Original Article

Prevalence of Hyperuricemia and the Relationship between Serum Uric Acid and Metabolic Syndrome in the Asian Mongolian Area

Lili You¹, Aiping Liu¹, Gaowa Wuyun², Heping Wu² and Peiyu Wang¹

Aiping Liu and Peiyu Wang contributed equally to this work.

¹Department of Social Medicine& Health Education, School of Public Health, Peking University Health Science Center, Beijing, PR China

²Hospital of Xilinguole Meng, Xilinguole City, Inner Mongolia, PR China

Aim: To investigate the prevalence of hyperuricemia and the association between the serum uric acid (SUA) levels and incidence of metabolic syndrome (MetS) in the Mongolian area of China.

Methods: This cross-sectional survey was based on a population of 1,426 subjects (809 men and 617 women) 20-80 years of age who were recruited from Inner Mongolia, China. Metabolic and anthropometric indicators were measured according to standard methods. Hyperuricemia was defined as an SUA level of ≥ 7.0 mg/dL for men and ≥ 6.0 mg/dL for women. MetS was diagnosed based on the consensus criteria released in 2009 from a joint collaboration organization.

Results: The prevalence of hyperuricemia was 17.7% in men and 5.2% in women. The prevalence of MetS in men was higher than that observed in women (36.7% vs 17.8%). Waist circumference, BMI and the level of triglycerides were most strongly correlated with the SUA level in both sexes. Men with hyperuricemia had an increased risk of MetS [OR (95%CI)=2.95 (2.00-4.35)], while men with a "normal" SUA level (> 5.0 mg/dL and < 6.3 mg/dL) had a higher risk of MetS, central obesity and hypertriglyceridemia than men in the lower level group (≤ 5 mg/dL). Women with a higher SUA level (≥ 4.3 mg/dL) had an increased risk of MetS, central obesity, hypertriglyceridemia and hypertension compared with women in the lowest tertile SUA group (≤ 3.5 mg/dL).

Conclusions: The SUA level is significantly associated with various metabolic indicators. In this study, waist circumference and the level of triglycerides were most strongly correlated with the SUA level in both sexes. Individuals with a normal level of SUA had an increased risk of MetS and other metabolic disorders. Further research on appropriate cut-off values for pre-hyperuricemia is expected, and the early detection of hyperuricemia is essential for the prevention of MetS.

J Atheroscler Thromb, 2014; 21:355-365.

Key words: Metabolic syndrome, Serum uric acid, Hyperuricemia

Introduction

Mongolians have played a pivotal role in the peopling of Central and East Asia. They live across Northern Asia, including Russia, Mongolia, China and many of the former Soviet Union states. Over half of

Mongolians live in China, primarily in either Inner Mongolia or, less commonly, Xinjiang. The Inner Mongolia autonomous region of China is home to aboriginal Mongolians who have maintained their nomadic lifestyle for hundreds of years and are currently also engaged in agriculture and various industries. However, owing to the influence of the long-term nomadic herding tradition, the Mongolian people's lifestyle is strongly affected by a nomadic culture, although a portion of the population is not genetically Mongolian. Meanwhile, ethnic Mongolians living in cities are also partly influenced by modernization.

Address for correspondence: Peiyu Wang, Department of Social Medicine& Health Education, School of Public Health, Peking University Health Science Center, Beijing, PR China
E-mail: wpeiuyu@bjmu.edu.cn

Received: July 12, 2013

Accepted for publication: October 29, 2013

Therefore, the people living in the Mongolian region maintain some traditional habits, such as consuming a large amount of red meat with an insufficient amount of fruits and vegetables and excessive drinking, while those living in modern society are physically inactive with a poor lifestyle. The result is the clustering of various cardiovascular risk factors in this mixed ethnicity population. As Yu *et al.*¹⁾ reported, the prevalence of obesity, elevated blood pressure, increased triglycerides, reduced HDL-cholesterol and elevated fasting glucose among the Mongolian population is much higher than that observed in other ethnic populations. A cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus that occur together more often than by chance alone is known as MetS²⁾. Hyperuricemia has also been reported to be another neglected independent risk factor for cardiovascular disease (CVD). Studies have demonstrated that a high serum uric acid level is closely associated with arterial stiffness, arteriosclerosis³⁾ and the severity of coronary disease⁴⁾. Individuals with MetS often exhibit an elevated serum uric acid (SUA) level⁵⁻⁹⁾. Therefore, the relationship between the SUA level and the incidence of MetS has recently received greater attention.

