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Relationship Between Hyperuricemia and Cardiovascular Disease Risk Factors in a Chinese Population: A Cross-Sectional Study

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Data Collection B
Statistical Analysis C
Data Interpretation D
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Background: To study the relationship between hyperuricemia and cardiovascular diseases (CVDs) risk factors in a Chinese population.

Material/Methods: Data analyzed in this study were from the Chinese Hyperuricemia and Gout Database. Indicators of serum uric acid (SUA) level, height, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), smoking status, alcohol consumption, blood glucose, cholesterol, and triglycerides were measured. T test, one-way analysis of variance, Pearson's correlation, multivariate linear regression, and multivariate logistic regression were used.

Results: Compared with normouricemic men, hyperuricemic men had greater height ($P<0.01$), weight ($P<0.001$), body mass index (BMI) ($P<0.001$), SBP ($P<0.01$), DBP ($P<0.001$), cholesterol ($P<0.01$), and triglyceride ($P<0.001$). Compared with normouricemic women, hyperuricemic women were older ($P<0.01$) and had greater weight ($P<0.05$), BMI ($P<0.01$), SBP ($P<0.01$), DBP ($P<0.05$), glucose ($P<0.05$), and triglyceride ($P<0.001$). In men, an increase of 1 mg/dL in SUA was associated with a 0.279 kg/m^2 increase in BMI ($P<0.001$), a 2.438 mg/dL increase in cholesterol ($P<0.05$), a 10.358 mg/dL increase in triglyceride ($P<0.001$), and a 3.1 mg/dL decrease in glucose ($P<0.01$). In women, an increase of 1 mg/dL SUA was associated with a 0.168 kg/m^2 increase in BMI ($P<0.01$) and a 3.708 mg/dL increase in triglyceride ($P<0.01$). After adjustment, SUA was strongly associated with obesity and hyperlipidemia in both sexes.

Conclusions: Elevated serum uric acid concentration was strongly associated with obesity and hyperlipidemia in both men and women. These results indicated that, among hyperuricemia patients, we should pay more attention to the possibility of cardiovascular complications. These results might provide a novel target or a possible new treatment for cardiovascular diseases by lowering the level of serum uric acid.

MeSH Keywords: Cardiovascular Diseases • Hyperuricemia • Risk Factors

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Background

Cardiovascular diseases (CVDs) are a set of multiple disorders of the heart and blood vessels, including coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, deep vein thrombosis, and pulmonary embolism [1]. According to WHO data [2], approximately 17.3 million people world-wide died from CVDs in 2008, over 80% of which lived in low- and middle-income countries. In 2012, cardiovascular diseases were the leading cause of non-communicable disease deaths (17.5 million deaths), and it has been predicted that there will be more than 23 million people world-wide dying annually from CVDs by 2030 [3]. There are various risk factors involved for CVDs, including heredity/family history, sex, race/ethnicity, age, hypertension, hypercholesterolemia, diabetes mellitus, obesity, smoking/tobacco, stress/depression, and risk behaviors [4–8]. Genetic risk factors such as carotid intima-media thickness are related to cardiovascular morbidity and mortality [4,9], and socioeconomic factors and social environment also affect the deterioration and prognosis of CVDs [6,7].

Hyperuricemia has been viewed as being connected with CVDs risk factors since the last century [10]. Hyperuricemia was observed with an increased morbidity and mortality of CVDs such as hypertension, coronary heart disease (CHD), and myocardial infarction (MI) [11–13]. Many CVDs risk factors were thought to be associated with increased serum uric acid (SUA), such as: indicators of obesity, including body mass index (BMI), waist circumference (WC), and waist-to-hip ratio (WHR); indicators of hyperlipidemia including cholesterol, triglyceride, low-density lipoprotein (LDL), and high-density lipoprotein (HDL); and indicators of hypertension, including systolic blood pressure (SBP), and blood glucose and insulin level [13–21]. These results indicate that SUA-lowing treatment may be useful in offering a possible novel target for controlling CVDs [20,22–24].

