using a multistage, stratified sampling design, a total of 2,854 adults from both urban and rural areas of the Jiangsu and Fujian Provinces were selected and enrolled in this study. Adults who had lived in these areas for at least six months were included. The exclusion criteria were as follows: pregnancy; individuals who suffered from severe adrenal insufficiency, renal failure, or other severe comorbidities; and patients taking drugs that affect UA concentration and lipid metabolism. Finally, 2,482 subjects met our criteria and were included in the analysis. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine (2021-LWKY-007), and all participants provided written informed consent.

Laboratory tests and physical examination

Blood samples were collected after overnight fasting for at least 10 h. Blood centrifugation was performed within 30 min after collection, and samples were stored at –20 ℃. Fasting blood glucose (FBG), two-hour blood glucose, serum triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and UA levels were measured using an automatic biochemical machine (COBAS 8000, Roche, Basel, Switzerland). Hemoglobin A1c (HbA1c) was measured using high-performance liquid chromatography (VARIANT II Hemoglobin Analyzer, Bio-Rad, Hercules, CA, USA). Blood pressure was measured using an electronic blood pressure monitor (Omron HEM 7430, Omron Corporation, Kyoto, USA) twice after a five-minute rest.

Reference ranges and diagnosis criteria

In the present study, hyperuricemia was defined as UA >420 μmol/L, following the Guidelines for the Diagnosis and Management of Hyperuricemia and Gout in China (4). UA levels were classified into four categories according to their interquartile ranges: Q1 <243 μmol/L, 243≤ Q2 <283 μmol/L, 283≤ Q3 <343 μmol/L, and Q4 ≥343 μmol/L.

Lipid profile stratifications were classified in accordance with the Guidelines for Prevention and Treatment of Dyslipidemia in Adults in China (13). Body mass index (BMI) was categorized as underweight (<18.5 kg/m^2), normal weight (18.5≤ BMI <24.0 kg/m^2), overweight (24.0≤ BMI <28.0 kg/m^2), and obese (≥28 kg/m^2) (14). Chinese guidelines are available on blood pressure and serum glucose concentration categories (15,16). Normal thyroid-stimulating reference values ranged from 0.27 to 4.20 mIU/L, according to the manufacturer's instructions.

Statistical analysis

All statistical analyses were performed using SPSS software (version 26.0; SPSS, Inc., Chicago, IL, USA). Normally distributed data are presented as means (SD), while variables with skewed distributions are presented as medians (interquartile ranges). Differences among age groups or UA quartile groups were compared using one-way analysis of variance tests. Chi-square tests were performed to determine the distributions, percentages, and associations between UA and other factors. Pearson correlation analysis was performed to determine the association between UA and lipid profiles. Both univariate and multivariate logistic regression analyses were used to investigate the risk factors for hyperuricemia. For all measures, a two-tailed P value of <0.05 was considered as indicating statistical significance.

Results

Characteristics of individuals in the study cohort

A total of 2,482 participants (1,249 males and 1,233 females) were enrolled in the present study (*Table 1*). The majority of individuals were younger than 60 years (84.5% men and 85.6% women). UA concentrations displayed an opposite tendency between the sexes, decreasing with age in males and increasing with age in females. According to the results above, the following analyses revealed that menopausal women were prone to have a higher UA concentration (Tables S1 and S2). The 18–29-year-old group had high levels of UA in both sexes. TC and LDL-c levels increased with aging but had a relatively lower level among women. Older participants had higher average blood pressure compared to younger participants. As for metabolic biomarkers, most participants had a normal weight and a normal range of FBG, two-hour postprandial blood glucose (2hPB), and HbA1c. Regarding thyroid-related values, TSH levels also showed an increasing trend with age in both sexes.

