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Original Article

Association of Serum Uric Acid with Body Mass Index: A Cross-Sectional Study from Jiangsu Province, China

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Abstract

Background: Body mass index (BMI) has been demonstrated to be associated with serum uric acid (SUA) level in many developed countries, however, there is still a lack of large sample study in Jiangsu Province, one of the most economically developed regions in China, where fat-rich diet is common.

Methods: Through retrospective analysis in healthy subjects, we determined the association of BMI with hyperuricemia risk. Data of 39,736 participants from January 2011 to June 2013 in China were analyzed for parameters including physical examinations and biochemical blood analysis.

Results: On univariate analysis, SUA was positively correlated with age, SBP, DBP, BMI, FPG, red blood cell count, hemoglobin, white blood cell count, platelet, cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, ALT, AST, bilirubin, albumin, BUN and creatinine. SUA was significantly elevated in a linear fashion as BMI increased, and SUA in obesity was significantly higher than underweight. The prevalence of hyperuricemia remained approximately 2.98 times greater among individuals with overweight, and 5.96 times greater among obesity, compared to individuals with underweight.

Conclusion: There is a positive relationship between BMI and SUA among healthy subjects in Jiangsu province, China.

Keywords: Serum uric acid, Body mass index, Association

Introduction

Uric acid is a byproduct of purine metabolism (1, 2) and elevated serum uric acid (SUA) levels have an underlying role in gout (3). Hyperuricemia was defined as SUA concentration > 420 μmol/l in males or 340 μmol/l in female. The prevalence of hyperuricemia is increasing rapidly in China. In the coastal city Tianjin of China, hyperuricemic prevalence was 12.16%, with male significantly higher than female, which was reported in 2011 (4). Increasing evidence has shown that hyperuricemia was also associated with dyslipid-emia (5), increased systemic inflammation (6), insulin resistance (7), diabetes mellitus (8), hypertension (9), chronic kidney disease (10), and cardiovascular disease (11).

Several studies have focused on possible risk factors of hyperuricemia. Gout patients have significantly greater body mass index (BMI) in the Framingham study (12). After two years follow up of 3,153 individuals, Ishizaka reported SUA change was related with for BMI change (13). As the association between obesity and SUA is well

established, BMI is an important modifiable risk factor for hyperuricemia in USA, Japan, and other countries (13, 14).

However, according to our knowledge, there is a lack of large sample study in Jiangsu Province, one of the most economically developed regions in China, where fat-rich diet is common. In the present study, we investigated the relationship of BMI and SUA in 39,736 healthy subjects.

Methods

This study was approved by the Ethics Committee of Nanjing Medical University.

Our study consisted of 39,736 healthy subjects from health checkups at the Health Care Center of the Second Affiliated Hospital of Nanjing Medical University. All subjects completed the physical and blood examinations performed from January 2011 to June 2013.

A physical examination was performed on all subjects by a qualified doctor per established standard methods (15). Weight was obtained with participants wearing light clothing and no shoes. BMI was calculated by dividing body weight (kg) by the square of height (m^2). Using diagnostic criteria for obesity in BMI for Asian populations recommended by the WHO, we categorized BMI into four categories: underweight (<18.5 kg/m^2), normal weight (18.5-23.0 kg/m^2), overweight (23.0-27.5 kg/m^2), and obese (≥27.5 kg/m^2) (16). Two consecutively readings of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were taken on the right arm using a calibrated mercury sphygmomanometer with the participant in a seated position and arm supported at heart level. The participants rested for at least 5 minutes before blood pressure measurement. The mean of these two measures was used in the subsequent analysis. After an overnight fast of at least 10 hours and rest for 20 minutes, fasting blood samples (without venous stasis) were drawn from an antecubital vein. Measurement of fasting plasma glucose (FPG), red blood cell count, hemoglobin, white blood cell count, platelet, total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, albumin, urea nitrogen (BUN), creatinine and SUA were done in the laboratory. All procedures were conducted by trained technicians followed standardized protocols. Hyperuricemia was defined as serum uric acid concentration > 420 μmol/l in males or 340 μmol/l in female as previously defined (17).