However, the relationship between hyperuricemia and CVDs risk factors is controversial and conflicting. First, the debate focuses on whether hyperuricemia is an independent risk factor for CVDs or is only associated with CVDs because of confounding factors. Some studies reported that increased SUA was an independent risk factor contributing to CVDs [13,19,20], but other studies found that SUA was not a truly independent risk factor for CVDs. Increased SUA appeared to be an integral part of the cluster of risk factors associated with CVDs, including obesity, raised serum triglycerides, and cholesterol [17,18]. Second, the debate focuses on the sex difference in this relationship. Some studies found that the significant association between hyperuricemia and CVDs only existed in women but not in men [13,18]. However, other studies indicated that the positive association was observed in men [11,17]. Also, there were studies demonstrating that the relationship was seen in both sexes [21]. Third, the prevalence of hyperuricemia was different in different racial populations [14,25–27].

However, there are few studies on this relationship in the Chinese population. We designed the present study to investigate the relationship between hyperuricemia and CVDs risk factors in Chinese men and women. Indicators of CVDs were evaluated and the association with SUA levels was analyzed.

Material and Methods

Participants

The data analyzed in the present study were based on Chinese Hyperuricemia and Gout Database, provided by the Chinese National Scientific Data Sharing Platform for Population and Health. The participants were composed of health checkup residents in the Beijing Xiehe Hospital and part of the community population in Beijing, China. There were 940 participants in total, including 599 men, 288 women, and other 53 participants without sex information, ranging from 18 to 90 years old. Those cases without sex information were excluded from further analysis.

Measures

Indicators of SUA level, height, weight, SBP, DBP, fatty liver, smoking status, alcohol consumption, blood glucose, cholesterol, and triglycerides were measured in the participants. SUA was measured to the nearest 0.1 mg/dL. Hyperuricemia was defined as SUA ≥7.0 mg/dL for men and SUA ≥6.0 mg/dL for women [28,29]. Complications were analyzed by the diagnostic history, including CHD, hypertension, stroke, hyperlipidemia, DM, and gout. Fatty liver was observed by B-mode ultrasonography. Smoking status was divided into 3 groups: current smoker, non-smoker, and former smoker. Alcohol consumption was classified into current drinker, non-drinker, and former drinker. Among current drinkers, the frequency of alcohol consumption was recorded as frequency/week, and the alcoholic beverage classifications (spirits, beer, and wine) were also recorded. Physical activities were recorded by frequency per week, light activity defined as less than 2 times/week, mediate activity defined as 3–5 times/week, and heavy activity defined as more than 6 times/week [30].

Height was measured to the nearest 1 cm, weight was measured to the nearest 0.1 kg, and BMI was calculated as body weight/height^2 (kg/m^2). Obesity was defined as BMI ≥30.0 kg/m^2, overweight was defined as 25.0 kg/m^2 ≤BMI ≤29.9 kg/m^2, normal was defined as 18.5 kg/m^2 ≤BMI ≤24.9 kg/m^2, and underweight was defined as BMI ≤18.4 kg/m^2 [30]. Both SBP and DBP were measured to the nearest 1 mmHg. Hypertension was defined as having blood pressure ≥140/90

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Table 1. The comparison of cardiovascular disease risk factors between men and women.

	Unit	Men		Women		*P* value
		Mean	SD	Mean	SD	
Number		599		288		
SUA	mg/dL	5.60	1.20	4.21	1.08	***
Age	years	46.61	16.17	48.28	17.49	*P*=0.175
Height	cm	170.60	6.05	158.90	6.46	***
Weight	kg/m^2	72.35	10.56	58.36	8.81	***
BMI	mmHg	24.83	3.10	23.22	3.44	***
SBP	mmHg	123.63	15.78	115.76	15.08	***
DBP	mmHg	75.69	9.49	69.57	9.13	***
Serum glucose	mg/dL	102.44	26.28	97.04	13.88	***
Cholesterol	mg/dL	181.19	32.70	184.47	37.83	*P*=0.211
Triglyceride	mg/dL	139.55	85.51	118.61	78.12	***

SD – standard deviation; SUA – serum uric acid; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; *P* value was compared between men and women; *** means *P*<0.001.

mm Hg, or currently undergoing anti-hypertensive pharmacologic treatment [31]. Fasting plasma glucose was measured to the nearest 1 mg/dL. Diabetes mellitus (DM) was defined as fasting plasma glucose (FPG) ≥126 mg/dL or currently undergoing pharmacologic treatment, impaired fasting glucose (IFG) was defined as 110 mg/dL ≤FPG <126 mg/dL, and normal state was defined as FPG <110 mg/dL [32]. Cholesterol and triglyceride were measured to the nearest 1 mg/dL. Hyperlipidemia was defined as serum triglyceride level ≥150 mg/dL or total cholesterol level ≥200 mg/dL [33].

