Cohort Study on Relationship Between Hyperuricemia and Metabolic Syndrome

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ABSTRACT

Objective: To explore the relationship between hyperuricemia and metabolic syndrome.

Methods: The physical examination data of a business unit's employees, selected from our hospital from August 1, 2012 to August 1, 2016, were analyzed using a retrospective cohort study method. These employees were divided into case and control groups depending on whether they suffered from a hyperuricemia, in order to compare the morbidity of metabolic syndrome between the two groups.

Results: The difference in morbidity of metabolic syndrome between the case group and the control group was statistically significant ($p < 0.05$). controlling for age, gender and metabolic score, Logistic regression analysis showed that the The relative risk of metabolic syndrome in the hyperuricemia group relative to the normal uric acid group was OR 1.676, with a 95 % of its confidence interval (CI) 1.057-2.658.

Conclusion: A history of hyperuricemia is associated with the occurrence of metabolic syndrome, thus it is an important risk factor of the metabolic syndrome.

Keywords: Hyperuricemia; Metabolic Syndrome; Cohort Study; Morbidity

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1 INTRODUCTION

Metabolic syndrome (MS) refers to an aggregation phenomenon of risk factors of obesity, hypertension, abnormal glucose metabolism and dyslipidemia and other cardiovascular diseases in the same individual [1]. With the improvement of living standards, the morbidity of metabolic syndromes is increasing year by year, and is currently approximately 25 % in China [2]. It has gradually become the focus of clinical attention on how to better prevent the occurrence of metabolic syndromes. In recent years, a close relationship between hyperuricemia and various components of metabolic syndrome has been found, but the

current studies are mostly based on the cross-sectional and case-controlled methods. There are less cohort studies on whether the hyperuricemia is independently associated with the metabolic syndrome. Therefore, we designed this cohort study.

2 SUBJECT AND METHODS

2.1 Subject

A business unit had chosen our hospital for the physical examination of its employees for eight successive times, and the physical examination archives have been preserved. The physical examination datum dated from August 1, 2012 to August 1, 2016 were selected for analysis. The physical examination data in 2012 was used as a baseline, excluding the individuals who were already suffering from the metabolic syndrome. The employees were divided into the case group and the control group depending on whether they suffered from hyperuricemia at the end of the period of four years.

2.2 Study Indicator

2.2.1 Metabolic Syndrome

The diagnostic criteria for metabolic syndrome jointly developed by International Diabetes Federation (IDF) and American Heart Association (AHA) in 2009 was used [3], with the following three or more conditions: a. abdominal obesity: different criteria were used for different races and countries, with male waist ≥ 90 cm and female waist ≥ 85 cm in China [4]; b. triglycerides ≥ 1.7 mmol/L or Or undergoing treatment; c. high-density lipoprotein: male < 1.0 mmol/L, female < 1.3 mmol/L or receiving the appropriate treatment; d. fasting blood glucose (FBG) ≥ 5.6 mmol/L or diagnosed with Type-II diabetes or receiving the appropriate treatment; e. elevated blood pressure: systolic blood pressure ≥ 130 mmHg (1 mmHg = 0.133 kPa) or diastolic blood pressure 85 mmHg, or diagnosed with hypertension and receiving the appropriate treatment.

2.2.2 Hyperuricemia

BUA level: Male > 420 μmol/L, and female > 360 μmol/L [5];

2.2.3 Grouping Criteria of Other Indicators

Table 1. Grouping Criteria of Other Indicators

Subject	Criteria	Definition
BMI	Underweight	Underweight
	18.5 - 23.9 Kg/m2	Normal
	24-27.9 Kg/m2	Overweight
	28 Kg/m2	Obesity
waist-hip ratio (WHR)	WHR > 0.9 (male) WHR > 0.8 (female)	High waist-hip ratio
	WHR ≤ 0.9 (male) WHR ≤ 0.8(female)	Normal waist-hip ratio
Age	≤ 35 years old	a
	35-44 years old	b
	45-54 years old	c
	55-64 years old	d
	≥ 65 years old	e

2.3 Data Collection

2.3.1 Survey Method and Quality Control

The physical examination data for the years 2012 - 2016 were retrieved, including the baseline data in 2012: age, gender, diet, exercise, alcohol and tobacco preferences and other personal habits; symptom indicators associated with metabolic syndrome, and their disease diagnosis & treatment history, including abdominal obesity or overweight, dyslipidemia, hypertension, diabetes, insulin resistance and/or impaired glucose tolerance, etc. The morbidity of metabolic syndromes in 2013 and of the following four years was collected. The data was retrieved by computer, and was verified and cleaned up by the researchers. A nurse was arranged to sample at random for the second verification in accordance with SPSS random number generators.