Statistical analyses were performed using SPSS 18.0 software for Windows (SPSS Inc., Chicago, IL). All variables were normal distribution and presented as mean±standard error (SE) for continuous variables. Comparisons among groups were tested by t test or one-way ANOVA. Partial correlation analysis determined the relationship between SUA and related variables. Multivariate logistic regression models examined the association between BMI and concentrations of SUA, after adjusting for age, FPG, red blood cell count, hemoglobin, white blood cell count, platelet, cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, ALT, AST, bilirubin, albumin, BUN, creatinine. All statistical tests were two-tailed with type I error set at 0.05, and *P* values, 0.05 considered statistically significant.

Results

On univariate analysis, SUA was positively correlated with age, SBP, DBP, BMI, FPG, red blood cell count, hemoglobin, white blood cell count, platelet, cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, ALT, AST, bilirubin, albumin, BUN and creatinine (Table 1). On multiple regression analysis, SUA was positively associated with age, SBP, BMI, FPG, red blood cell count, hemoglobin, white blood cell count, platelet, triglyceride, HDL-cholesterol, LDL-cholesterol, ALT, AST, bilirubin, albumin, BUN and creatinine, while *P* value for DBP was 0.652 (>0.05), and for cholesterol was 0.847 (>0.05) (Table 2). Table 3 compares individuals with and without hyperuricemia. The two groups were statistically significantly different in majority of the variables evaluated.

Table 1: Serum uric acid: univariate analysis (n=39736)

Characteristics	Serum uric acid	
	r	*P* value
Age (yr)	0.038	<0.001
SBP (mmHg)	0.250	<0.001
DBP (mmHg)	0.244	<0.001
BMI (kg/m^2)	0.354	<0.001
FPG (mmol/L)	0.048	<0.001
Red blood cell count (×10^{12}/L)	0.326	<0.001
Hemoglobin (g/L)	0.388	<0.001
White blood cell count (×10^{12}/L)	0.196	<0.001
Platelet (×10^9/L)	-0.017	=0.001
Cholesterol (mmol/L)	0.106	<0.001
Triglyceride (mmol/L)	0.322	<0.001
HDL-cholesterol (µmmol/L)	-0.318	<0.001
LDL-cholesterol (µmmol/L)	0.112	<0.001
ALT (IU/L)	0.294	<0.001
AST (IU/L)	0.223	<0.001
Bilirubin (µmmol/L)	0.140	<0.001
Albumin (g/L)	0.153	<0.001
BUN (mmol/L)	0.195	<0.001
Creatinine (µmmol/L)	0.547	<0.001

Pearson correlation analysis was used between serum uric acid and the other independent variables. r, pearson correlation coefficient; *P* value, significance level.

Table 2: Serum uric acid: multivariate analysis (n=39736)

Independent variables	Serum uric acid		
	β	*t* value	*P* value
Age (yr)	-0.023	-4.54	<0.001
SBP (mmHg)	0.037	4.77	<0.001
DBP (mmHg)	-0.003	-0.451	0.652
BMI (kg/m^2)	0.132	27.2	<0.001
FPG (mmol/L)	-0.049	-11.7	<0.001
Red blood cell count (×10^{12}/L)	0.013	2.12	0.034
Hemoglobin (g/L)	0.045	6.78	<0.001
White blood cell count (×10^{12}/L)	0.041	9.55	<0.001
Platelet (×10^9/L)	0.009	2.04	0.041
Cholesterol (mmol/L)	0.003	0.193	0.847
Triglyceride (mmol/L)	0.128	17.7	<0.001
HDL-cholesterol (µmmol/L)	-0.077	-11.7	<0.001
LDL-cholesterol (µmmol/L)	0.041	3.56	<0.001
ALT (IU/L)	0.038	5.56	<0.001
AST (IU/L)	0.060	9.56	<0.001
Bilirubin (µmmol/L)	0.024	5.78	<0.001
Albumin (g/L)	0.089	21.1	<0.001
BUN (mmol/L)	0.043	10.3	<0.001
Creatinine (µmmol/L)	0.404	86.3	<0.001

Linear Regression Analysis was used to analysis the relationship between serum uric acid and other independent variables. *β*, standardized coefficients; *t* value, *t* test statistic; *P* value, significance level

Table 3: Comparison of baseline characteristics between hyperuricemia subjects and control group (n=39736)