Statistical analyses

Continuous variables are provided as mean with standard deviation (SD). Categorical variables were classified into groups as described above. The *t* test was used to detect the difference between men and women, or to compare patients with hyperuricemia and participants with normouricemia. One-way analysis of variance (ANOVA) was used when there were more than 2 groups. Pearson's correlation coefficients were calculated to detect the correlation between the level of SUA and other CVDs risk factors in both men and women. Two multivariate linear regression models were applied to determine the different effects of different covariates contributed to the variation of the SUA. The first model was a stepwise section procedure and the second model was an enter section procedure. Also, for those categorical variables, multivariate logistic regression models (adjusted by age and other confounding factors) were used to determine the relationship between hyperuricemia and CVDs risk factors. *P*<0.05 was regarded as statistical significance.

Results

We calculated the mean value of each indicator in Chinese men and women, as shown in Table 1. By comparing the indicators between men and women, we found that, except for age and cholesterol, other indicators, such as SUA, height, weight, BMI, SBP, DBP, the level of serum glucose, and triglyceride, were significantly different for men and women. These results indicated that the study should be implemented for each sex separately, instead of a mixed-sex study. In Table 2, the portions of different status were also calculated in both sexes. The comparison between the 2 sexes was similar with the results of Table 1, except for the DM, IFG, and normal state divided by the level of glucose. However, we noted that in Chinese women, the numbers of current and former smokers were too small to be included as accurate factors.

In Table 3, for both sexes, we compared the mean value of each indicator between patients with hyperuricemia and participants with normouricemia. In men, the age of hyperuricemic patients was not significantly different from that of normal participants (*P*=0.644). However, the height, weight, and BMI of patients with hyperuricemia were significantly higher than those of participants with normouricemia. Also, both SBP and DBP of patients with hyperuricemia were significantly higher than those of normal participants. In addition, the level of cholesterol and triglyceride were also higher for patients. In women, hyperuricemic patients were older, with higher value of weight, BMI, SBP, DBP, glucose, and triglyceride.

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Table 2. The portions of different status of cardiovascular disease risk factors between men and women.

			Men		Women		*P* value
			Number	Percentage	Number	Percentage	
Smoking status							
	Current smoker		116	32.13%	6	2.94%	
	Non-smoker		198	54.85%	194	95.10%	
	Former smoker		47	13.02%	4	1.96%	***
Alcohol consumption							
	Current drinker		217	60.11%	48	23.53%	
	Non-drinker		117	32.41%	154	75.49%	
	Former drinker		27	7.48%	2	0.98%	***
Physical activities							
	Light activity	≤2 times/week	91	25.35%	76	37.25%	
	Mediate activity	3–5 times/week	136	37.88%	49	24.02%	
	Heavy activity	≥6 times/week	132	36.77%	79	38.73%	**
Body mass index							
	Obesity	BMI ≥30.0 kg/m^2	25	4.48%	10	3.51%	
	Overweight	25.0 kg/m^2 ≤BMI ≤29.9 kg/m^2	244	43.73%	73	25.61%	
	Normal state	18.5 kg/m^2 ≤BMI ≤24.9 kg/m^2	279	50.00%	184	64.56%	
	Underweight	BMI ≤18.4 kg/m^2	10	1.79%	18	6.32%	***
Blood pressure							
	Hypertension	BP ≥140/90 mm Hg	80	14.41%	19	6.71%	
	Normal state	BP <140/90 mm Hg	475	85.59%	264	93.29%	***
Serum glucose							
	DM	FPG ≥126 mg/dL	41	7.11%	11	3.83%	
	IFG	110 mg/dL ≤FPG <126 mg/dL	52	9.01%	20	6.97%	
	Normal state	FPG <110 mg/dL	484	83.88%	256	89.20%	*P*=0.082
Cholesterol							
	Hyperlipidemia	Chol ≥200 mg/dL	167	28.99%	99	34.49%	
	Normal state	Chol <200 mg/dL	409	71.01%	188	65.51%	*P*=0.101
Triglyceride							
	Hyperlipidemia	TG ≥150 mg/dL	187	32.47%	73	25.52%	
	Normal state	TG <150 mg/dL	389	67.53%	213	74.48%	*

SD – standard deviation; SUA – serum uric acid; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; DM – diabetes mellitus; FPG – fasting plasma glucose; IFG – impaired fasting glucose; Chol – cholesterol; TG – triglyceride; *P* value was compared between men and women; * means $P<0.05$; ** means $P<0.01$; *** means $P<0.001$.