Although previous studies have investigated the prevalence of hyperuricemia and found positive associations between the SUA level and MetS in Asian populations¹⁰⁾, most studies of the uric acid levels were performed in populations selected from coastal regions¹¹⁻¹⁸⁾. The prevalence of hyperuricemia and whether an association between the SUA level and MetS exists in the Mongolian population, which exhibits a high risk of CVD, remain unclear.

Aim

The present study investigated the prevalence of hyperuricemia and the association between the SUA level and the incidence of MetS in a representative sample of adults living in the Mongolian area.

Methods

Study Design and Subjects

A cross-sectional study was conducted among 1,426 participants (809 men and 617 women) 20-80 years of age. In this survey, two populations were covered. Urban subjects ($n=1,060$) were recruited through a health checkup program during the period of September 2006 and August 2009 in Xilinguole Meng, Inner Mongolia, China. The survey was conducted at one health examination center located in the central region of the city as a unique third-grade general hos-

pital. Rural subjects ($n=366$) were recruited from Taibus Banner country, Inner Mongolia, China. One community in this village was selected as the survey spot. All inhabitants 20-80 years of age were recruited, excluding those with hypertension, diabetes or hyperlipidemia receiving drug treatment. Face-to-face interviews were conducted at the participants' homes, and examinations were performed by nurses in the village clinics. This study was reviewed and approved by the Institutional Review Board of Xilinguole Meng Hospital.

Data Collection and Measurements

A self-designed questionnaire was used to collect the demographic characteristics and lifestyle information of the participants. The investigators included well-trained medical school students and nurses working at the hospital. Fasting blood was drawn from each subject, and the SUA level and other parameters of biochemistry and hematology were measured according to standard methods. In addition, some physiological parameters were measured. All of the above measurements were obtained by professional nurses. Anthropometric measurements of body weight, height and waist circumference were obtained twice, and the average of the two measurements was used in the present study. Height was measured to the nearest 0.1 cm, and weight was measured to the nearest 0.1 kg with light clothing. The body mass index (BMI) was calculated as the weight (in kg) divided by the height (in m²). Waist circumference was measured midway between the lowest border of the ribs and the iliac crest in the horizontal plane to the nearest 0.5 cm with anthropometric tape. Well-trained nurses measured the systolic blood pressure (SBP) and diastolic blood pressure (DBP) two times in the left arm of the seated participants according to a standardized protocol. The average of the two readings was calculated to determine the reported blood pressure for each participant. Overnight fasting blood specimens were collected for measurement of the SUA, lipid and plasma glucose levels. A blood sample was collected into an EDTA anticoagulant tube for each participant. The SUA level was assayed using the colorimetric uricase-peroxidase system.

Diagnostic Criteria

In the present study, hyperuricemia was defined according to sex-specific SUA levels: SUA ≥ 420 mmol/L (7.0 mg/dL) for men and ≥ 360 mmol/L (6.0 mg/dL) for women^{19, 20)}.

MetS was defined according to the joint interim statement criteria established by the International Dia-

Table 1. Characteristics of the participants according to area and sex

	Men (<i>n</i> =809)			Women (<i>n</i> =617)		
	Urban	Rural	<i>p</i> value	Urban	Rural	<i>p</i> value
Count	630	179		430	187	
Age (year; mean $\pm$ SD)	51.3 $\pm$ 14.2	50.1 $\pm$ 11.1	0.305	48.2 $\pm$ 12.8	49.9 $\pm$ 10.0	0.312
Serum Uric acid (mg/dL)	5.8 $\pm$ 1.2	5.1 $\pm$ 1.8	<0.001	4.2 $\pm$ 1.9	3.6 $\pm$ 1.5	0.015
Waist circumference (cm)	90.2 $\pm$ 10.8	78.3 $\pm$ 10.1	<0.001	75.9 $\pm$ 10.0	74.4 $\pm$ 9.6	0.098
BMI (kg/m ²)	25.6 $\pm$ 3.7	22.8 $\pm$ 3.8	<0.001	23.6 $\pm$ 3.8	22.6 $\pm$ 3.2	0.005
SBP (mmHg)	135.3 $\pm$ 19.1	126.7 $\pm$ 20.7	<0.001	121.0 $\pm$ 19.8	128.2 $\pm$ 20.4	<0.001
DBP (mmHg)	89.5 $\pm$ 11.6	83.6 $\pm$ 14.9	0.002	79.2 $\pm$ 11.7	79.8 $\pm$ 10.2	0.508
Fasting plasma glucose (mg/dL)	101.3 $\pm$ 30.2	89.2 $\pm$ 20.8	<0.001	93.2 $\pm$ 21.4	83.4 $\pm$ 19.8	<0.001
TG (mg/dL)	200.8 $\pm$ 160.1	145.1 $\pm$ 101.0	<0.001	123.5 $\pm$ 73.3	130.5 $\pm$ 76.2	0.283
HDL-C (mg/dL)	54.2 $\pm$ 12.8	59.7 $\pm$ 16.0	<0.001	59.4 $\pm$ 12.9	58.4 $\pm$ 13.9	0.103
Smoke (%)	43.2	64.8	<0.001	2.3	6.4	0.002
Drink (%)	44.4	41.3	0.483	4.4	5.3	0.616