Characteristics of individuals stratified by UA quartiles

To investigate the association between UA and other metabolic biomarkers, we stratified individuals according to UA quartiles: Q1 (UA <234 μmol/L), Q2 (234≤ UA <284 μmol/L), Q3 (284≤ UA <345 μmol/L), and Q4 (UA ≥345 μmol/L). The average age of each group was slightly more than 40 years (*Table 2*). Similar to the age-stratified groups, we also found an inverse tendency for sex in this UA quartile stratification. The Q4 was composed mainly of males (42.2% males, 7.5% females). By contrast, the Q1 group had the largest proportion of females (43.3%) (*Table 2*). Further investigations showed that women who were menopausal had higher serum UA levels compared with those who premenopausal (Table S2). Regarding the lipid profile, TG, TC, and LDL-c increased from Q1 to Q4. Notably, participants in the Q3 and Q4 groups were overweight, with an average BMI of 24.06 and 25.20 kg/m^2, respectively. However, the first two groups had a normal weight. No statistical differences were found for FBG, 2hPBG, and HbA1c levels.

Prevalence of hyperuricemia in groups with different age stratifications

The total prevalence of hyperuricemia was 5.9% in our study, with 10.7% and 1.1% for men and women, respectively. Stratified by age groups, the prevalence of hyperuricemia presented as a U-shaped curve with the nadir at the 60–69-year-old group for both sexes, with peaks appearing for the youngest group (16.7% for men and 1.3% for women). Regardless of age group, the prevalence was consistently higher in men than in women (*Figure 1*).

Association between UA and lipid profile

Spearman correlation analysis was performed to investigate the association between UA and lipid profiles (*Figure 2*). A statistically significant positive association was revealed between UA and TG, TC, and LDL-c (r=0.275, r=0.117, r=0.180, respectively; all P<0.001). By contrast, *Figure 2C* shows that only HDL-c had a negative correlation with UA (r=–0.268, P<0.001).

Logistic regression analyses were also performed to evaluate the key risk factors for hyperuricemia (*Table 3*). In

Table 1 Characteristics of individuals across different age-stratified groups by sex

Characteristics	Total	Age group (years)						P
		18–29	30–39	40–49	50–59	60–69	≥70	