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Table 3. The comparison of cardiovascular disease risk factors between patients with hyperuricemia and participants with normouricemia.

	Unit	Men					Women				
		Hyperuricemia		Normouricemia		*P* value	Hyperuricemia		Normouricemia		*P* value
		Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Number		66		512			20		266		
SUA	mg/dL	7.75	0.69	5.33	0.95	***	6.55	0.45	4.04	0.89	***
Age	years	46.14	14.95	47.05	16.45	*P*=0.644	60.25	14.23	47.46	17.42	**
Height	cm	172.29	4.93	170.37	6.18	**	158.37	6.54	158.94	6.49	*P*=0.715
Weight	kg	78.57	10.21	71.52	10.38	***	62.71	8.79	58.24	8.78	*
BMI	kg/m^2	26.45	3.04	24.61	3.05	***	25.00	3.05	23.08	3.49	**
SBP	mmHg	129.12	14.89	123.03	15.87	**	127.68	16.38	114.93	14.66	**
DBP	mmHg	80.22	9.32	75.18	9.37	***	72.84	10.22	69.36	9.05	*
Serum glucose	mg/dL	101.56	13.79	102.56	27.49	*P*=0.634	106.35	19.65	96.33	13.16	*
Cholesterol	mg/dL	195.69	36.20	179.75	30.86	**	200.30	37.87	183.22	37.69	*P*=0.065
Triglyceride	mg/dL	201.74	103.16	131.83	79.79	***	189.70	98.35	113.68	73.75	**

SD – standard deviation; SUA – serum uric acid; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; *P* value was compared between patients with hyperuricemia and participants with normouricemia; * means *P*<0.05; **means *P*<0.01; *** means *P*<0.001.

Table 4. Pearson's correlation coefficients of serum uric acid with those components of cardiovascular disease risk factors.

	Men		Women	
	r	*P* value	r	*P* value
Serum uric acid	1.000		1.000	
Age	–0.083	*	0.300	***
Height	0.143	**	–0.062	*P*=0.301
Weight	0.276	***	0.347	***
BMI	0.244	***	0.385	***
SBP	0.161	***	0.292	***
DBP	0.219	***	0.203	**
Serum glucose	–0.070	*P*=0.092	0.215	***
Cholesterol	0.150	***	0.295	***
Triglyceride	0.268	***	0.432	***

SUA – serum uric acid; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; * means *P*<0.05; ** means *P*<0.01; *** means *P*<0.001

The sex-specific Pearson's correlation coefficients of SUA with those components of CVDs risk factors are shown in Table 4. In both men and women, we observed that weight, BMI, and the level of triglyceride showed the strongest positive correlation. In men, the positive correlation coefficients were age, height, weight, BMI, SBP, DBP, cholesterol, and triglyceride. In women, the positive correlation coefficients were age, weight, BMI, SBP, DBP, glucose, cholesterol, and triglyceride. Using the stepwise section procedure of multivariate linear regression models, we observed that for men, age, BMI, DBP, glucose, cholesterol, and triglyceride were the major determinants for the variation of the level of SUA (Table 5),

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Table 5. The major determinants of the level of serum uric acid by stepwise section procedure of multivariate linear regression models.

	Men		Women	
	R^2=0.130		R^2=0.219	
	beta	*P* value	beta	*P* value
Age	–0.008	*	–	–
BMI	0.053	**	0.072	***
SBP	–	–	–	–
DBP	0.014	*	–	–
Serum glucose	–0.008	**	–	–
Cholesterol	0.003	*	–	–
Triglyceride	0.002	***	0.004	***

BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; * means $P<0.05$; ** means $P<0.01$; *** means $P<0.001$.

but for women, the major determinants were only BMI and triglyceride.

