Cross-sectional Study on the Association Between Hyperuricemia and Other Metabolic Diseases

Baosheng Guan

Jiamusi University School of Basic Medicine <https://orcid.org/0000-0002-4275-6661>

Jiaxin Chen

Jiamusi University School of Public Health

Rongyu Lan

Jiamusi University School of Public Health

Xue Bai

Jiamusi University School of Basic Medicine

Liling Zhu

Jiamusi University School of Public Health

Songpo Yao

Jiamusi University School of Public Health

Yang Song

First Affiliated Hospital of Qiqihar Medical University

Xianglin Yin

Jiamusi University School of Public Health

Xiaoqing Niu

Jiamusi University School of Basic Medicine

Hongbin Qiu (✉ jms_guan@163.com)

Jiamusi University

Research article

Keywords: hyperlipidemia, hypertension, prevalence, serum uric acid, hyperuricemia

Posted Date: March 7th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1342350/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Purpose: Hyperuricemia (HUA) is a metabolic disease caused by overproduction and/or underexcretion of serum uric acid (SUA). The study was conducted to find the association between Hyperuricemia and hypertension, diabetes and hyperlipidemia.

Methods: A total of 1632 people aged older than 18 years were selected through cluster random sampling in 2015 from two hospitals in Qiqihar, China. Epidemiological investigations were conducted to determine SUA, blood pressure, blood lipids, blood glucose and other indicators. Statistical comparisons of the results were evaluated by using *t* test, *chi*-square test, and logistic regression analysis with SPSS 19.0.

Results: The prevalence of HUA, hypertension, diabetes and hyperlipidemia were 21.68%, 37.26%, 10.98% and 57.45% in the male population and 1.34%, 19.91%, 4.59% and 40.38% in the female population, respectively. There was a significant difference in the prevalence of HUA, hypertension, diabetes and hyperlipidemia between males and females ($p \leq 0.001$). Using the lowest SUA range as a reference group, the risk of hyperlipidemia increased with SUA levels in population (Q2: $OR=1.570$, $p=0.003$; Q3: $OR=2.049$, $p \leq 0.001$; Q4: $OR=3.519$, $p \leq 0.001$). (This trend persisted after adjusting for BMI, sex and age, Q2: $OR=1.632$, $p=0.002$; Q3: $OR=2.091$, $p \leq 0.001$; Q4: $OR=3.719$, $p \leq 0.001$). However, there was no statistically significant difference between the levels of SUA in the context of diabetes and hypertension, not even been adjusted.

Conclusion: The level of SUA is associated with hyperlipidemia. It may be useful to maintain normal SUA level in the prevention and treatment of hyperlipidemia.

Introduction

Uric acid is the final metabolite of purines in humans [1]. Hyperuricemia (HUA) is a metabolic disease caused by overproduction and/or underexcretion of serum uric acid (SUA) [2]. When SUA exceeds its saturation in blood or tissue fluid, sodium urate crystals can be formed and deposited locally in joints, inducing local inflammatory response and tissue destruction, namely gout[3]. It can cause acute nephropathy, chronic interstitial nephritis, or kidney stones in the kidney deposition, called uric acid nephropathy. HUA and gout are systemic diseases in which multiple systems are involved. HUA is related not only to gouty arthritis and kidney stones but also to lipid metabolism, diabetes, cardiovascular disease and other diseases [4]. The prevalence of HUA and gout has been increasing annually in the world with changes in diet and lifestyle[3]. As health costs increase, an economic burden is imposed on many families.

The study was conducted at the First and Third Affiliated Hospital of Qiqihar Medical College to investigate the relationship between uric acid and metabolic diseases such as hypertension, hyperlipidemia and diabetes mellitus through a cross-sectional investigation of the population and to provide theoretical evidence for the prevention and treatment of HUA and other metabolic diseases.

Materials And Methods

1.1 Subjects

This cross-sectional study included 1632 (738 males, 894 females) subjects registered from two hospitals in Qiqihar, China examination registry without anti-hypertensive or anti-hyperuricemic or anti-lipidemic agent administration. All subjects aged older than 18 years were selected through cluster random sampling from January to December 2015. The exclusion criteria were as follows: those with clinical manifestations of gout and with serious liver or kidney diseases, lung insufficiency or other organic diseases. Participants with incomplete clinical data were also excluded. All subjects provided written informed consent (ethics committee license number: JMSU-213).

1.2 Methods

1.2.1 Biochemical determination

Blood samples were collected after subjects had fasted for more than 8 h for the determination of SUA, urea nitrogen (BUN), creatinine (CREA), triglycerides (TGs), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FPG) and other indicators by biochemical analyzer. Blood pressure was measured using a mercury sphygmomanometer to auscultate the Korotkoff sound. To measure blood pressure, use the same arm and take the average of the two after at least one minute. Body mass index (BMI) was defined as weight in kilograms divided by height in square meters. Normal weight was defined as a BMI of 18.5 to 23.9 kg/m², low weight as less than 18.5 kg/m², overweight as 24.0 to 27.9 kg/m², and obesity as 28.0 kg/m² or greater, on the basis of recommendations from the Working Group on Obesity in China [5]. All measurements were taken by trained nurses.

