An observational study on the relationship between serum uric acid and hypertension in a Northern Chinese population aged 45 to 59 years

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Abstract

Little is known about the relationship serum uric acid (SUA) and hypertension in Chinese population. Therefore, the aim of this study was to determine the association between SUA and hypertension in a northern Chinese population. The participants were a group of 1730 Chinese adults aged 45 to 59 years in Shandong Province, who were recruited from the Linyi Nutrition and Health Survey (2015–2016). Hypertension was defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg. Hyperuricemia was defined as SUA >420 μmol/L (7.0 mg/dL) for men and >360 μmol/L (6.0 mg/dL) for women. All anthropometric measurements and biochemical data were collected following standard protocols. Multivariate logistic regression analysis was used to examine the association between SUA and hypertension with adjustment of confounding variables. Body mass index, waist circumference, waist-to-hip ratio, systolic blood pressure, diastolic blood pressure, fasting blood glucose, triglycerides, alanine aminotransferase, aspartate aminotransferase, SUA, and the prevalence of hypertension and hyperuricemia were significantly higher in males than in females ($P < .001$). The females had significantly higher levels of total cholesterol and high-density lipoprotein cholesterol. Besides, after adjustment for confounding variables, hyperuricemia was associated with an increased risk of hypertension in both male and female patients, with odds ratios of 2.152 (95% confidence interval 1.324–3.498) and 2.133 (95% confidence interval 1.409–3.229), respectively.

Hyperuricemia was significantly associated with the risk of hypertension. Further longitudinal studies and trails are needed to confirm our findings.

Abbreviations: ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, CI = confidence interval, DBP = diastolic blood pressure, FPG = fasting blood glucose, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, OR = odds ratio, SBP = systolic blood pressure, SUA = serum uric acid, TC = total cholesterol, TG = triglycerides, WC = waist circumference, WHR = waist-to-hip ratio.

Keywords: blood pressure, Chinese population, hypertension, hyperuricemia

1. Introduction

Hypertension is 1 of the most common chronic diseases, affecting more than one billion people worldwide.[1] In United States, it is a significant health problem, with an estimated 65 million adults suffering from hypertension.[2] Meanwhile, the prevalence of hypertension in China has also dramatically increased by almost one-third from 1991 to 2002, which comprises approximately 18% of adult population.[3,4] It is well-known that hypertension

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is considered as a multifactorial chronic disease that may be related to some risk factors, including genetic factors, alcohol intake, smoking, dietary factors, family history of hypertension, and overweight/obesity.[2]

Hyperuricemia is a metabolic disturbance of purine nucleotide, and considered as a precursor of gout. Over the past decade, although its incidence in Chinese population has not been extensively investigated, a remarkable increasing trend has been observed.[5,6] Similarly, previous studies have shown that increased uric acid concentrations are significantly associated with the elements of metabolic syndrome, for example, hypertension, obesity, diabetes, and insulin resistance.[7,8] However, to the best of our knowledge, data on the relation between hyperuricemia and hypertension in Chinese population have scarcely been reported,[9,10] especially among a middle-aged and northern Chinese population. Therefore, the aim of the present study was to investigate the association between serum uric acid (SUA) and hypertension among a northern Chinese population aged 45 to 59 years.

2. Subjects and methods

2.1. Study population

During the period from June 2015 through September 2016, this cross-sectional study was performed in the city of Linyi,

Table 1

Comparison of clinical and biochemical characteristics between subjects with hypertension and nonhypertension.