Male								
UA	330.37 (67.58)	348.96 (66.73)	339.32 (65.70)	328.63 (65.83)	315.59 (69.11)	310.46 (63.60)	310.46 (64.31)	<0.001
TG	1.57 (1.29)	1.25 (0.85)	1.80 (1.40)	1.94 (1.85)	1.54 (0.83)	1.35 (0.96)	1.06 (0.50)	<0.001
TC	5.00 (0.97)	4.08 (0.78)	4.73 (0.89)	4.94 (0.95)	5.00 (1.03)	5.16 (0.91)	4.98 (0.99)	<0.001
HDL-c	1.38 (0.34)	1.31 (0.27)	1.31 (0.29)	1.36 (0.36)	1.44 (0.39)	1.53 (0.40)	1.52 (0.36)	<0.001
LDL-c	2.60 (0.71)	2.24 (0.63)	2.63 (0.68)	2.69 (0.69)	2.74 (0.75)	2.86 (0.66)	2.80 (0.72)	<0.001
SBP	124 [15]	117 [12]	120 [12]	125 [14]	129 [17]	132 [18]	134 [16]	<0.001
DBP	82 [10]	77 [8]	81 [9]	84 [10]	85 [11]	85 [11]	84 [10]	<0.001
BMI	24.46 (3.56)	22.52 (4.00)	25.27 (3.08)	25.41 (3.46)	24.75 (2.86)	24.66 (3.15)	24.34 (3.22)	<0.001
FBG	5.58 (1.42)	5.12 (1.32)	5.39 (1.23)	5.65 (1.22)	5.99 (1.72)	6.08 (1.55)	5.82 (1.45)	<0.001
2hPG	6.33 (2.35)	5.21 (1.22)	5.98 (2.12)	6.62 (2.57)	7.14 (2.16)	7.65 (3.25)	6.90 (2.27)	<0.001
HbA1c	5.33 (0.74)	5.05 (0.36)	5.25 (0.77)	5.36 (0.64)	5.51 (0.84)	5.63 (0.92)	5.47 (1.02)	<0.001
TSH	2.78 (4.60)	2.83 (1.39)	2.88 (6.17)	2.41 (1.20)	2.30 (1.39)	2.47 (1.64)	5.06 (12.64)	<0.001
Female								
UA	249.99 (59.34)	257.43 (60.57)	240.09 (56.55)	237.33 (58.39)	253.57 (54.39)	264.35 (57.36)	266.55 (67.41)	<0.001
TG	1.30 (0.88)	0.96 (0.47)	1.10 (0.66)	1.39 (1.04)	1.56 (1.03)	1.74 (1.13)	1.48 (0.65)	<0.001
TC	4.62 (0.95)	4.00 (0.71)	4.30 (0.74)	4.73 (0.84)	5.00 (0.88)	5.31 (0.95)	5.54 (0.93)	<0.001
HDL-c	1.52 (0.36)	1.52 (0.32)	1.49 (0.31)	1.51 (0.36)	1.53 (0.38)	1.52 (0.45)	1.67 (0.45)	0.002
LDL-c	2.43 (0.67)	2.01 (0.53)	2.25 (0.53)	2.50 (0.63)	2.70 (0.64)	2.84 (0.60)	3.03 (0.71)	<0.001
SBP	118 [17]	106 [9]	111 [11]	120 [15]	125 [19]	131 [20]	137 [16]	<0.001
DBP	78 [10]	72 [6]	75 [8]	81 [10]	82 [11]	83 [11]	85 [10]	<0.001
BMI	23.10 (3.58)	20.80 (3.06)	22.55 (3.05)	23.82 (3.20)	24.74 (3.17)	24.88 (3.73)	24.39 (4.06)	<0.001
FBG	5.41 (1.24)	4.94 (0.50)	5.18 (0.59)	5.40 (1.23)	5.84 (1.71)	6.13 (2.03)	5.85 (1.01)	<0.001
2hPG	6.74 (2.11)	5.58 (1.22)	6.45 (1.61)	6.98 (1.96)	7.47 (2.17)	8.28 (2.87)	7.97 (2.94)	<0.001
HbA1c	5.31 (0.79)	4.99 (0.41)	5.11 (0.40)	5.27 (0.69)	5.63 (1.06)	5.83 (1.11)	5.69 (0.94)	<0.001
TSH	3.20 (4.71)	3.19 (5.76)	2.86 (2.35)	3.08 (4.68)	3.31 (3.12)	2.88 (1.52)	4.78 (9.39)	0.037