1.2.2 SUA level grading

Subjects were divided into four groups in accordance with the quartiles of SUA level: Males: Q1<301.25 μmol/L, 301.25 μmol/L≤Q2<350.00 μmol/L, 350.00 μmol/L≤Q3<409.00 μmol/L, Q4≥409.00 μmol/L. Females: Q1<183.00 μmol/L, 183.00 μmol/L≤Q2<224.70 μmol/L, 224.00 μmol/L≤Q3<273.00 μmol/L, Q4≥273.00 μmol/L.

1.2.3 Diagnostic criteria

The HUA diagnostic criteria were as follows: According to the sixth edition of "Internal Medicine", HUA is defined as an SUA level> 417 μmol/L (7.0 mg/ml) in males and > 357 μmol/L (6.0 mg/ml) in females.

The hypertension diagnostic criteria were as follows: According to "Guidelines for the Prevention and Treatment of Hypertension in China", systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg or anti-hypertensive drug treatment in a patient with a history of hypertension.

The diabetes diagnostic criteria were as follows: According to the 2010 edition of the "Guideline for Type 2 Diabetes in China" formulated by the Chinese Medical Association Diabetes Branch: FPG $\geq$ 7.0 mmol/L (110 mg/dL) or those receiving drug treatment for elevated glucose.

The diagnostic criteria for hyperlipidemia were as follows: According to the "Guideline for the prevention and treatment of dyslipidemia in Chinese adults", individuals who have TGs $\geq$ 1.70 mmol/L, LDL-C $\geq$ 4.14 mmol/L, HDL-C $<$ 1.04 mmol/L or TC $\geq$ 5.72 mmol/L can be diagnosed with hyperlipidemia.

1.3 Statistical analysis

A database was established by EpiData3.0 software. Statistical analysis was performed using SPSS 19.0 software. The quantitative data conforming to normality were expressed as the mean $\pm$ SD and compared by *t*-test, and non-normal measurement data and categorical variables were assessed by *chi*-square test. Correlation analysis used logistic multiple regression analysis, and odds ratios (*ORs*), 95% confidence intervals (*CIs*) and *p* values were calculated. *p* $<$ 0.05 was considered significant.

Results

2.1 Basic Situation of Subjects

2.1.1 Demographic characteristics

The study investigated a total of 1632 subjects, including 738 males and 894 females, with an average age of 42.67 $\pm$ 13.21 years, including 43.25 $\pm$ 12.47 years males and 42.20 $\pm$ 13.77 years females, with no significant difference between males and females. The average level of SUA was 355.09 $\pm$ 78.14 μ mol/L in males and 231.49 $\pm$ 69.77 μ mol/L in females, with a significant difference between the two groups (*p* $<$ 0.001). The BMI was 25.38 $\pm$ 3.35 kg/m² for males and 22.88 $\pm$ 3.13 kg/m² for females, and the difference was statistically significant (*p* $<$ 0.001) (Table 1).

Table 1
Baseline Characteristics of Participants by Gender (Mean±SD)

	Males	Females	<i>t</i>	<i>p</i>
Total	738	894	-	-
Age (year)	43.25±12.47	42.20±13.77	1.62	0.107
BMI (kg/m ²)	25.38±3.35	22.88±3.13	15.55	<0.001
SUA (μmol/L)	355.09±78.14	231.49±69.77	33.37	<0.001
Data are presented as mean ± standard deviation (SD).				
BMI, body mass index; SUA, serum uric acid.				
The <i>p</i> -values are obtained from independent sample <i>t</i> -test in comparison between the gender groups.				

2.1.2 The prevalence of HUA, hypertension, diabetes and hyperlipidemia among study population

In this study, the prevalence rates of HUA, hypertension, diabetes and hyperlipidemia in the total population were 10.54%, 27.76%, 7.47% and 48.10%, respectively. The prevalence of HUA, hypertension, diabetes and hyperlipidemia were 21.68%, 37.26%, 10.98% and 57.45% in the male population and 1.34%, 19.91%, 4.59% and 40.38% in the female population, respectively. There was a significant difference in the prevalence of HUA, hypertension, diabetes and hyperlipidemia between males and females ($p<0.001$) and the prevalence of male was significantly higher than that of female. After grouping the population according to age, with the increase of age, the prevalence of hypertension, diabetes and hyperlipidemia increased. Compared with the group less than 30 years old, the prevalence of hypertension, diabetes and hyperlipidemia increased significantly, and the differences were statistically significant ($p<0.001$), while HUA showed no correlation with age. However, with the increase of BMI, the prevalence of HUA, hypertension, diabetes and hyperlipidemia was significantly increased, which was significantly higher than that of BMI<18.5 ($p<0.001$) (Table 2).