Characteristics (mean±SE)	Hyperuricemia (n=4523)	Control (n=35213)	*t* value	*P* value
Age (yr)	52.7±0.26	48.3±0.08	16.7	<0.001
SBP (mmHg)	131.1±0.25	125.1±0.09	23.3	<0.001
DBP (mmHg)	81.4±0.19	77.7±0.07	18.7	<0.001
BMI (kg/m^2)	25.6±0.05	23.8±0.02	32.1	<0.001
FPG (mmol/L)	5.39±0.01	5.20±0.01	12.8	<0.001
Red blood cell count (×10^{12}/L)	4.80±0.01	4.79±0.01	1.13	0.259
Hemoglobin (g/L)	145.1±0.22	145.5±0.08	-1.37	0.170
White blood cell count (×10^{12}/L)	6.73±0.02	6.35±0.01	14.8	<0.001
Platelet (×10^9/L)	205.7±0.76	202.8±0.27	3.61	<0.001
Cholesterol (mmol/L)	5.26±0.01	4.95±0.01	20.9	<0.001
Triglyceride (mmol/L)	1.86±0.02	1.34±0.01	28.5	<0.001
HDL-cholesterol (µmmol/L)	1.24±0.01	1.33±0.01	-20.1	<0.001
LDL-cholesterol (µmmol/L)	3.06±0.01	2.90±0.01	13.1	<0.001
ALT (IU/L)	27.6±0.28	22.6±0.08	17.6	<0.001
AST (IU/L)	23.8±0.13	21.2±0.04	19.1	<0.001
Bilirubin (µmmol/L)	12.4±0.08	12.2±0.03	2.49	0.013
Albumin (g/L)	48.0±0.05	47.5±0.02	10.6	<0.001
BUN (mmol/L)	5.72±0.02	5.31±0.01	18.1	<0.001
Creatinine (µmmol/L)	81.2±0.25	74.4±0.08	25.6	<0.001

Data were expressed as the mean mean±SE. *t* test was taken to compare factors associated with hyperuricemia between the two groups in study population.

Table 4: Baseline characteristics according to BMI (kg/m^2) (n=39736)

Characteristics (mean±SE)	Obese (≥27.5) (n=5542)	Overweight (23–27.5) (n=18744)	Normal (18.5–23.0) (n=14108)	Underweight (<18.5) (n=1342)	*P* value
Age (yr)	50.1±0.20	50.6±0.11	46.5±0.13	42.1±0.47	<0.001
SBP (mmHg)	136.7±0.21	128.7±0.11	119.1±0.12	111.5±0.37	<0.001
DBP (mmHg)	85.9±0.17	80.1±0.09	73.3±0.09	68.9±0.27	<0.001
FPG (mmol/L)	5.48±0.01	5.31±0.007	5.04±0.006	4.90±0.02	<0.001
Red blood cell count (×10^{12}/L)	4.96±0.007	4.86±0.004	4.67±0.004	4.51±0.01	<0.001
Hemoglobin (g/L)	150.6±0.19	147.7±0.11	141.2±0.13	136.1±0.38	<0.001
White blood cell count (×10^{12}/L)	6.94±0.02	6.5±0.01	6.08±0.01	5.85±0.04	<0.001
Platelet (×10^9/L)	207.8±0.68	203.3±0.37	201.6±0.42	196.2±1.32	<0.001
Cholesterol (mmol/L)	5.14±0.01	5.06±0.007	4.86±0.008	4.69±0.02	<0.001
Triglyceride (mmol/L)	1.87±0.02	1.54±0.007	1.07±0.005	0.84±0.01	<0.001
HDL-cholesterol (µmmol/L)	1.16±0.01	1.25±0.01	1.44±0.01	1.61±0.01	<0.001
LDL-cholesterol (µmmol/L)	3.09±0.01	3.00±0.01	2.78±0.006	2.52±0.02	<0.001
ALT (IU/L)	32.8±0.26	24.8±0.11	18.2±0.09	14.8±0.23	<0.001
AST (IU/L)	24.5±0.12	21.9±0.05	20.0±0.06	19.4±0.18	<0.001
Bilirubin (µmmol/L)	12. 4±0.07	12.3±0.04	11.9±0.05	12.2±0.15	<0.001
Albumin (g/L)	47.4±0.04	47.5±0.02	47.6±0.03	48.1±0.09	<0.001
BUN (mmol/L)	5.53±0.02	5.44±0.01	5.22±0.01	5.01±0.04	<0.001
Creatinine (µmmol/L)	78.9±0.20	77.5±0.10	71.4±0.13	67.4±0.37	<0.001
SUA (µmmol/L)	376.5±1.16	344.9±0.59	302.0±0.64	274.8±1.89	<0.001