Analyzed by multivariate linear regression models, Table 6 shows the relationship between SUA concentration and each CVDs risk factor by adjusting for other potential confounding factors, including age, BMI, SBP, DBP, the level of glucose, cholesterol, and triglyceride. In men, after adjustment, SUA concentration showed significant positive associations with BMI, cholesterol, and triglyceride, and an inverse association with glucose. The results indicate that, after adjustment, an increase of 1 mg/dL in SUA concentration was associated with a 0.279 kg/m^2 increase in BMI ($P<0.001$), a 2.438 mg/dL increase in cholesterol ($P<0.05$), a 10.358 mg/dL increase in triglyceride ($P<0.001$), and a 3.1 mg/dL decrease in glucose ($P<0.01$). In women, after adjustment, only BMI and triglyceride showed significant associations with the level of SUA. The results indicated that, after adjustment, an increase of 1 mg/dL the level of SUA was associated with a 0.168 kg/m^2 increase in BMI ($P<0.01$) and a 3.708 mg/dL increase in triglyceride ($P<0.01$).

Analyzed by multivariate logistic regression models, Table 7 showed the odds ratio for hyperuricemia according to different status of smoking, drinking, physical activities and so on. In men, before adjustment or after age adjusted, drinking, overweight/obesity, hypertension, and hyperlipidemia all played positive roles in increasing the odds ratio of hyperuricemia. After adjustment for other potential confounding factors, drinking, overweight, and high level of triglyceride played positive roles in increasing the odds ratio of hyperuricemia. In women, before adjustment, heavy activities, overweight/obesity, hypertension, IFG/DM, and hyperlipidemia all played positive roles in increasing the odds ratio of hyperuricemia. After adjustment for age, only overweight/obesity and hyperlipidemia played positive roles in increasing the odds ratio of hyperuricemia.

Discussion

According to our results, there was a significant relationship between hyperuricemia and CVDs risk factors in both Chinese men and women. The participants with higher levels of serum uric acid tended to sustain more risk factors in cardiovascular diseases, and those patients with higher CVDs risk factors were easier to diagnose with hyperuricemia.

Compared with normouricemic men, hyperuricemic men had greater height, weight, BMI, SBP, DBP, cholesterol, and triglyceride. Compared with normouricemic women, hyperuricemic women were older and had higher weight, BMI, SBP, DBP, glucose, and triglyceride. In men, the associated CVDs risk factors included age, alcohol consumption, BMI, DBP, glucose, cholesterol, and triglyceride. After adjustment, SUA was strongly associated with alcohol consumption, obesity, and hyperlipidemia. In women, the strong determinants were obesity and hyperlipidemia.

Unfortunately, the mechanism to account for this association is still unclear. One possible reason is about the impaired kidney function, which was the main cause of hyperuricemia. Patients' SUA levels increased mainly as a consequence of impaired renal excretion. In conditions of local ischemia, an increased production of uric acid occurred in parallel with that of reactive oxygen species (ROS). The pro-oxidant and pro-inflammatory effects of ROS accumulation might further affect those CVDs indicators [20]. The second possible reason was the damage to endothelial cells (ECs) and vascular smooth muscle cells (VSMCs) caused by hyperuricemia. *In vitro* and *in vivo* research suggests that uric acid might contribute to endothelial dysfunction by inducing anti-proliferative effects on endothelium and impairing nitric oxide production. Pro-inflammatory and proliferative effects of soluble uric acid have

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Table 6. The relationship between serum uric acid concentration and each cardiovascular disease risk factor by adjusting for other potential confounding factors.