betes Federation Task Force on Epidemiology and Prevention, National Heart, Lung and Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity²¹), and the cut-off point for waist circumference was determined based on the WHO recommendations for the Asian population²¹). Accordingly, the presence of three of the following five criteria was grounds for diagnosis: (1) elevated blood pressure: a blood pressure of at least 130/85 mmHg or the use of antihypertensive medications; (2) elevated triglycerides: a serum triglyceride level of at least 150 mg/dL or the use of medications for elevated triglycerides; (3) reduced HDL-C: an HDL-C level of <40 mg/dL in men and <50 mg/dL in women or the use of medications for reduced HDL-C; (4) elevated fasting plasma glucose (FPG): an FPG level of 100 mg/dL or more or the use of medications for elevated glucose; and (5) elevated waist circumference: a waist circumference of 90 cm in men and 80 cm in women.

The smoking and alcohol consumption status was also surveyed. Never-smokers were defined as participants who had never smoked, whereas ex-smokers were defined as participants who had smoked at least one cigarette per day for more than six months but were currently not smoking. Current smokers were defined as people who had smoked at least one cigarette per day in the past six months. Alcohol consumption was assessed in two stages. In the first stage, the subjects were categorized according to the frequency of alcohol drinking: never, occasionally but less than once a week, once or twice a week, every other day or almost every day. Those who reported

consuming at least one drink per week were further questioned about their weekly average consumption of different alcoholic beverages in the second stage.

Statistical Analysis

A Pearson's correlation analysis was used to evaluate independent associations between the factors under study and the relative importance of these factors as covariates of the SUA levels. We classified the participants according to sex-specific tertiles of the SUA level. For descriptive analyses across the tertile groups of SUA, we used chi-square analyses for categorical variables and ANOVA for continuous traits. A multivariable logistic regression analysis was used to quantify the strength of the association between the SUA level and the prevalence of MetS after controlling for potential confounding factors. All analyses were performed using the SPSS version 13.0 software program for Windows (SPSS Inc., Chicago, IL, USA), and all statistical tests were two-tailed with a level of 0.05.

Results

Characteristics of the Participants

Table 1 shows the mean $\pm$ S.D. values of the SUA level and other variables according to sex. The results are given for the urban and rural populations separately, as the mean SUA concentration was significantly lower in the rural population for both men and women. No age-related changes in the SUA level were observed in men; however, the mean value increased with age in women. Compared with that observed in the rural men, most of the indicators were signifi-

Table 2. Serum uric acid levels and the prevalence of hyperuricemia and metabolic syndrome according to area and gender

	Both		Urban		Rural	
	Men (<i>n</i> =809)	Women (<i>n</i> =617)	Men (<i>n</i> =630)	Women (<i>n</i> =430)	Men (<i>n</i> =179)	Women (<i>n</i> =187)
Hyperuricemia [n (%)]	143 (17.7)	32 (5.2)	120 (19.0)	23 (5.3)	23 (12.8)	9 (4.8)
Metabolic syndrome [n (%)]	297 (36.7)	110 (17.8)	272 (43.2)*	79 (18.4)	25 (14.1)	31 (16.6)

* $p < 0.05$, compared with the same gender in the rural group

Fig. 1. Prevalence of hyperuricemia and metabolic syndrome by age and sex.

cantly higher in urban men. The levels of SUA, BMI, SBP and fasting plasma glucose were higher in urban women than in rural women. Other metabolic variables increased with age in both men and women, except for waist circumference, BMI and fasting plasma glucose in men. The prevalence of smoking was lower among the younger patients in both men and women. In contrast, the younger participants exhibited an increased prevalence of drinking in both genders.