Table 2
Prevalence of HUA and Metabolic Diseases among Study Population

	Total	HUA	Hypertension	Diabetes	Hyperlipidemia
Gender					
Males	738	160(21.68%)	275(37.26%)	81(10.98%)	424(57.45%)
Females	894	12(1.34%)	178(19.91%)	41(4.59%)	361(40.38%)
χ^2	-	177.36	60.70	23.86	47.20
p	-	<0.001	<0.001	<0.001	<0.001
Age group					
<30	373	37(9.92%)	41(10.99%)	7(1.88%)	127(34.05%)
30~	343	39(11.37%)	58(16.91%)	8(2.33%)	130(37.9%)
40~	365	44(12.05%)	101(27.67%)	23(6.3%)	178(48.77%)
50~	405	44(10.86%)	168(41.48%)	55(13.58%)	251(61.98%)
60~	146	8(5.48%)	85(58.22%)	29(19.86%)	99(67.81%)
χ^2	-	5.302	178.014	84.963	97.810
p	-	0.258	<0.001	<0.001	<0.001
BMI group					
<18.5	62	1(1.61%)	6(9.68%)	2(3.23%)	15(24.19%)
18.5~	773	40(5.17%)	131(16.95%)	35(4.53%)	310(40.1%)
24~	606	75(12.38%)	215(35.48%)	55(9.08%)	328(54.13%)
28~	191	56(29.32%)	101(52.88%)	30(15.71%)	132(69.11%)
χ^2	-	102.45	133.29	32.28	76.58
p	-	<0.001	<0.001	<0.001	<0.001
Data are presented as N (percent prevalence).					
The p -values are obtained from <i>Chi</i> -Square in comparison between the groups.					
BMI: body mass index, HUA: hyperuricemia.					

2.1.3 The prevalence of metabolic diseases according to quartiles of SUA level

Taking the population as a whole, the prevalence rates of hypertension and hyperlipidemia in different groups were related to SUA level ($p<0.001$), and the prevalence rates of hypertension and hyperlipidemia in the population increased with the increase of SUA level. At the same time, the prevalence of diabetes could not be considered to be related to SUA level. The groups were divided into four groups according to the quartile of SUA level. Among them, the prevalence of hyperlipidemia in men was correlated with the SUA level($p<0.001$). No correlation was found between the prevalence of hypertension and diabetes and SUA level in different groups of men. The prevalence of hypertension ($p<0.001$), diabetes ($p=0.004 < 0.05$) and hyperlipidemia ($p<0.001$) in women were correlated with SUA level (Table 3).

Table 3
Prevalence of Metabolic Diseases According to Quartiles of SUA level

	N	Hypertension	Diabetes	Hyperlipidemia
Males				
Q1	185	71(38.38%)	22(11.89%)	73(39.46%)
Q2	183	68(37.16%)	19(10.38%)	103(56.28%)
Q3	183	56(30.6%)	17(9.29%)	103(56.28%)
Q4	187	80(42.78%)	23(12.3%)	145(77.54%)
χ^2	-	6.009	1.093	55.575
<i>p</i>	-	0.111	0.779	<0.001
Females				
Q1	223	21(9.42%)	6(2.69%)	62(27.8%)
Q2	221	32(14.48%)	4(1.81%)	72(32.58%)
Q3	219	55(25.11%)	12(5.48%)	100(45.66%)
Q4	231	70(30.3%)	19(8.23%)	127(54.98%)
χ^2	-	38.851	13.114	43.225
<i>p</i>	-	<0.001	0.004	<0.001
Overall				
Q1	408	92(22.55%)	28(6.86%)	135(33.09%)
Q2	404	100(24.75%)	23(5.69%)	175(43.32%)
Q3	402	111(27.61%)	29(7.21%)	203(50.5%)
Q4	418	150(35.89%)	42(10.05%)	272(65.07%)
χ^2	-	21.11	6.12	89.69

Data are presented as N (percent prevalence).

The *p*-values are obtained from Pearson *Chi*-Square in comparison between the SUA quartiles.

BMI: body mass index, HUA: hyperuricemia.

Participants were classified into quintiles according to their serum uric acid levels. For males: Q1<301.25 $\mu\text{mol/L}$, 301.25 $\mu\text{mol/L}$ ≤Q2<350.00 $\mu\text{mol/L}$, 350.00 $\mu\text{mol/L}$ ≤Q3<409.00 $\mu\text{mol/L}$, Q4≥409.00 $\mu\text{mol/L}$. For females: Q1<183.00 $\mu\text{mol/L}$, 183.00 $\mu\text{mol/L}$ ≤Q2<224.70 $\mu\text{mol/L}$, 224.00 $\mu\text{mol/L}$ ≤Q3<273.00 $\mu\text{mol/L}$, Q4≥273.00 $\mu\text{mol/L}$.

	N	Hypertension	Diabetes	Hyperlipidemia
<i>p</i>	-	<0.001	0.106	<0.001
Data are presented as N (percent prevalence).				
The <i>p</i> -values are obtained from Pearson <i>Chi</i> -Square in comparison between the SUA quartiles.				
BMI: body mass index, HUA: hyperuricemia.				
Participants were classified into quintiles according to their serum uric acid levels. For males: Q1<301.25 µmol/L, 301.25 µmol/L≤Q2<350.00 µmol/L, 350.00 µmol/L≤Q3<409.00 µmol/L, Q4≥409.00 µmol/L. For females: Q1<183.00 µmol/L, 183.00 µmol/L≤Q2<224.70 µmol/L, 224.00 µmol/L≤Q3<273.00 µmol/L, Q4≥273.00 µmol/L.				