2.3.2 Statistical Analysis

Statistical analysis uses SPSS18.0 statistical analysis software. Summary statistics for normally

distributed quantitative variables were expressed as means and standard deviations; Enumeration data expressed by ratio or constituent ratio. The two independent samples t test was used to compare the normal data and the homogeneity of variance between the two groups. The influencing factors were analyzed by binary logistic regression. The difference of $p < 0.05$ or $p < 0.01$ was statistically significant.

3 RESULTS

3.1 Basic Information of Cohort Population

There were 1208 employees in the research unit, and the actual number of participants was 1091 with a screening rate 90.3 %. A total of 224 cases of metabolic syndrome were excluded from the study cohort. The subjects were divided into two groups: exposure group and non exposed group, according to whether there were hyperuricemia history in 867 subjects. To August 1, 2016, a total of 137 people were lost to visit, with a total loss rate of 15.8 %. Among the 730 patients who completed the follow-up visit, there were 135 cases of hyperuricemia and 595 cases of normal uric acid, and the morbidity of hyperuricemia was 18.49 %. The baseline BUA level was 337.45 ± 81.01 μmol/L, including male of 366.51 ± 75.06 μmol/L and female of 278.11 ± 56.77 μmol/L. Four hundred and nineteen males were enrolled i n the study, with a mean age of 55.50 ± 14.05 years old and a mean BMI level of 24.22 ± 2.73 Kg/m2, and 240 females, with a mean age of 49.17 ± 11.03 years old and a mean BMI level of 22.60 ± 2.58Kg/m2. The males' underweight incidence, overweight rate and obesity rate were 1.8 %, 46.1 %, and 8.8 % respectively and the females' rates were 4.2 %, 25.8 %, and 1.7 %, respectively.

3.2 Comparison of Different Uric Acid Grouping Indicators in Baseline Data

Except for high-density lipoprotein, other indicators of the hyperuricemia group were all higher than that of uric acid normal group, of which, BMI, waist circumference, systolic blood pressure, triglyceride, high-density lipoprotein, total cholesterol, and fasting blood glucose were statistically significant ($p < 0.001$), see Table 2 below.

Table 2. Comparison of Different Uric Acid Grouping Indicators

	SUA (n=595)	HUA (n=135)	t	*p*
Age (years old)	53.13 ± 13.21	54.69 ± 14.51	-1.213	0.226
BMI (Kg/m2)	23.36 ± 2.73	25.38 ± 2.62	-7.826	0.000
Waist circumference(cm)	78.51 ± 8.80	84.62 ± 7.14	-8.578	0.000*
SBP (mmHg)	119.33 ± 16.11	125.76 ± 14.75	-4.252	0.000
DBP (mmHg)	76.34 ± 10.28	80.44 ± 10.10	-4.191	0.000
Triglyceride (mmol/L)	1.15 ± 0.89	1.61 ± 0.93	-5.411	0.000
High-density lipoprotein (mmol/L)	1.42 ± 0.33	1.28 ± 0.29	4.153	0.000
Low-density lipoprotein (mmol/L)	2.82 ± 0.77	2.96 ± 0.89	-1.765	0.059
Total cholesterol (mmol/L)	4.76 ± 0.86	4.97 ± 0.99	-2.576	0.000
FBG (mmol/L)	5.00 ± 1.06	5.18 ± 1.41	-1.657	0.000

Notes: SUA refers to the control group (normal uric acid); * Approximate t-test is used.

3.3 Comparison of Baseline Characteristics among Metabolic Syndrome Groups

The BMI, SBP, DBP, triglyceride, low-density lipoprotein, total cholesterol, uric acid and FBG of the metabolic syndrome group were all higher than that of the control group, and except for the low-density lipoprotein, they were statistically significant ($p < 0.001$), see Table 3 below.

Table 3. Comparison of Baseline Characteristics among Metabolic Syndrome Groups

	Control Group (n=545)	Metabolic Syndrome Group (n=185)	t	*p*
Age (years old)	53.53 ± 13.50	53.11 ± 13.39	0.365	0.715
BMI (Kg/m2)	23.07 ± 2.48	25.72 ± 2.83	-12.10	0.000
Waist circumference(cm)	77.51 ± 8.18	85.92 ± 7.67	-12.29	0.000
SBP (mmHg)	118.12 ± 15.79	127.63 ± 14.71	-7.18	0.000
DBP (mmHg)	75.43 ± 10.01	82.07 ± 9.80	-7.82	0.000
Triglyceride (mmol/L)	1.05 ± 0.71	1.80 ± 1.174	-8.23	0.000*
High-density lipoprotein (mmol/L)	1.45 ± 0.32	1.23 ± 0.29	8.17	0.000
Low-density lipoprotein (mmol/L)	2.82 ± 0.81	2.94 ± 0.76	-1.89	0.059
Total cholesterol (mmol/L)	4.73 ± 0.87	5.00 ± 0.92	-3.53	0.000
Uric acid (μmol/L)	326.61 ± 76.76	369.38 ± 84.90	-6.06	0.000*
FBG (mmol/L)	4.90 ± 0.83	5.43 ± 1.68	-4.11	0.000*

Note: * Approximate t-test is used.