		SUA		BMI		SBP		DBP		glucose		CHOL		TG	
		beta	*P* value	beta	*P* value	beta	*P* value	beta	*P* value	beta	*P* value	beta	*P* value	beta	*P* value
Men															
	R^2	R^2=0.135		R^2=0.286		R^2=0.454		R^2=0.44		R^2=0.122		R^2=0.165		R^2=0.264	
	SUA	–	–	0.279	***	0.751	0.106	0.336	0.238	–3.1	**	2.438	*	10.358	***
	Age	–0.01	**	–0.002	**	0.281	***	–0.072	**	0.26	**	0.314	***	0.296	0.191
	BMI	0.049	**	–	–	0.551	**	0.617	***	0.15	0.727	0.531	0.273	6.336	***
	SBP	0.007	0.106	0.028	**	–	–	0.313	***	0.229	***	–0.129	0.237	–0.158	0.572
	DBP	0.008	0.238	0.083	0	0.834	0	–	–	–0.103	0.51	0.336	0.058	1.391	**
	Serum glucose	–0.006	**	0.002	0.727	0.048	*	–0.008	0.51	–	–	0.117	*	0.38	**
	Cholesterol	0.004	*	0.004	0.273	–0.021	0.237	0.021	0.058	0.091	*	–	–	0.554	***
	Triglyceride	0.002	***	0.008	***	–0.004	0.572	0.013	**	0.045	**	0.084	***	–	–
Women															
	R^2	R^2=0.234		R^2=0.421		R^2=0.596		R^2=0.51		R^2=0.278		R^2=0.304		R^2=0.443	
	SUA	–	–	0.168	**	0.623	0.201	0.417	0.269	0.775	0.99	2.055	0.077	3.708	**
	Age	0.004	0.952	0.012	***	0.043	***	0.03	**	0.055	**	0.143	***	0.271	0.712
	BMI	0.021	**	–	–	0.222	0.678	0.143	***	0.274	0.461	0.732	0.416	1.32	**
	SBP	0.006	0.201	0.017	0.678	–	–	0.032	***	0.073	***	0.2	0.206	0.366	0.053
	DBP	0.009	0.269	0.024	***	0.073	***	–	–	0.112	0.055	0.298	0.071	0.551	0.598
	Serum glucose	0.005	0.99	0.013	0.461	0.048	***	0.033	0.055	–	–	0.162	0.766	0.292	**
	Cholesterol	0.002	0.077	0.005	0.416	0.018	0.206	0.012	0.071	0.023	0.766	–	–	0.106	***
	Triglyceride	0.001	**	0.003	**	0.01	0.053	0.007	0.598	0.012	**	0.032	***	–	–

SUA – serum uric acid; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; Chol – cholesterol; TG – triglyceride; * means *P*<0.05; ** means *P*<0.01; *** means *P*<0.001.

been described in VSMCs. In animal models of mild hyperuricemia, hypertension developed in association with intrarenal vascular disease [31].

However, according many studies, the association between hyperuricemia and CVDs risk factors is conflicting and complicated. Some studies [17,25] reported that SUA was not a truly independent risk factor for CVD, but was secondary to its association with the insulin resistance syndrome (IRS). Also, there is research [18] showing that after additional adjustment for CVDs risk factors, uric acid level was no longer associated with CHD, death from CVDs, or death from all causes. However, according to our results, after adjustment for other potential risk factors of CVD, there was still a strong and significant connection between the level of SUA and obesity, as well as hyperlipidemia, in both men and women. Our results were similar to and consistent with some additional studies. In adolescents with new-onset essential hypertension, the prevalence of elevated SUA was more than 90%, and a preliminary clinical trial evidence suggested that agents that lower SUA may also lower BP [19]. For each increase of 1 mg/dL in uric acid level, the pooled multivariate risk ratio for CHD mortality was 1.12 [13]. In untreated subjects with essential hypertension, raised uric acid was a powerful risk marker for

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Table 7. The odds ratio for hyperuriceima according to different status of men and women.