2.2 Association of SUA levels with prevalence of hypertension

logistic regression analysis showed that the level of SUA had a positive significant correlation ($p<0.001$) with hyperlipidemia, and there was also a difference ($p<0.001$) after adjusting for age, sex and BMI. there was no difference in SUA level according to diabetes status and hypertension, not even been adjusted. (Table 4)

Table 4

Logistic Correlation Analysis of SUA and Hypertension, Hyperlipidemia and Diabetes in Two Models

		SUA	B	S.E	Wald	P	P'	OR (95% C.I.)
Hyperlipidemia	Model1	Q1	-	-	-	-	<0.001	1.000 (reference)
		Q2	0.451	0.150	9.008	0.003		1.570 (1.169-2.108)
		Q3	0.717	0.150	22.902	<0.001		2.049 (1.528-2.749)
		Q4	1.258	0.152	68.635	<0.001		3.519 (2.613-4.739)
	Model2	Q1	-	-	-	-	<0.001	1.000 (reference)
		Q2	0.490	0.156	9.864	0.002		1.632 (1.202-2.215)
		Q3	0.738	0.156	22.238	<0.001		2.091 (1.539-2.842)
		Q4	1.314	0.162	65.660	<0.001		3.719 (2.707-5.11)
Diabetes	Model1	Q1	-	-	-	-	0.637	1.000 (reference)
		Q2	-0.350	0.301	1.358	0.244		0.704 (0.391-1.27)
		Q3	-0.197	0.287	0.470	0.493		0.822 (0.468-1.441)
		Q4	-0.064	0.271	0.056	0.813		0.938 (0.552-1.595)
	Model2	Q1	-	-	-	-	0.663	1.000 (reference)
		Q2	-0.309	0.305	1.028	0.311		0.734 (0.404-1.335)
		Q3	-0.175	0.293	0.356	0.551		0.84 (0.473-1.491)
		Q4	-0.003	0.286	<0.001	0.992		0.997 (0.569-1.747)

Association of SUA quartiles with hyperlipidemia, diabetes and hypertension. The multiple logistic regressions were done to evaluate the association between SUA quartiles and hypertension. Model 1: No variables had been adjusted. Model 2: Age, sex and BMI were adjusted.

		SUA	B	S.E	Wald	<i>P</i>	<i>P'</i>	OR (95% C.I.)
Hypertension	Model1	Q1	-	-	-	-	0.172	1.000 (reference)
		Q2	0.048	0.174	0.077	0.781		1.049 (0.746-1.476)
		Q3	0.107	0.172	0.384	0.535		1.113 (0.794-1.560)
		Q4	0.336	0.168	4.004	0.045		1.400 (1.007-1.946)
	Model2	Q1	-	-	-	-	0.441	1.000 (reference)
		Q2	0.083	0.187	0.195	0.658		1.086 (0.753-1.567)
		Q3	0.080	0.187	0.183	0.669		1.083 (0.751-1.561)
		Q4	0.285	0.187	2.320	0.128		1.33 (0.922-1.919)
Association of SUA quartiles with hyperlipidemia, diabetes and hypertension. The multiple logistic regressions were done to evaluate the association between SUA quartiles and hypertension. Model 1: No variables had been adjusted. Model 2: Age, sex and BMI were adjusted.								

Discussion

3.1 Prevalence of HUA

HUA and gout are continuous and chronic pathophysiological processes with significant heterogeneity in clinical phenotypes. The boundary between asymptomatic HUA and gout is becoming blurred with the wide use of new more sensitive and specific imaging methods [6, 7]. The prevalence of HUA which is associated with genetic factors and environmental factors varies in different regions [8]. The prevalence of gout was 3.9% among US adults in 2015–2016 (5.2% and 2.7% among men and women, respectively) [9]. While a cross-sectional study in Thailand showed the prevalence of HUA was 10.6% (18.4% in men and 7.8% in women) [10], which is higher than in the US, obviously. A community-based cross-sectional study showed the prevalence of HUA among adults aged 35-79 years was 13.5% (17.3% in men and 10.0% in women) in southwestern China [11]. Meta-analysis indicated that the pooled prevalence of HUA was 17.4% (ranged from 15.5 to 24.6% by regions) among the general population in mainland China, which had become another common metabolic disease after diabetes [12]. In our study, the prevalence of HUA was 10.54% in the population, and in males (21.68%) was significantly higher than that in females (1.34%), which is consistent with the above scholars' studies.

The prevalence of HUA in different regions was mainly associated with regional financial conditions and residents' daily exercise, diet and drinking habits. Increased SUA is due to abnormalities in purine metabolism, excessive uric acid production and/or reduced excretion; higher levels of estrogen in women favor the excretion of SUA, whereas androgens promote reabsorption of UA and inhibit the excretion of SUA [13] and affect the liver's purine metabolism [14]. Besides, the high prevalence of HUA in men may also be related to lifestyle habits such as unhealthy diet, alcohol consumption, smoking habits, and little exercise.