Prevalence of Metabolic Syndrome and Hyperuricemia

Table 2 presents the prevalence of MetS and hyperuricemia according to sex. The prevalence of MetS was significantly higher among men than women in both the urban and rural populations. Over 40% of urban men suffered from MetS; this prevalence was higher than that observed in rural men. There were no significant differences between the urban and rural women. Additionally, as shown in Fig. 1, the prevalence of MetS gradually increased with age, such that

a notable upward trend was observed in the prevalence of MetS with age in women: women younger than 35 years of age rarely suffered from MetS, whereas, among women over sixty years of age, the prevalence of MetS was higher than that observed in men. Meanwhile, the prevalence of hyperuricemia decreased with age in men: men younger than 35 years of age exhibited the highest probability of having hyperuricemia. This trend was opposite in women. The overall prevalence of hyperuricemia was 19.0% in urban men, which was higher than that observed in rural men (12.8%, $p=0.055$), while the prevalence of hyperuricemia was not significantly different between urban and rural women.

Association between Hyperuricemia and MetS

As shown in Table 3, the prevalence of MetS was approximately 60% in hyperuricemic men, who also exhibited a nearly three-fold increased risk of MetS compared with men without hyperuricemia. A difference in MetS prevalence associated with the hyperuricemia status was also observed in women; however, it

Table 3. Relationships between hyperuricemia and metabolic syndrome by sex

Hyperuricemia		Participants of metabolic syndrome (+/-)	Prevalence of metabolic syndrome	Adjusted-OR (95%CI) [§]	<i>p</i> value
Men	(-)	222/444	33.3	1.0	< 0.001
	(+)	84/59	58.7	2.95 (2.00-4.35)	
Women	(-)	96/489	16.4	1.0	0.229
	(+)	13/19	40.6	1.67 (0.72-3.87)	

[§] Odds ratios and 95% CIs adjusted for age, area, smoking status and alcohol consumption

Table 4. Correlation coefficients (Pearson's) between the uric acid levels and other metabolic variables after adjustments for age and sex

variables	Men		Women	
	Pearson's correlation (r)	<i>p</i> -value	Pearson's correlation (r)	<i>p</i> -value
Waist circumference	0.33	< 0.001	0.21	< 0.001
BMI	0.32	< 0.001	0.21	< 0.001
Triglyceride	0.29	< 0.001	0.19	< 0.001
DBP	0.21	< 0.001	0.10	0.018
SBP	0.16	< 0.001	0.06	0.114
HDL-C	0.12	0.001	0.18	< 0.001
Fasting plasma glucose	-0.04	0.251	0.13	0.001

was not significant after adjusting for confounding variables.

Correlations between the SUA Level and Other Metabolic Disorders

Table 4 shows the Pearson's correlation coefficients between the uric acid level and other metabolic variables according to sex, after adjusting for age. In men, the SUA levels were positively correlated with the following factors: waist circumference, BMI, triglycerides, DBP, SBP and HDL-C; no associations were observed for fasting plasma glucose. In women, the SUA levels were positively correlated with all of the variables listed above, except for SBP. Waist circumference, BMI and triglycerides were most strongly correlated with the SUA level in both sexes.

Association between the SUA Level and the Incidence of MetS and its Components

Fig. 2 and **3** indicate that more metabolic abnormalities were clustered in the upper third group than in the lower third group in both sexes ($p_{\text{trend}} < 0.001$). Only 6% of men and 20% of women in the upper third group exhibited no metabolic risk factors. In the upper third group, 15% of men and 12% of women had 4-5 metabolic abnormalities.

We further separated the participants according

to tertiles of the SUA level for each gender. The range and mean values of each tertile group are presented in **Table 5**, which also shows the associations between different tertiles of SUA and the incidence of MetS and its components. Subjects with a higher SUA level tended to exhibit a higher likelihood of having MetS. This positive gradient for the prevalence of MetS across the tertiles of the SUA level was more robust in men than in women. Men in the highest tertile uric acid group had a 2.8-times higher risk of having MetS compared with men in the lowest tertile group ($p < 0.001$). In women, the adjusted risk for MetS was 1.8 among the subjects in the highest tertile group compared with that observed in those in the lowest tertile group ($p < 0.001$).

Next, we analyzed the prevalence of each MetS-associated abnormality in the SUA tertile groups according to sex; the results are presented in **Table 5**. The prevalence of abdominal obesity, hypertriglyceridemia, high blood pressure and high fasting glucose increased in association with an increased level of SUA (trend $p < 0.001$) in both men and women. Among the five components evaluated, the largest increases in the upper SUA tertile group compared with the lowest tertile group were seen in central obesity in both men and women (increased by 37% and 30%, respectively) hypertriglyceridemia in men (increased by 32.5%) and

Fig. 2. Proportions of metabolic syndrome risk number gathered in each tertiles for men (%).