	OR				Age-adjusted OR				Full-adjusted OR			
	OR	95% CI		*P* value	OR	95% CI		*P* value	OR	95% CI		P value
Men												
Smoking status												
Non-smoker												
Current smoker	1.087	0.901	1.312	0.382	1.07	0.88	1.301	0.496	0.931	0.733	1.182	0.556
Former smoker	1.013	0.781	1.313	0.924	1.04	0.804	1.346	0.764	0.899	0.658	1.23	0.506
Alcohol consumption												
Non-drinker												
Current drinker	1.382	1.13	1.69	**	1.38	1.121	1.7	**	1.416	1.115	1.797	**
Former drinker	1.242	0.869	1.774	0.234	1.196	0.827	1.73	0.341	1.432	0.93	2.205	0.103
Physical activities												
Light activity ≤2 times/week												
Mediate activity 3–5 times/week	0.901	0.726	1.118	0.344	0.877	0.698	1.101	0.259	0.733	0.557	0.963	*
Heavy activity ≥6 times/week	0.874	0.703	1.087	0.225	0.905	0.721	1.135	0.386	0.863	0.664	1.12	0.267
Body mass index												
Normal state 18.5 kg/m^2 ≤BMI ≤24.9 kg/m^2												
Underweight BMI ≤18.4 kg/m^2	0.354	0.195	0.643	**	0.352	0.178	0.698	**	0.113	0.019	0.667	*
Overweight 25.0 kg/m^2 ≤BMI ≤29.9 kg/m^2	1.349	1.153	1.578	***	1.389	1.179	1.638	***	1.266	1.009	1.588	*
Obestiy BMI ≥30.0 kg/m^2	1.459	1.033	2.06	*	1.514	1.076	2.13	*	1.437	0.907	2.279	0.123
Blood pressure												
Normal state BP <140/90 mm Hg												
Hypertension BP ≥140/90 mm Hg	1.286	1.055	1.569	**	1.508	1.209	1.881	***	1.244	0.883	1.752	0.212
Serum glucose												
Normal state FPG <110 mg/dL												
IFG 110 mg/dL ≤FPG <126 mg/dL	1.249	0.985	1.583	0.067	1.308	1.034	1.655	*	1.004	0.711	1.418	0.981
DM FPG ≥126 mg/dL	0.951	0.723	1.251	0.719	1.004	0.765	1.318	0.978	0.932	0.645	1.346	0.706
Cholesterol												
Normal state Chol <200 mg/dL												
Hyperlipidemia Chol ≥200 mg/dL	1.263	1.081	1.476	**	1.281	1.094	1.501	**	1.07	0.862	1.328	0.541
Triglyceride												
Normal state TG <150 mg/dL												
Hyperlipidemia TG ≥150 mg/dL	1.639	1.39	1.932	***	1.67	1.409	1.98	***	1.396	1.101	1.771	**

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Table 7 continued. The odds ratio for hyperuriceima according to different status of men and women.

	OR				Age-adjusted OR				Full-adjusted OR			
	OR	95% CI		*P* value	OR	95% CI		*P* value	OR	95% CI		P value
Women												
Alcohol consumption												
Non-drinker												
Current drinker	0.868	0.637	1.185	0.373	1.016	0.73	1.413	0.927	0.917	0.622	1.353	0.662
Former drinker	1.739	0.531	5.699	0.361	1.699	0.538	5.363	0.366	0	0	.b	0.989
Physical activities												
Light activity ≤2 times/week												
Mediate activity 3–5 times/week	1.202	0.845	1.71	0.306	1.379	0.936	2.031	0.104	1.243	0.787	1.963	0.351
Heavy activity ≥6 times/week	1.516	1.113	2.065	**	1.33	0.957	1.85	0.089	1.397	0.955	2.042	0.085
Body mass index												
Normal state 18.5 kg/m*2* ≤BMI ≤24.9 kg/m^2												
Underweight BMI ≤18.4 kg/m^2	0.786	0.461	1.342	0.378	0.938	0.561	1.57	0.809	1.038	0.577	1.867	0.901
Overweight 25.0 kg/m^2 ≤BMI ≤29.9 kg/m^2	1.842	1.399	2.424	***	1.509	1.121	2.033	**	1.225	0.805	1.863	0.344
Obestiy BMI ≥30.0 kg/m^2	2.588	1.443	4.642	**	1.84	1.115	3.035	*	1.824	0.864	3.849	0.115
Blood pressure												
Normal state BP <140/90 mm Hg												
Hypertension BP ≥140/90 mm Hg	0.527	0.349	0.798	**	1.589	0.97	2.603	0.066	1.135	0.403	3.2	0.811
Serum glucose												
Normal state FPG <110 mg/dL												
IFG 110 mg/dL ≤FPG <126 mg/dL	1.624	1.086	2.426	*	1.235	0.787	1.938	0.359	0.942	0.47	1.89	0.867
DM FPG ≥126 mg/dL	1.83	1.085	3.085	*	1.396	0.752	2.592	0.291	1.392	0.546	3.546	0.488
Cholesterol												
Normal state Chol <200 mg/dL												
Hyperlipidemia Chol ≥200 mg/dL	1.91	1.485	2.458	***	1.595	1.212	2.099	**	1.466	0.993	2.164	0.054
Triglyceride												
Normal state TG <150 mg/dL												
Hyperlipidemia TG ≥150 mg/dL	2.278	1.719	3.018	***	1.849	1.356	2.523	***	1.47	0.899	2.403	0.125