Our study also showed that increased BMI was a risk factor for HUA, which was consistent with the conclusions of Wang YY et al [15] and Ali N et al [16]. The reasons may be related as follow. On the one hand, the accumulation of visceral fat leads to a large amount of plasma free fatty acids flowing into the liver and hepatic portal vein, which stimulates the synthesis of triglyceride, and then leads to the surge of uric acid generation by activating the uric acid synthesis pathway [17]. On the other hand, in participants with visceral fat and obesity, urate excretion, clearance, and creatinine clearance were significantly reduced, leading to high uric acid accumulation in the body [18]. However, the correlation between age and HUA was not shown in this study, which may be due to the fact that the population included in this study was employed population, and its distribution trend in different ages was not obvious.

3.2 The association between SUA levels and hypertension, diabetes and hyperlipidemia

The number of patients suffering from hypertension is 245 million in China in 2015 [19]. Data from CHS [20] showed that the prevalence in people ≥ 18 years was higher among men than women (crude rate: 28.6% vs 27.2%, weighted rate: 24.5% vs 21.9%), and increased with age and BMI. In 2002, 2010, 2011 and 2012, the prevalence rates of dyslipidemia in Chinese people aged ≥ 18 years were 18.60%, 33.97%, 39.91% and 40.40%, respectively, demonstrating an increasing trend [21]. The age-standardized prevalence of dyslipidemia aged ≥ 35 years during 2015-2017 in Inner Mongolia was 31.2%, and male sex and obesity were positively correlated with dyslipidemia [22]. Furthermore, a cohort study from Japan also showed that the prevalence of dyslipidemia was higher in men than in women and tended to increase with age [23]. In 2013, a large sample of 170287 urban and rural residents in 31 provinces showed that the standardized prevalence rate of diabetes mellitus in Chinese adults was 10.9%, with males (11.7%) higher than females (10.2%) [24]. A Meta-analysis involving 80,775 persons showed that the pooled prevalence of diabetes in the general population in Bangladesh was 7.8% (95% *CI*: 6.4-9.3), and age was a risk factor [25]. Conforming with the above studies, the prevalence rates of hypertension, hyperlipidemia and diabetes in this study were 27.76% (male 37.26% higher than female 19.91%), 48.10% (male 57.45% higher than female 40.38%) and 7.47% (male 10.98% higher than female 4.59%), respectively. The prevalence of hypertension, hyperlipidemia and diabetes increased with age and BMI.

In recent years, a number of studies worldwide have shown that SUA levels are closely associated with the occurrence and development of hypertension. A survey by Kuwabara [26] in Japan showed that being in the highest quartile of SUA level increased the risk of hypertension by 3.7 times compared with being in the lowest. Baker [27] also reported that HUA was one of the causes of cardiovascular disease and might

predict the development of hypertension. A systematic review and meta-analysis of 17 prospective cohort studies with 32,000 participants published in 2020 showed a dose-response relationship between SUA levels and the prevalence of hypertension, with each 1 mg/dL increase in uric acid concentration increasing the risk of hypertension by 10% [28]. A possible reason is that a high level of SUA can stimulate renin secretion, causing renin-angiotensin activation and triggering the proliferation of arterial smooth muscle cells, resulting in increased blood pressure [29]. Another possible cause is a mutation in the uricase gene in humans[30], it not only mediates microvascular changes in uric acid levels, but also induces reversible salt-sensitive hypertension [31, 32]. However, there was no correlation between hypertension and uric acid in our study, suggesting that such correlation was not obvious in the northeast China and regional differences may exist. This could not exclude the selective bias in the selection of research subjects as well. We will pay more attention to this content in the later study.

As early as 1975, Bansal [33] reported that SUA levels were associated with dyslipidemia. Our previous study also showed that total TC, TGs, and LDL-C were risk factors for HUA [34]. The reason for this may be related to the inhibition of lipoprotein lipase activity by an increase in SUA levels [35]. The decrease in lipoprotein lipase activity in vivo limits the catabolism of TGs and triggers increased triglyceride levels in the blood. On the other hand, HUA is often accompanied by low adiponectin [36], which can increase the oxidation of free fatty acids, reduce blood TGs and low-density lipoprotein levels and increase high-density lipoprotein. Adiponectin may be a key factor in abnormal HUA lipid metabolism [37]. Dyslipidemia and increased SUA levels may aggravate atherosclerosis [38]. The results of this study showed that the higher the SUA levels were in population, the higher the prevalence of hyperlipidemia. The prevalence of hyperlipidemia in the higher three quartiles of SUA was 3.519-, 2.049- and 1.570- times that of the lowest quartile in model 1. After adjusting for BMI, sex, and age, the prevalence of hyperlipidemia in the higher three quartiles of SUA was 3.719-, 2.091- and 1.632-times that of the lowest quartile, respectively.