1. UA, TG, TC, HDL-C, LDL-C, SBP, DBP, BMI, FBG, 2hPB, HbA1c, and TSH are presented as means (SD). 2. Missing values: 1 for SBP, 1 for DBP, 4 for FBG, 179 for PBG, 21 for HbA1c. UA, serum uric acid; TG, serum triglyceride; TC, serum total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FBG, fasting blood glucose; 2hPB, two-hour postprandial blood glucose; HbA1c, hemoglobin A1c; TSH, thyroid-stimulating hormone.

the univariate model, compared with TG <1.70 mmol/L, both 1.70≤ TG <2.30 mmol/L and TG ≥2.30 mmol/L were risk factors for hyperuricemia [odds ratio (OR) =2.279, 95% confidence interval (CI): 1.463–3.549; OR =3.095 95% CI: 2.061–4.648, respectively]. The multivariate model further confirmed that 1.70≤ TG <2.30 mmol/L was an independent risk factor for hyperuricemia (OR =2.028, 95% CI: 1.250–3.291). In comparison with the individuals in the TC <5.20 mmol/L group, those in the group with TC ≥6.20 mmol/L were more likely to suffer from hyperuricemia

Table 2 Characteristics of different uric-acid-stratified groups

Characteristics	Q1	Q2	Q3	Q4	P
Age*	43.36 (14.33)	43.28 (15.68)	43.23 (16.39)	40.32 (16.17)	0.001
Sex*					<0.001
Male	7.5% (n=94)	17.2% (n=215)	33.1% (n=413)	42.2% (n=527)	
Female	43.3% (n=534)	32.0% (n=394)	17.2% (n=212)	7.5% (n=93)	
TG*	1.12 (0.72)	1.27 (0.78)	1.46 (1.00)	1.87 (1.58)	<0.001
TC*	4.50 (0.91)	4.67 (0.93)	4.72 (0.97)	4.82 (1.03)	<0.001
HDL-c*	1.56 (0.36)	1.49 (0.38)	1.42 (0.34)	1.33 (0.32)	<0.001
LDL-c*	2.33 (0.63)	2.50 (0.68)	2.58 (0.70)	2.67 (0.74)	<0.001
SBP*	117 [16]	120 [17]	123 [17]	124 [16]	<0.001
DBP*	78 [10]	79 [11]	81 [10]	82 [10]	<0.001
BMI*	22.60 (3.26)	23.27 (3.47)	24.06 (3.71)	25.20 (3.55)	<0.001
FBG	5.48 (1.55)	5.53 (1.31)	5.56 (1.45)	5.43 (0.97)	0.381
2hPBG*	6.48 (1.79)	6.75 (2.71)	6.45 (2.18)	6.46 (2.19)	0.071
HbA1c	5.33 (0.92)	5.34 (0.79)	5.32 (0.75)	5.28 (0.55)	0.585
TSH	3.08 (4.78)	3.07 (5.92)	2.81 (1.90)	2.99 (5.08)	0.693

1. Q1 serum uric acid (UA) <234 μmol/L; Q2 234≤ UA <283 μmol/L; Q3 283≤ UA <343 μmol/L; Q4 UA ≥343 μmol/L. 2. *, P<0.05. 3. Age, TG, TC, HDL-C, LDL-C, TSH, SBP, DBP, BMI, FBG, 2hPB, HbA1c are presented as means (SD). Sex is presented as percentage (counts). 4. Missing values: 1 for SBP, 1 for DBP, 4 for FBG, 179 for PBG, 21 for HbA1c. TG, serum triglyceride; TC, serum total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TSH, thyroid-stimulating hormone; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FBG, fasting blood glucose; 2hPB, two-hour postprandial blood glucose; HbA1c, hemoglobin A1c.

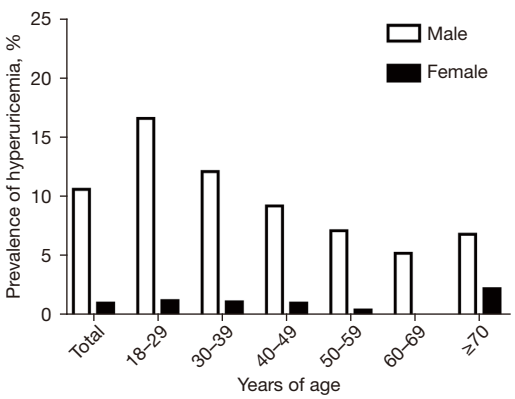

Figure 1 Prevalence of hyperuricemia by age-stratified groups.

(OR =7.746, 95% CI: 2.323–17.427). With LDL-c <2.60 mmol/L as reference group, both 2.60≤ LDL-c <3.40 mmol/L and LDL-c ≥4.10 mmol/L were risk factors for hyperuricemia (OR =2.846, 95% CI: 1.628–4.975; OR =5.029, 95% CI: 2.707–9.341). By contrast, participants who had a higher level of HDL-c (HDL-c >1.0 mmol/L) seemed to be affected less by hyperuricemia (OR =0.405, 95% CI: 0.257–0.640). Additionally, female sex was also a protective factor against hyperuricemia (OR =0.089, 95% CI: 0.050–0.158), while people who were obese were at increased risk for hyperuricemia (OR =2.914, 95% CI: 1.874–4.530, adjusted OR =1.974, 95% CI: 1.183–3.293).