Variables	Hypertension (n = 553)	Nonhypertension (n = 1177)	P
Clinical variables			
Age, y[*]	54.50 ± 5.15	48.03 ± 5.68	<.001
Sex[†]			<.01
Male	359 (64.92%)	662 (56.24%)	
Female	194 (35.08%)	515 (43.76%)	
BMI, kg/m^2[*]	26.04 ± 2.96	24.41 ± 2.71	<.001
WC, cm[*]	90.70 ± 8.39	86.35 ± 8.06	<.001
WHR[*]	0.91 ± 0.05	0.88 ± 0.06	<.001
SBP, mm Hg[*]	149.68 ± 15.13	123.54 ± 9.47	<.001
DBP, mm Hg[*]	96.34 ± 9.84	76.05 ± 8.15	<.001
Biochemical variables			
FPG, mmol/L[*]	6.34 ± 1.45	6.16 ± 1.90	.123
TG, mmol/L[*]	2.16 ± 2.37	1.84 ± 1.50	<.05
TC, mmol/L[*]	5.22 ± 1.20	5.07 ± 0.86	<.05
HDL-C, mmol/L[*]	1.30 ± 0.53	1.27 ± 0.32	.348
LDL-C, mmol/L[*]	3.31 ± 0.86	3.28 ± 0.85	.666
SUA, μmol/L[*]	369.90 ± 80.08	355.05 ± 71.16	<.01
Hyperuricemia, %[†]	96 (17.40%)	147 (12.49%)	<.01

Data for continuous variables are mean ± SD.
BMI = body mass index, DBP = diastolic blood pressure, FG = fasting blood glucose, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SBP = systolic blood pressure, SUA = serum uric acid, TC = total cholesterol, TG = triglycerides, WC = waist circumference, WHR = waist-to-hip ratio.
[*] Student t tests.
[†] Chi-square test.

Shandong Province, China. Participants aged 45 to 59 years were recruited in present study. In these areas and countries, we randomly chose 2 residential villages or communities, according to resident health records. A total of 1906 eligible participants (1143 male, 763 female) were invited to attend a health examination at the Medical Center for Physical Examination, Linyi People's Hospital, where the participant was face to face interviewed by a trained interviewer using written questionnaires. Thirty-six participants with missing or incomplete information in their questionnaires were included. Besides, we also excluded 140 participants who did not examine the SUA or/and blood pressure. Overall, a total of 1730 participants (1021 male and 709 female) remained in our analyses. Written informed consent was obtained from all subjects, and the protocol of this study was approved by the institutional review and ethic committee of Linyi People's Hospital, Shandong Province, China.

2.2. Anthropometric measurements

Height was measured with subject not wearing shoes to the nearest 0.1 cm. Weight in light clothes and without shoes was measured with a digital scale to the nearest 100 g. Body mass index (BMI) was calculated using weight (in kilograms) divided by squared height (in meters). Waist circumstance (WC) was measured midway between the lowest rib and the superior border of the iliac crest with an inelastic measuring tape at the end of normal expiration to the nearest 1 mm[11] and hip circumference was measured to the nearest 0.5 cm at the maximum level over light clothing by using an inelastic plastic tape.[12] All measurements were performed by trained nurses to use standardized procedures.

2.3. Assessment of biomarker

Blood samples were obtained after 12 hours of fasting overnight. After blood was collected, samples were allowed to clot at room temperature for 1 to 3 hours and serum was separated. After clotting, serum was separated by centrifugation for 15 minutes at

3000 r.p.m. Then samples were analyzed in the Medical Center for Physical Examination, Linyi People's Hospital, fasting blood glucose (FPG), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), SUA, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) using the Hitachi 7180 auto-analyzer (Hitachi, Tokyo, Japan).

2.4. Blood pressure measurement

After participants rested for 5 minutes in the sitting position, blood pressure was measured by using a standard mercury sphygmomanometer. Then, a trained nurse measured the blood pressure 2 times in seated participants, and thereafter the means of 2 measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated and considered for analysis.