At present, the association between SUA levels and diabetes is controversial and requires further investigation. In our study, there was no clear correlation between the different levels of SUA and the prevalence of diabetes in men and women. This is different from the finding of Xu Y [39] in the US, but consistent with the findings of Taniguchi Y in Japan [40]. There are also studies that have shown a negative correlation between diabetes and SUA levels [41], which may be due to different geographical, temporal or age differences in surveys. A systematic review and meta-analysis [42] of the prevalence of SUA and type 2 diabetes mellitus (T2DM) showed that for each 1 mg/ dL increase in SUA, the risk of T2DM increased by 13.1% (pooled *RR*) and 48.4% (pooled *OR*). However, another meta-analysis [43] indicated that it is still debatable whether SUA is an independent risk factor for T2DM or it only emphasizes the association between other independent risk factors such as age, obesity, hypertension, gender, and dyslipidemia and T2DM. Therefore, the association between SUA and T2DM requires further evaluation.

The present study is characterized with several strengths. First, through a large sample of population epidemiological studies, we deeply studied the correlation between uric acid and metabolic indicators such as blood glucose and blood pressure, providing a useful reference for revealing the etiology and

pathogenesis of HUA. Second, adjustments for some potential confounding factors, such as age, gender and BMI, increased reliability of the results. It should be noted that this work had several potential limitations. First, because this research was a cross-sectional study, it was not possible to find the causal relationship between SUA levels and hypertension, diabetes and hyperlipidemia. Second, a selection bias could be introduced, for the study participants volunteered for the health examination. Third, parameters of lifestyle factors such as diet and physical activity were not included in the questionnaire, which may affect the SUA levels. Fourth, the sample size of this study was relatively small; therefore, the findings may not represent for the whole population of China. However, this study findings are worthy as a reference for future investigations. Further, a longitudinal study is necessary for a deeper explanation and to clarify these issues.

Conclusion

In conclusion, our research explores the association between SUA and other metabolic diseases. Our results could be significant for the clinical prevention and control of hyperlipidemia and other diseases. Maintaining normal SUA level may be useful for the prevention and treatment of hyperlipidemia.

Declarations

Funding

This paper was funded by the basic research business fees of universities in Heilongjiang (2016-KYYWF-0591).

Conflict of Interest

The authors declare that they have no conflict of interest.

Availability of data and material

All data generated or analysed during this study are included in this manuscript.

Code availability

A database was established by EpiData3.0 software. Statistical analyzes were performed using SPSS 19.0 software.

Authors' contributions

All authors contributed to the study conception and design. Hongbin Qiu was responsible for directing the experiment. Material preparation and data collection were performed by Xue Bai, Liling Zhu, Yang Song, Xianglin Yin and Xiaoqing Niu. Songpo Yao and Rongyu Lan processed the experimental data. The first

draft of the manuscript was written by Baosheng Guan and Jiaxin Chen and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Medical Ethics Committee of Jiamusi University, Jiamusi, China. (Data: 2015-01-07/ No. JMSU-213)

Consent to participate

All patients provided written informed consent prior to participation in this study. Consent to publish was also obtained from all patients in this study.

Acknowledgments

The authors would like to thank the gout research key laboratory in Heilongjiang Province, and Northern medicine and functional food special subject construction project for assistance with some of the experiments. This paper was supported by the basic research business fees of universities in Heilongjiang (2016-KYYWF-0591).

References

1. A. V. Yeldandi, X. D. Wang, K. Alvares et al. Human urate oxidase gene: cloning and partial sequence analysis reveal a stop codon within the fifth exon. *Biochemical and biophysical research communications*. 1990; 171: 641-646.
2. X. Chen, H.-Z. Ge, S.-S. Lei et al. *Dendrobium officinalis* six nostrum ameliorates urate under-excretion and protects renal dysfunction in lipid emulsion-induced hyperuricemic rats. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*. 2020; 132: 110765. <https://doi.org/10.1016/j.biopha.2020.110765>
3. N. Dalbeth, A. L. Gosling, A. Gaffo, A. Abhishek. Gout. *Lancet*. 2021; 397: 1843-1855. [https://doi.org/10.1016/S0140-6736\(21\)00569-9](https://doi.org/10.1016/S0140-6736(21)00569-9)
4. X. Li, X. Meng, M. Timofeeva et al. Serum uric acid levels and multiple health outcomes: umbrella review of evidence from observational studies, randomised controlled trials, and Mendelian randomisation studies. *BMJ*. 2017; 357: j2376. <https://doi.org/10.1136/bmj.j2376>
5. B.-F. Zhou, Cooperative Meta-Analysis Group of the Working Group on Obesity in China. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults—study on optimal cut-off points of body mass index and waist circumference in Chinese adults. *Biomed Environ Sci*. 2002; 15: 83-96.