Discussion

Compared with the other age groups, our results showed that individuals aged 18 to 29 years presented with high serum UA concentrations, which may be related to their living standards and lifestyles. First, the improvements in living standards mean that there is no shortage of food supply. Indeed, individuals in this younger age group may have excessive food intake, which significantly increases the risk of hyperuricemia. Young people with heavy study loads also typically have a sedentary lifestyle and may thus be

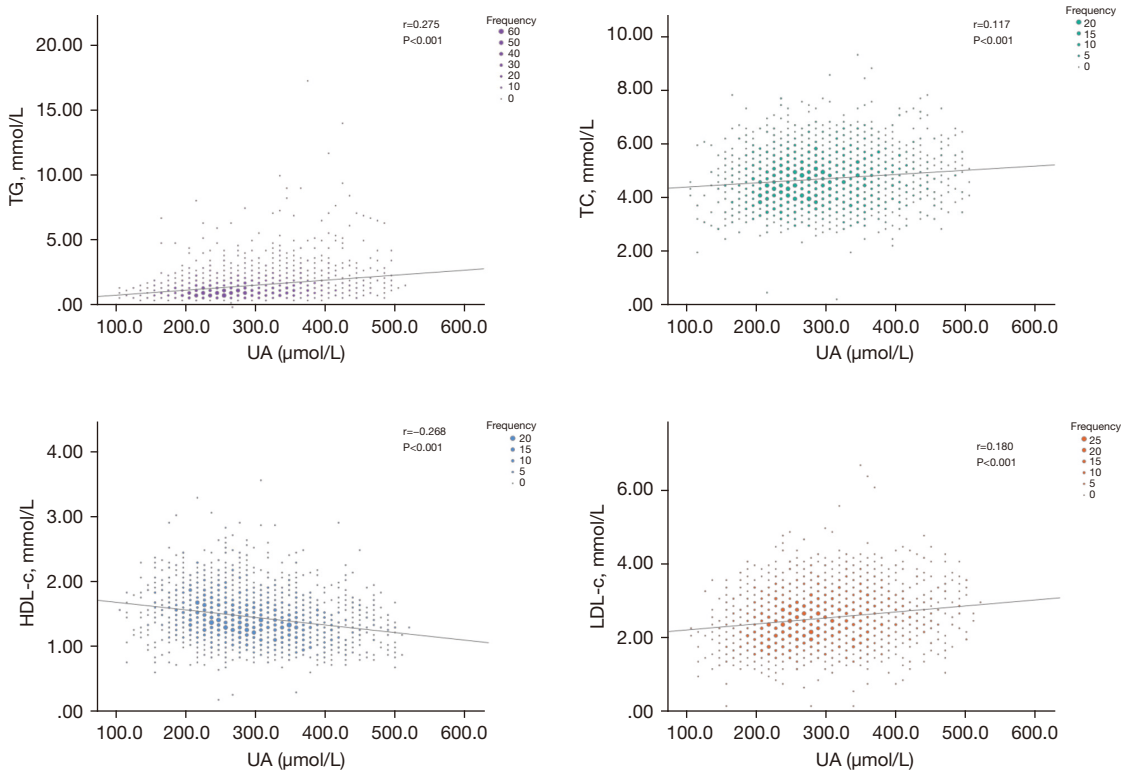

Figure 2 Associations between serum uric acid and serum triglycerides, serum total cholesterol, and high- and low-density lipoprotein cholesterol.

compromising their physical health to excel academically. Several studies have reported that unhealthy lifestyles, such as staying up late, excessive amounts of alcohol, and a sedentary lifestyle, are all risk factors for hyperuricemia (17,18). The two main risk factors of excessive food intake and unhealthy lifestyle, might explain why participants aged 18–29 years presented with a higher UA concentration than participants in the other age groups.

Additionally, we found that in all the age groups, the prevalence of hyperuricemia was higher among men than in women (*Figure 1*). Moreover, we also found that the level of serum UA increased with age in women, whereas the opposite trend was observed in men. A similar result has been reported in southwestern China (7). Investigating the association between sex and age, our results show that menopausal women showed a higher level of serum UA compared with premenopausal women. Several factors contribute to these differences (Tables S1 and S2). First, men consume higher levels of purine and alcohol as part of their diet, which are risk factors for hyperuricemia (19,20). Second, sex hormones may partly explain these differences. Serum UA levels have been reported to be negatively correlated with testosterone levels (21). Testosterone affects the expression pattern of urate transporters in the kidneys, such as urate transporter 1, glucose transporter 9, and sodium-coupled monocarboxylate transporter 1, which induces UA reabsorption in males (22). In the liver, testosterone increases the activity of the rate-limiting enzyme xanthine oxidase, which generates UA (7). In females, the lower levels of serum UA may be related to the effect of estrogen on postsecretory tubular reabsorption of UA (23). Hence, we hypothesized that the prevalence of hyperuricemia in men would be higher than that in women. Moreover, estrogen levels decrease following menopause, which may explain why the prevalence of hyperuricemia increases in postmenopausal women.