2.5. Definitions

Obesity was defined by BMI ≥28 kg/m^2 and abdominal adiposity was defined as male WC ≥85 cm and female WC ≥80 cm).[13] Hyperuricemia was defined as SUA >420 μmol/L (7.0 mg/dL) for men and >360 μmol/L (6.0 mg/dL) for women.[14] Hypertension was defined as SBP ≥140 mm Hg and/or DBP ≥90 mm Hg, and/or the current use of antihypertensive medication.[15]

2.6. Statistical analysis

The data for continuous variables were reported as the mean ± SD, and the data for categorical variables were reported as sum (proportions). The chi-square test and independent-samples t test or Mann–Whitney U test were used to compare categorical variables and continuous variables, respectively. Pearson bivariate correlation was made between SUA and other variables. Besides, multivariate logistic regression analysis was used to examine the association between SUA and hypertension with

Table 2

Demographic, and clinical characteristics of subjects by sex.

Variables	Male	Female	P
Demographic			
N (%)	1021 (59.0%)	709 (41.0%)	
Age, y	51.8 ± 5.38	51.3 ± 4.57	.748
Clinical characteristics			
BMI, kg/m^2	24.73 ± 2.35	23.79 ± 2.46	<.001
WC, cm	87.65 ± 7.45	81.26 ± 7.03	<.001
WHR	0.89 ± 0.07	0.83 ± 0.04	<.001
SBP, mm Hg	133.48 ± 17.42	129.01 ± 17.51	<.001
DBP, mm Hg	83.76 ± 13.23	78.31 ± 12.37	<.001
FPG, mmol/L	6.17 ± 1.04	5.76 ± 1.75	<.001
TG, mmol/L	1.86 ± 2.09	1.33 ± 1.54	<.001
TC, mmol/L	5.02 ± 0.96	5.43 ± 0.87	<.001
HDL-C, mmol/L	1.18 ± 0.21	1.61 ± 0.27	<.001
LDL-C, mmol/L	3.21 ± 0.83	3.19 ± 0.80	.411
SUA, μmol/L	401.74 ± 47.28	303.51 ± 59.82	<.001
ALT, U/L	34.76 ± 15.28	25.48 ± 13.80	<.001
AST, U/L	26.37 ± 7.44	23.26 ± 6.65	<.001
Hypertension, %	380 (37.22%)	153 (21.58%)	<.05
Hyperuricemia, %	188 (18.40%)	55 (7.76%)	<.001

Data for continuous variables are mean ± SD.
BMI = body mass index, DBP = diastolic blood pressure, FPG = fasting blood glucose, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SBP = systolic blood pressure, SUA = serum uric acid, TC = total cholesterol, TG = triglycerides, WC = waist circumference.

adjustment of confounding variables. Two-sided P values <.05 were considered statistically significant. All analyses were performed on the Statistical Package for Social Sciences (version 20.0, SPSS Inc, Chicago, IL).

3. Results

Comparison of clinical and biochemical characteristics between subjects with hypertension and nonhypertension are shown in Table 1. Total prevalence of hyperuricemia in our study population was 14.05%. In hypertension subjects, it was 17.40% and in nonhypertension subjects it was 12.49%. Age, BMI, WC, waist-to-hip ratio (WHR), SBP, DBP, TG, TC, SUA, and the prevalence of hyperuricemia were significantly higher in hypertension subjects than in nonhypertension subjects(P <.05).

Demographic and clinical characteristics of subjects by sex are presented in Table 2, which indicated higher levels of BMI, WC, WHR, SBP, DBP, FPG, TG, SUA, ALT, AST, and prevalence of hypertension and hyperuricemia in males than in females (P <.001). Besides, females had significantly higher levels of TC and HDL-C (5.43 ± 0.87 vs 5.02 ± 0.96, 1.61 ± 0.27 vs 1.18 ± 0.21; P <.001, respectively) than males.