6. M. Andrés, M.-A. Quintanilla, F. Sivera et al. Silent Monosodium Urate Crystal Deposits Are Associated With Severe Coronary Calcification in Asymptomatic Hyperuricemia: An Exploratory Study. *Arthritis & rheumatology* (Hoboken, N.J.). 2016; 68: 1531-1539. <https://doi.org/10.1002/art.39581>
7. N. Dalbeth, M. E. House, O. Aati et al. Urate crystal deposition in asymptomatic hyperuricaemia and symptomatic gout: a dual energy CT study. *Annals of the rheumatic diseases*. 2015; 74: 908-911. <https://doi.org/10.1136/annrheumdis-2014-206397>
8. C.-F. Kuo, M. J. Grainge, W. Zhang, M. Doherty. Global epidemiology of gout: prevalence, incidence and risk factors. *Nature reviews. Rheumatology*. 2015; 11: 649-662. <https://doi.org/10.1038/nrrheum.2015.91>
9. M. Chen-Xu, C. Yokose, S. K. Rai, M. H. Pillinger, H. K. Choi. Contemporary Prevalence of Gout and Hyperuricemia in the United States and Decadal Trends: The National Health and Nutrition Examination Survey, 2007-2016. *Arthritis & rheumatology* (Hoboken, N.J.). 2019; 71: 991-999. <https://doi.org/10.1002/art.40807>
10. V. Lohsoonthorn, B. Dhanamun, M. A. Williams. Prevalence of hyperuricemia and its relationship with metabolic syndrome in Thai adults receiving annual health exams. *Arch Med Res*. 2006; 37: 883-889. <https://doi.org/10.1016/j.arcmed.2006.03.008>
11. X.-B. Huang, W.-Q. Zhang, W.-W. Tang et al. Prevalence and associated factors of hyperuricemia among urban adults aged 35-79 years in southwestern China: a community-based cross-sectional study. *Scientific reports*. 2020; 10: 15683. <https://doi.org/10.1038/s41598-020-72780-3>
12. J. Huang, Z. F. Ma, Y. Zhang et al. Geographical distribution of hyperuricemia in mainland China: a comprehensive systematic review and meta-analysis. *Glob Health Res Policy*. 2020; 5: 52. <https://doi.org/10.1186/s41256-020-00178-9>
13. Z. Li, Q. Liu, H. Mao et al. Gender difference in the association of hyperuricemia with chronic kidney disease in southern China. *Kidney Blood Press Res*. 2012; 36. <https://doi.org/10.1159/000341486>
14. R. Yahyaoui, I. Esteva, J. J. Haro-Mora et al. Effect of long-term administration of cross-sex hormone therapy on serum and urinary uric acid in transsexual persons. *The Journal of clinical endocrinology and metabolism*. 2008; 93: 2230-2233. <https://doi.org/10.1210/jc.2007-2467>
15. Y.-Y. Wang, L. Li, J. Cui et al. Associations between anthropometric parameters (body mass index, waist circumference and waist to hip ratio) and newly diagnosed hyperuricemia in adults in Qingdao, China: A cross-sectional study. *Asia Pac J Clin Nutr*. 2020; 29: 763-770. [https://doi.org/10.6133/apjcn.202012_29\(4\).0011](https://doi.org/10.6133/apjcn.202012_29(4).0011)
16. N. Ali, R. Perveen, S. Rahman et al. Prevalence of hyperuricemia and the relationship between serum uric acid and obesity: A study on Bangladeshi adults. *PloS one*. 2018; 13: e0206850. <https://doi.org/10.1371/journal.pone.0206850>
17. K. Tanaka, S. Ogata, H. Tanaka et al. The relationship between body mass index and uric acid: a study on Japanese adult twins. *Environ Health Prev Med*. 2015; 20: 347-353. <https://doi.org/10.1007/s12199-015-0473-3>

18. F. Matsuura, S. Yamashita, T. Nakamura et al. Effect of visceral fat accumulation on uric acid metabolism in male obese subjects: visceral fat obesity is linked more closely to overproduction of uric acid than subcutaneous fat obesity. *Metabolism*. 1998; 47: 929-933.
[https://doi.org/10.1016/s0026-0495\(98\)90346-8](https://doi.org/10.1016/s0026-0495(98)90346-8)
19. National Center for Cardiovascular Diseases (2020) Report on Cardiovascular Health and Diseases in China 2019. China Science Publishing & Media Ltd, Beijing.
20. Z. Wang, Z. Chen, L. Zhang et al. Status of Hypertension in China: Results From the China Hypertension Survey, 2012-2015. *Circulation*. 2018; 137: 2344-2356.
<https://doi.org/10.1161/CIRCULATIONAHA.117.032380>
21. The Disease Prevention Control Bureau of the National Health Family Planning Commission (2015) A report on the status of nutrition and chronic diseases among Chinese residents (2015). People's Medical Publishing House, Beijing.
22. Y. Xi, L. Niu, N. Cao et al. Prevalence of dyslipidemia and associated risk factors among adults aged ≥ 35 years in northern China: a cross-sectional study. *BMC Public Health*. 2020; 20: 1068.
<https://doi.org/10.1186/s12889-020-09172-9>
23. T. Okui. An Age-Period-Cohort Analysis of Prevalence and Consultation Rate for Dyslipidemia in Japan. *Asia Pac J Public Health*. 2021; 33: 46-52. <https://doi.org/10.1177/1010539520963643>
24. L. Wang, P. Gao, M. Zhang et al. Prevalence and Ethnic Pattern of Diabetes and Prediabetes in China in 2013. *JAMA*. 2017; 317: 2515-2523. <https://doi.org/10.1001/jama.2017.7596>
25. S. Akhtar, J. A. Nasir, A. Sarwar et al. Prevalence of diabetes and pre-diabetes in Bangladesh: a systematic review and meta-analysis. *BMJ Open*. 2020; 10: e036086.
<https://doi.org/10.1136/bmjopen-2019-036086>
26. M. Kuwabara, K. Niwa, S. Nishihara et al. Hyperuricemia is an independent competing risk factor for atrial fibrillation. *Int J Cardiol*. 2017; 231: 137-142. <https://doi.org/10.1016/j.ijcard.2016.11.268>
27. J. F. Baker, E. Krishnan, L. Chen, H. R. Schumacher. Serum uric acid and cardiovascular disease: recent developments, and where do they leave us? *Am J Med*. 2005; 118: 816-826.
<https://doi.org/10.1016/j.amjmed.2005.03.043>
28. L. Liu, X. Zhang, R. Qie et al. Dose-response association between serum uric acid levels and incident hypertension: a systematic review and meta-analysis of 17 prospective cohort studies of 32 thousand participants. *Acta Cardiol*. 2020: 1-6. <https://doi.org/10.1080/00015385.2020.1779476>
29. J. Wang, T. Qin, J. Chen et al. Hyperuricemia and risk of incident hypertension: a systematic review and meta-analysis of observational studies. *PLoS One*. 2014; 9: e114259.
<https://doi.org/10.1371/journal.pone.0114259>
30. X. W. Wu, D. M. Muzny, C. C. Lee, C. T. Caskey. Two independent mutational events in the loss of urate oxidase during hominoid evolution. *J Mol Evol*. 1992; 34: 78-84.
<https://doi.org/10.1007/BF00163854>
31. D. I. Feig, D.-H. Kang, T. Nakagawa, M. Mazzali, R. J. Johnson. Uric acid and hypertension. *Curr Hypertens Rep*. 2006; 8: 111-115. <https://doi.org/10.1007/s11906-006-0005-z>