The present study also found a significant positive relationship between serum UA levels and TG, TC, LDL-c, and BMI and an inverse relationship between serum UA and HDL-c, which was also observed in previous studies (8,10). Furthermore, we found that 1.70≤ TG <2.30 mmol/L and a BMI ≥28.0 kg/m^2 (obesity) were independent risk

Table 3 Risk factors for hyperuricemia

Variable	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Female	0.089 (0.050, 0.158)	<0.001	0.105 (0.059, 0.189)	<0.001
Age				
30–39-year group	1.000 (reference)	–	1.000 (reference)	
18–29-year group	1.313 (0.884, 2.043)	0.227	2.322 (1.415, 3.808)	–
40–49-year group	0.750 (0.453, 1.243)	0.264	0.713 (0.418, 1.217)	0.215
50–59-year group	0.542 (0.292, 1.004)	0.051	0.595 (0.310, 1.144)	0.119
60–69-year group	0.400 (0.176, 0.913)	0.029	0.433 (0.182, 1.031)	0.059
≥70-year group	0.660 (0.301, 1.448)	0.300	0.875 (0.377, 2.029)	0.755
TG				
TG <1.70 mmol/L	1.000 (reference)	–	1.000 (reference)	–
1.70≤ TG <2.30 mmol/L	2.279 (1.463, 3.549)	<0.001	2.028 (1.250, 3.291)	0.004
TG ≥2.30 mmol/L	3.095 (2.061, 4.648)	<0.001	1.327 (0.538, 3.273)	0.539
TC				
TC <5.20 mmol/L	1.000 (reference)	–	1.000 (reference)	–
5.20 ≤TC <6.20 mmol/L	3.351 (0.389, 28.878)	0.271	1.529 (0.127, 18.409)	0.738
TC ≥6.20 mmol/L	7.746 (2.323,17.427)	<0.001	3.197 (0.811, 12.613)	0.097
HDL-c				
HDL-c <1.0 mmol/L	1.000 (reference)	–	1.000 (reference)	–
HDL-c ≥1.0 mmol/L	0.405 (0.257,0.640)	<0.001	1.218 (0.697, 2.129)	0.489
LDL-c				
LDL-c <2.60 mmol/L	1.000 (reference)	–	1.000 (reference)	–
2.60 ≤LDL-c <3.40 mmol/L	2.846 (1.628, 4.975)	<0.001	2.154 (0.776, 5.982)	0.141
3.40 ≤LDL-c <4.10 mmol/L	1.454 (0.294,5.275)	0.776	0.856 (0.156, 4.687)	0.858
LDL-c ≥4.10 mmol/L	5.029 (2.707, 9.341)	<0.001	1.935 (0.509 ,7.352)	0.332
SBP				
SBP <140 mmHg	1.000 (reference)	–	1.000 (reference)	–
SBP ≥140 mmHg	1.145 (0.756, 1.733)	0.522	1.145 (0.644 ,2.034)	0.644
DBP				
DBP <90 mmHg	1.000 (reference)	–	1.000 (reference)	–
DBP ≥90 mmHg	1.285 (0.188,1.285)	0.188	0.908 (0.548,1.505)	0.708
BMI				
18.5≤ BMI <24.0 kg/m^2	1.000 (reference)		1.000 (reference)	–
BMI <18.5 kg/m^2	0.274 (0.066, 1.135)	0.074	0.212 (0.050, 0.900)	0.035
24.0≤ BMI <27.9 kg/m^2	1.628 (1.101, 2.406)	0.015	1.374 (0.889, 2.124)	0.153
BMI ≥28.0 kg/m^2	2.914 (1.874, 4.530)	<0.001	1.974 (1.183, 3.293)	0.009