3.4 Morbidity of Metabolic Syndrome in Four Years

As of August 1, 2016, 185 cases of the cohort population suffered from the metabolic syndrome in the previous four years, with a morbidity of 25.34 % and an average annual morbidity of 5.93 %, of which, the morbidity of hyperuricemia group was 43.70 % and the morbidity of the control group (normal uric acid) was 21.18 %. The morbidity of metabolic syndromes in different uric acid groups was statistically significant in chi-square test ($p < 0.05$).

3.5 Multivariate Analysis of Metabolic Syndrome

To rule out the effects of other confounding factors on the metabolic syndrome and to understand the correlation between the hyperuricemia and the metabolic syndrome, a logistic regression model was used to analyze the influencing factors. Taking the morbidity of metabolic syndrome as a dependent variable, age, gender, score of metabolic syndrome group, and occurrence of hyperuricemia were subject to a binary logistic regression analysis using the forward progressive method ($\alpha in = 0.05$, and $\alpha out = 0.10$). The analysis results showed that, after the effects of age, gender, and metabolic composition were adjusted for, the relative risk of normal metabolic syndrome morbidity between hyperuricemia group and BUA group was 1.676 and 95 % confidence interval was among 1.057-2.658, see Table 4 below.

Table 4. Logistic Regression Result of Risk Factors for Metabolic Syndrome

	β value	S.E.	Waldχ2 value	p value	RR(95 %CI value)
Age Subgroup	-0.203	0.086	5.581	0.018	0.817 (0.690, 0.966)
Score of Metabolic Group	1.782	0.152	137.630	0.000	5.944 (4.413, 8.006)
High uric acid	0.517	0.235	4.825	0.028	1.676 (1.057, 2.658)
Constant	-2.680	0.269	99.561	0.000	0.069

Notes: assignment of risk factors: female = 0, male = 1, age (years old) < 35 = 1, 35-44 = 2, 45-54 = 3, 55-64 = 4, and ≥ 65 = 5; score of 0 metabolic group = 0, score of 1 metabolic group = 1, score of 2 metabolic groups = 2; normal uric acid = 0 and high uric acid = 1.

4 DISCUSSION

The populations under survey in this study are the employees of a business unit. The cumulative morbidity of metabolic syndrome was 25.34 % in the four years, with an average annual morbidity of 5.93 %. These results are significantly increased compared with the cumulative morbidity (12.7 %) and average annual morbidity (2.54 %) of metabolic syndrome in natural populations in Beijing from 1999 to 2004, as reported by Jing Liu [6], which indicates that the morbidity of metabolic syndrome is on the rise. Hence, the metabolic syndrome has become one of the important diseases that seriously threatens the lives and health of the people in China, and thus it is even more important to research how to effectively prevent, identify, and treat it.

In recent years, increasingly more studies show that the hyperuricemia is closely associated with various components of the metabolic syndrome [7]. In addition, some researchers believed that the hyperuricemia was an independent risk factor of cardiovascular diseases [8], and therefore called for the inclusion of hyperuricemia into the diagnostic criteria as a new component of metabolic syndrome [9]. The findings from NHANES III (the Third National Health and Nutrition Examination Survey) show that the morbidity of metabolic syndrome increased significantly with the increase of BUA level [10]. The survey findings of 2174 healthy controls in Beijing show that the risk of metabolic syndrome increased with the increase of serum uric acid level [11]. However, because of the lack of powerful evidence-based medical evidences, the issue on whether the hyperuricemia can serve as an independent risk factor for the metabolic syndrome remains controversial. Hence, the relationship between hyperuricemia and metabolic syndrome was explored in this study using the retrospective cohort study methods. The waist circumference, blood glucose, lipids, blood pressure and other components in the metabolic syndrome are often accompanied by each other and interact with each other. Therefore, this article takes into consideration the interaction of these factors,the results of this study show that the relative risk of metabolic syndrome morbidity in the patients with hyperuricemia was 1.639 and 95 % confidence interval was among 1.057 - 2.658, suggesting that the hyperuricemia is an independent risk factor for metabolic syndrome.

With the development of China's economic level and the change of diet and lifestyle, the morbidity of hyperuricemia and metabolic syndrome continues to grow, which poses great harm to the health of the people. This study has revealed the prevalence of metabolic syndrome, explored the relationship between hyperuricemia and metabolic syndrome and clarified that the hyperuricemia is an independent risk factor for metabolic syndrome. This study is of course a retrospective cohort study, thus further prospective cohort studies are still needed to understand whether the morbidity risk of metabolic syndrome can be reduced after the treatment of hyperuricemia. Furthermore, the samples for this study are those who have taken

the physical examinations in our hospital for a long time, therefore it is likely that these people may have better health awareness. Therefore, there might be a selective bias, and some further clinical studies are still needed for a larger scope.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest regarding the publication of this paper.

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