32. R. J. Johnson, J. Herrera-Acosta, G. F. Schreiner, B. Rodriguez-Iturbe. Subtle acquired renal injury as a mechanism of salt-sensitive hypertension. *N Engl J Med.* 2002; 346: 913-923.
<https://doi.org/10.1056/NEJMra011078>
33. B. C. Bansal, R. R. Gupta, M. R. Bansal, C. Prakash. Serum lipids and uric acid relationship in ischemic thrombotic cerebrovascular disease. *Stroke.* 1975; 6: 304-307.
<https://doi.org/10.1161/01.str.6.3.304>
34. B. Guan, Y. Wang, X. Bai et al. Risk factors for hyperuricemia. *Chinese Journal of Gerontology.* 2016; 36(1):69-70.
35. Q.-X. Han, D. Zhang, Y.-L. Zhao et al. Risk Factors For Hyperuricemia In Chinese Centenarians And Near-Centenarians. *Clin Interv Aging.* 2019; 14: 2239-2247. <https://doi.org/10.2147/CIA.S223048>
36. D. Gradinaru, D. Margina, C. Borsa et al. Adiponectin: possible link between metabolic stress and oxidative stress in the elderly. *Aging Clin Exp Res.* 2017; 29: 621-629.
<https://doi.org/10.1007/s40520-016-0629-z>
37. N. Katsiki, C. Mantzoros, D. P. Mikhailidis. Adiponectin, lipids and atherosclerosis. *Curr Opin Lipidol.* 2017; 28: 347-354. <https://doi.org/10.1097/MOL.0000000000000431>
38. C. Bianchi, G. Penno, L. Malloggi et al. Non-traditional markers of atherosclerosis potentiate the risk of coronary heart disease in patients with type 2 diabetes and metabolic syndrome. *Nutr Metab Cardiovasc Dis.* 2008; 18: 31-38. <https://doi.org/10.1016/j.numecd.2006.07.007>
39. Y. Xu, J. Zhu, L. Gao et al. Hyperuricemia as an independent predictor of vascular complications and mortality in type 2 diabetes patients: a meta-analysis. *PloS one.* 2013; 8: e78206.
<https://doi.org/10.1371/journal.pone.0078206>
40. Y. Taniguchi, T. Hayashi, K. Tsumura et al. Serum uric acid and the risk for hypertension and Type 2 diabetes in Japanese men: The Osaka Health Survey. *J Hypertens.* 2001; 19: 1209-1215.
<https://doi.org/10.1097/00004872-200107000-00005>
41. P. Bandaru, A. Shankar. Association between Serum Uric Acid Levels and Diabetes Mellitus. *Int J Endocrinol.* 2011; 2011: 604715. <https://doi.org/10.1155/2011/604715>
42. Y. L. Xu, K. F. Xu, J. L. Bai et al. Elevation of serum uric acid and incidence of type 2 diabetes: A systematic review and meta-analysis. *Chronic Dis Transl Med.* 2016; 2: 81-91.
<https://doi.org/10.1016/j.cdtm.2016.09.003>
43. L. Ismail, H. Materwala, J. Al Kaabi. Association of risk factors with type 2 diabetes: A systematic review. *Comput Struct Biotechnol J.* 2021; 19: 1759-1785. <https://doi.org/10.1016/j.csbj.2021.03.003>