Pearson bivariate correlation between SUA and other factors disclosed top 4 correlation coefficients belonged to TG (r = 0.269, P <.001), WHR (r = 0.214, P <.001), WC (r = 0.188, P <.001), and TC (r = 0.184, P <.01) in hypertension subjects, and BMI (r = 0.255, P <.001), weight (r = 0.251, P <.001), WC (r = 0.227, P <.001), and WHR (r = 0.190, P <.001) in nonhypertension subjects (Table 3). In addition, FPG and HDL-C were inversely associated with SUA in both nonhypertension and hypertension

Table 3

Pearson bivariate correlations between serum uric acid levels and other factors in the subjects with hypertension and nonhypertension.

Factors	SUA in hypertension (n = 931)		SUA in nonhypertension (n = 658)	
	r	P*	r	P*
Age, y	−0.129	.015	−0.075	.070
Height, cm	0.173	.001	0.083	.047
Weight, kg	0.175	.001	0.251	.000
BMI, kg/m^2	0.110	.040	0.255	.000
WC, cm	0.188	.000	0.227	.000
WHR	0.214	.000	0.190	.000
SBP, mm Hg	0.021	.697	0.074	.077
DBP, mm Hg	0.098	.066	0.103	.014
FPG, mmol/L	−0.128	.016	−0.138	.001
TG, mmol/L	0.269	.000	0.151	.000
TC, mmol/L	0.184	.001	0.026	.535
HDL-C, mmol/L	−0.162	.010	−0.184	.000
LDL-C, mmol/L	0.132	.036	0.036	.467

BMI = body mass index, DBP = diastolic blood pressure, FPG = fasting blood glucose, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SBP = systolic blood pressure, SUA = serum uric acid TC = total cholesterol, TG = triglycerides, WC = waist circumference, WHR = waist-to-hip ratio.
* Pearson correlation test.

Table 4

Multivariable-adjusted odds ratios and 95% confidence intervals of hyperuricemia for hypertension stratified by sex.

| | Male | | | Female | | |
Variables	OR	95% CI	P	OR	95% CI	P
Model 1	1.710	(1.334–2.011)	.000	1.627	(1.263–1.935)	.000
Model 2	1.586	(1.387–1.814)	.001	1.446	(1.214–1.689)	.003
Model 3	1.260	(1.105–1.536)	.034	1.037	(1.033–1.108)	.040

CI = confidence interval, OR = odds ratio.
Model 1 was unadjusted; model 2 was adjusted for age, physical activity, educational level, and income; model 3 was adjusted for age, physical activity, educational level, income, fasting glucose, total cholesterol, high-density lipoprotein cholesterol, and body mass index.

subjects ($P < .05$). Furthermore, age was inversely associated with SUA in hypertension subjects ($r = -0.129$, $P < .05$).

Multivariable-adjusted odds ratios (OR) (95% confidence interval [CI]) of hyperuricemia for the risk of hypertension stratified by sex are shown in Table 4. In the model 1, males were more likely to suffer from hypertension compared with females (OR 1.710, 95% CI 1.334–2.011; OR 1.627, 95% CI 1.263–1.935, $P < .001$, respectively). In models 2 and 3, our results indicated that the odds of having hypertension was significantly higher in males (OR 1.586, 95% CI 1.387–1.814, $P < .01$; OR 1.260, 95% CI 1.105–1.536, $P < .05$, respectively) than in females (OR 1.446, 95% CI 1.214–1.689, $P < .01$; OR 1.037, 95% CI 1.033–1.108, $P < .05$, respectively).

4. Discussion

In the present study, the results indicate that hyperuricemia is associated with an elevated risk of hypertension, and the prevalence of hyperuricemia was significantly higher in hypertension subjects than that in nonhypertension subjects. Moreover, our findings also show that the relation between hyperuricemia and risk of hypertension in males is significantly stronger than in females. To our knowledge, this is the first study reporting the association between hyperuricemia and risk of hypertension in a middle-aged and northern Chinese population.