TG, triglyceride; TC, total cholesterol; HDL-c, lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index.

factors for hyperuricemia, while a BMI <18.5 kg/m^2 was an independent protective factor. It is indisputable that obesity is an important component of metabolic syndrome. In particular, it is known that accumulation of visceral adipose tissue may be detrimental to UA metabolism. Specifically, the accumulation of visceral fat induces a large influx of plasma-free fatty acids into the liver and hepatic portal vein, which stimulates the synthesis of TG followed by an associated surge in the production of UA via activation of the UA synthesis pathway (24). However, both obesity and dyslipidemia are associated with a high risk of hyperuricemia, and elevated UA levels are also associated with an increased risk of obesity and dyslipidemia. Experimentally, UA has been shown to increase TG accumulation in cultured liver cells (25,26). Apart from this, a restricted lifestyle does benefits on preventing hyperuricemia, which can be elucidated as restraining the intake of alcohol, high-purine food and abundant fructose. On the contrary diary and fresh vegetables are high recommended. Hyperuricemia increases the level of TG in the liver tissue of rats (27). This mechanism may be mediated by intracellular and mitochondrial oxidative stress. UA induces the activation of nicotinamide adenine dinucleotide phosphate oxidase preceding endoplasmic reticulum stress, which further induces the mitochondrial production of reactive oxygen species in hepatocytes (25). Furthermore, allopurinol treatment reduces the levels of TG, TC, and fat lipid accumulation in rats (28). Considering all of these factors, the interactions between lipid and uric metabolism should be considered in the clinical treatment of metabolic diseases.

Hyperuricemia is commonly found in patients with obesity, metabolic syndrome, and type 2 diabetes. However, we found no association between serum UA levels and FBG, 2hPG, and HbA1c levels. Hyperuricemia was previously considered a secondary consequence of insulin resistance. However, recent studies have shown that it may have a certain causal role, especially given that elevated serum UA levels often precede the development of insulin resistance (29-31). It is well known that thyroid hormones affect the synthesis, mobilization, and degradation of lipids. As such, thyroid dysfunction (especially overt or subclinical hypothyroidism) has a negative effect on lipid metabolism, leading to hypercholesterolemia, which in turn results in an increased risk of cardiovascular diseases (32). It has been reported that thyroid hormones can modulate UA metabolism in patients with late-onset subclinical hypothyroidism. In normal thyroid function, UA levels have a linear correlation with FT3 and FT4 (33). However, in this cross-sectional study, we found no association between serum UA and TSH levels.

This study had several limitations. First, it is a cross-sectional study that was undertaken in the Jiangsu and Fujian Provinces of China, and as such may reflect local conditions. We recommend that further studies be carried out to confirm our results. Our sample size was limited. Thus, future studies with larger samples are needed to confirm our results. Lastly, we did not measure lipid and purine levels of participants' diets, and the rigor of the study would have been enhanced had such measurements been included.

In conclusion, the present study demonstrated a significant association between serum UA levels and lipid profiles in inhabitants of the Jiangsu and Fujian Provinces of China. Further studies are required to identify the underlying mechanisms.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures

performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine (2021-LWKY-007), and all participants provided written informed consent.

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Supplementary

Table S1 Serum uric acid concentration by age-stratified groups in females

Menopausal	18-29	30-39	40-49	50-59	60-69	≥70	P
Yes	345.00 (1.41)	267.20 (15.14)	258.44 (64.26)	257.75 (56.74)	264.35 (57.36)	266.55 (67.41)	<0.001
No	256.85 (60.35)	239.76 (56.79)	232.07 (55.76)	238.58 (42.21)	--	--	

Some young participants were rendered menopausal due to medicine, surgery or other reasons.

Table S2 Serum uric acid concentrations in uric-acid-stratified groups in females

Menopausal	Q1	Q2	Q3	Q4	P
Yes	35.3% (146)	29.7% (123)	24.9% (103)	10.1% (42)	<0.001
No	47.4% (388)	33.1% (271)	13.3% (109)	6.2% (51)	

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