OR – odds ratio; CI – confidence interval; SUA – serum uric acid; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; DM – diabetes mellitus; FPG – fasting plasma glucose; IFG – impaired fasting glucose; Chol – cholesterol; TG – triglyceride; * means $P<0.05$; ** means $P<0.01$; *** means $P<0.001$.

subsequent CVDs and all-cause mortality [21]. Also, some studies noted that hypertriglyceridemia was related to hyperuricemia independent of obesity and central body fat distribution [16]. Children and young adults with hyperuricemia had significantly higher plasma glucose, insulin levels, cholesterol, triglyceride, very low-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and total protein levels than subjects without hyperuricemia; high-density lipoprotein cholesterol level was significantly lower in subjects with hyperuricemia than in those without it [14].

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Besides the conflict on the relation itself, there were also debates on different sex patterns of this relationship. According to Kim's study [13], there was no significant association between hyperuricemia and CHD incidence/mortality in men, but an increased risk for CHD mortality was found in women. Culleton [18] reported that in men, after adjustment for age, elevated SUA level was not associated with increased risk for an adverse outcome. In women, after adjustment for age, uric acid level was predictive of CHD, and death from CVDs. Liese found [11] a strong positive association of elevated SUA with all-cause mortality of CVDs in men. According to Wannamethee's study [17], when the association between SUA and risk of CHD was examined by the presence and grade of pre-existing CHD, a positive association was seen only in men with previous definite MI, even after full adjustment. Verdecchia [21] found that the relationship between uric acid and CVDs event rate was J-shaped in both sexes. According to our study results, the relationship between SUA and CVDs risk factors exist in both sexes, but some details were different. In men, there were many related CVDs risk factors, while in women only BMI and triglyceride were related. In both sexes, obesity and hyperlipidemia showed the strongest association with hyperuricemia.

Considering all these differences in various studies, we suggest there might be several explanations. First, the definition of hyperuricemia was not exactly the same among various studies. In some studies, the definition of hyperuricemia was described as SUA >7.7 mg/dL for men and SUA >6.6 mg/dL for women [33]. In other studies, including the present one, hyperuricemia was defined as SUA ≥7.0 mg/dL for men and SUA ≥6.0 mg/dL for women [28,29]. Actually, the definition of hyperuricemia is currently arbitrary and varies from 5.6 to 7.7 mg/dL in men and from 4.7 to 7.0 mg/dL in women [13]. Second, the studied population was unique in each study. For example, black men might have lower SUA levels and a lower prevalence of hyperuricemia when compared with white men [25]. Third, since genes and environment can affect obesity and cardiovascular diseases, diet, genetics, and environmental factors of each population might explain the differences found in this association [34–36].

Our study has certain strengths. First, we studied the relationship between hyperuricemia and CVDs risk factors in a Chinese population, which has rarely been studied. Second, we detected and calculated many CVDs risk factors, including: height, weight, and BMI, which reflect obesity; SBP and DBP, which reflect hypertension; the level of glucose, which reflects DM; and the level of cholesterol and triglyceride, which reflect CHD and MI. Third, to better study the relationship between SUA and each factor, we ran the adjustment to exclude the effect of other confounding factors. Fourth, we studied the relationship in both sexes and compared the differences between men and women. However, our study also has some limitations. First, it was a cross-sectional study without any longitudinal observations. Second, the simple number of hyperuricemic women was too small, which might make the results disputable when we divided women into 2 groups: hyperuricemic and normouricemic. Third, the population in our study was only Chinese, which limits generalization of our results to other populations.

Conclusions

We found that elevated serum uric acid concentration was strongly associated with obesity and hyperlipidemia in both men and women, indicating that, among hyperuricemic patients, we should pay more attention to the possibility of cardiovascular complications. These results might provide a novel target or a new treatment for cardiovascular diseases by lowering the level of serum uric acid.

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Ethical standards

The data used in this study were based on Chinese Hyperuricemia and Gout Database, provided by the Chinese National Scientific Data Sharing Platform for Population and Health. Protocols used in this database were approved by the Ethics Committee of the Chinese National Scientific Data Sharing Platform for Population and Health.

Conflict of interest

The authors declare that they have no conflicts of interest.

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