Data were expressed as the mean mean±SE. All data were analyzed by one-way analysis of variance (ANOVA)

We found that BMI was higher in hyperuricemia subjects than control group. To elucidate the association of SUA with BMI, the subjects were divided into 4 groups according to the classification

of BMI in adults based on WHO (2004) criterion: underweight, normal weight, overweight, and obese. As shown in Table 4, SUA was significantly elevated in a linear fashion as BMI increased, and SUA in subjects with obese was significantly higher than that in subjects with underweight. The prevalence of hyperuricemia remained approximately 2.98 times greater among individuals with overweight (n=18744), and 5.96 times greater among obesity (n=5542), compared to individuals with underweight (n=1342) (Table 5).

Table 5: Effect of BMI on serum uric acid in Chinese subjects by multiple logistic regression (n=39736)

Diagnostic criteria in BMI	OR (95% CI)	*P* value
Underweight (<18.5) (n=1342)	1.000	-
Normal (18.5-23.0) (n=14108)	1.558 (1.193-2.035)	=0.001
Overweight (23-27.5) (n=18744)	2.980 (2.292-3.874)	<0.001
Obese (≥27.5) (n=5542)	5.968 (4.571-7.792)	<0.001

Multivariate logistic regression analysis was performed to determine the association of BMI and serum uric acid, after adjusting for age, FPG, red blood cell count, hemoglobin, white blood cell count, platelet, cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, ALT, AST, bilirubin, albumin, BUN, creatinine. OR, odds ratio; CI, confidence interval

Discussion

It has been demonstrated that BMI is strongly associated with prevalent hyperuricemia, which has important public health ramifications given that approximately 34% of Americans are overweight, approximately 20% are obese, and approximately 14% are obese at stages II or greater (18). BMI is thought to be a more valuable prediction marker for the risk of elevated SUA level. For the clinical doctors, BMI is more attractive for it is easy to get. Therefore, doctors are easier to predict the individuals' risk of hyperuricemia or gout.

Previous published paper indicated that weight loss was thought to be an effective non-medical strategy for SUA level reduction in the Japanese population (13). Men losing 10 pounds or more had a 39% lower risk of developing gout (19). The Framingham Heart Study established the dangerous relationship between SUA level elevation and coronary heart disease occurrence, cardiovascular death, and all-cause mortality in females (12). An eight years follow-up study upon 128,569 adults conducted by Pan in Taiwan, China, concluded the hyperuricemia was independently associated with the development of ischemic heart disease not only in the general population but also in those without any metabolic risk factor (20). As known, weight fluctuation can also alter various other metabolic factors such as blood pressure, blood sugar, HDL-cholesterol and obesity (21).

Although several studies have previously demonstrated association between SUA and body weight (14, 22), the relationship between BMI and the risk of hyperuricemia in Jiangsu province, China was not well known. Jiangsu is one of the most economically developed provinces in China, where the number of obesity and hyperuricemia patients is large. Therefore, it is necessary to explore the relationship between BMI and SUA in Jiangsu. This study has demonstrated that SUA was positively correlated with BMI in healthy subjects. Multiple regression analysis showed that BMI was closely related to SUA. When subjects were divided into different groups according to BMI levels, the level of SUA increased in higher BMI groups, especially in obesity subjects. How to explain the correlation? So far, it has not been studied in depth. According to Tsushima's report (23), uric acid secretion from adipose tissue in obese was increased. Among obese subjects, excessive fat accumulation in obesity could produce and secrete uric acid and is relatively associated with overproduction-type hyperuricemia. This may provide a possible mechanism for the relationship between BMI and SUA. However, our study has several limitations. Firstly, we have no information regarding the extent to which lifestyle

and dietary habit modifications affect our study population. Secondly, our study's data was from only one hospital in Jiangsu, which might not assess the true prevalence of hyperuricemia. Thirdly, as our study was observational, we could not rule out the possibility unmeasured factors that may contribute to observed associations. Finally, the study design was cross-sectional, and thus might not necessarily represent the role of SUA as the result of high BMI. Further studies are needed to determine the role of BMI in hyperuricemia in multi-center in China and long-term follow-up should be taken.

Conclusion

Our retrospective study indicates that there is a positive relationship between BMI and SUA among healthy subjects in Jiangsu province, China. Obesity may potentially serve as a novel clinical indicator for identifying patients with hyperuricemia.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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