The major finding in the present study is that hyperuricemia is significantly associated with an elevated risk of hypertension. To date, studies on the relation between hyperuricemia and risk of hypertension have reported inconsistent findings. Although some epidemiological and clinical studies have demonstrated that hyperuricemia is an independent risk factor for hypertension,[16,17] others also reported a null association.[18] Besides, the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and the American Heart Association have not recognized elevated SUA as an important risk factor for hypertension.[19,20] However, an emerging body of research in recent years has examined the relationship between hyperuricemia and risk of hypertension, and found that hyperuricemia plays an important role in the development of hypertension.[21,22] There are several potential explanations for the positive association between hyperuricemia and risk of hypertension. Firstly, elevated SUA level may induce renal vasoconstriction by reduction of circulating nitric oxide and activation of the rennin–angiotensin system, and thereby increasing the level of blood pressure.[23] Secondly, several studies have confirmed that elevated SUA may cause endothelial dysfunction by inducing antiproliferative effects and impairing nitric oxide production, and oxygen radicals generated by xanthine oxidase contributed to the pathogenesis of hypertension.[24] Thirdly, SUA may enter vascular smooth muscle cells stimulating multiple factors, for example, cycloxygenase-2 and

platelet-derived growth factor, which cause smooth muscle cellular proliferation, and thus lead to secondary arteriolosclerosis.[25] Furthermore, previous studies have shown that hyperuricemia is closely related to obesity and insulin resistance.[26,27] To the best of our knowledge, obesity and insulin resistance are considered as the key risk factors for hypertension. Meanwhile, recent a study reported that insulin resistance could promote the formation of hypertension through stimulating renal tubular sodium reabsorption, augmenting sympathetic nervous system reactivity and activating the rennin–angiotensin system.[28]

In this study, we also found the relationship of hyperuricemia with hypertension in males was significantly stronger than in females. This is in agreement with a previous study reporting the similar result.[10] The apparently protective effect of sex might be related to estrogen level. Estrogen is known to possess the effect of promoting excretion of uric acid. Here, the sex difference in the relation between hypeuricemia and risk of hypertension may lie in the fact that estrogen is a uricosuric agent. A previous study by Anton et al[29] showed that higher renal clearance of urate in women was due to their higher plasma estrogen levels and lower tuber urate postsecretory reabsorption. Moreover, higher consumption of alcohol is significantly associated with the risk of hyperuricemia. Previous study has shown that alcohol consumption can elevate SUA levels by increased uric acid synthesis.[30] Furthermore, there are significantly higher levels of BMI in males compared with that in females (24.73 ± 2.35 vs 23.79 ± 2.46). In a study by Wang et al,[11] the positive association between BMI and SUA level has been reported in a Chinese population.

4.1. Strengths and limitations

This study has its own strengths and limitations. Firstly, this is the first study reporting the relation between SUA and hypertension risk among a middle-aged and northern Chinese population. Findings from the present study add to existing literature by supporting the association between hyperuricemia and risk of hypertension. Secondly, our results are reliable because all biochemical data were obtained from the Medical Center for Physical Examination, Linyi People's Hospital. Thirdly, we also have adjusted for some potential known confounders for reliability in our analyses. However, some limitations need be considered in the interpretation of our findings. Firstly, due to the cross-sectional design of this study, one cannot infer causality. Thus, our findings need to be confirmed in future prospective study. Secondly, information on the risk factors for hyperuricemia (eg, history of kidney disease and dietary behavior) was not collected in the present study. Consequently, our findings may suffer from differing degrees of completeness and accuracy. Finally, the participants are only from the city of Linyi, Shandong

Province, China. Thus, our findings may not be extrapolated to a population in the whole China.

5. Conclusions

In conclusion, our findings indicate that hyperuricemia is significantly associated with risk of hypertension, and the association between hyperuricemia and hypertension risk is stronger in males than that in females among a middle-aged and northern Chinese population. However, prospective studies are needed to confirm the causal relation between hyperuricemia with risk of hypertension.

Acknowledgments

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