Fig. 3. Proportions of metabolic syndrome risk number gathered in each tertiles for women (%).

hypertension in women (increased by 32.6%). After adjusting for the other confounding variables listed in **Table 3**, men in the upper SUA tertile group had a 3.7-fold increased risk of central obesity and a 3.2-fold increased risk of hypertriglyceridemia, while women in the upper tertile group had a 2.8-fold increased risk of central obesity and a 2.5-fold increased risk of hypertriglyceridemia and hypertension.

Discussion

Previous studies of hyperuricemia and its association with MetS have been conducted among Asian populations²²⁻³⁰, mostly Taiwanese, Japanese, Korean and Han ethnic Chinese populations. In addition, previous studies have been primarily conducted in coastal

areas³⁰⁻³², where the intake of purine-rich marine products is dominant, contributing to hyperuricemia and possibly MetS. In contrast, many studies³²⁻³⁷ have found that an elevated SUA level is associated not only with purine intake from seafood, meat and beer, but also the presence of endogenous metabolic disorders. However, hyperuricemia is not as great of a concern as other metabolic disorders among people living in Mongolian regions, where the lifestyle is much different from that of other populations living in Asian regions. This study was conducted in the Mongolian region and found that, among the study population, the SUA levels differed according to gender and age. For example, possibly the SUA levels were lower in women than in men, as estrogen promotes the excretion of uric acid^{38, 39}. Furthermore, the SUA levels

Table 5. Multivariate analysis of the adjusted ORs and 95% CIs between the uric acid levels and the incidence of metabolic syndrome and its components[§]

	Men (n=809)			Women (n=617)		
	Lower third	Middle third	Upper third	Lower third	Middle third	Upper third
Count	281	283	245	242	153	222
SUA range (mg/dL)	(2.3, 5.0)	(5.1, 6.2)	(6.3, 13.3)	(1.7, 3.5)	(3.6, 4.2)	(4.3, 11.7)
Metabolic syndrome ^{††}	67 (23.8)	100 (35.5)	130 (53.1)	27 (11.2)	17 (11.1)	66 (29.7)
	1.0 (reference)	1.35 (0.92-2.00)	2.80 (1.89-4.15)	1.0 (reference)	0.71 (0.35-1.44)	1.85 (1.02-3.35)
Abdominal obesity [†]	70 (24.9)	127 (44.9)	152 (62.0)	47 (19.4)	39 (25.5)	112 (50.5)
	1.0	1.81 (1.23-2.65)	3.71 (2.48-5.54)	1.0	1.23 (0.74-2.06)	2.81 (1.75-4.53)
Elevated triglycerides [†]	90 (32.0)	153 (54.1)	158 (64.5)	41 (16.9)	27 (17.6)	88 (39.6)
	1.0	2.16 (1.51-3.10)	3.26 (2.23-4.76)	1.0	0.99 (0.59-1.67)	2.45 (1.49-4.03)
Elevated blood pressure [†]	185 (65.8)	209 (73.9)	201 (82.0)	76 (31.4)	54 (35.3)	142 (64.0)
	1.0	0.95 (0.62-1.46)	1.52 (0.95-2.41)	1.0	0.95 (0.55-1.66)	2.49 (1.59-3.90)
Elevated fasting glucose [†]	72 (25.6)	76 (26.9)	78 (31.8)	30 (12.4)	16 (10.5)	52 (23.4)
	1.0	0.94 (0.64-1.40)	1.18 (0.79-1.75)	1.0	0.64 (0.33-1.27)	1.17 (0.66-2.08)
Reduced HDL-C [†]	13 (4.6)	2 (0.7)	2 (0.8)	41 (16.9)	10 (6.5)	3 (1.4)
	1.0	0.51 (0.10-2.46)	0.74 (0.15-3.59)	1.0	0.56 (0.25-1.26)	0.23 (0.06-0.76)

[§] Odds ratios and 95% CIs for men and women adjusted for age, area, smoking status and alcohol consumption

[†] elevated waist circumference: a waist circumference of 90 cm in men and 80 cm in women.

[†] elevated blood pressure: a blood pressure of at least 130/85 mmHg or the use of antihypertensive medications

[†] elevated fasting plasma glucose (FPG): an FPG level of 100 mg/dL or more or the use of medications for elevated glucose

[†] elevated triglycerides: a serum triglyceride level of at least 150 mg/dL or the use of medications for elevated triglycerides

[†] reduced HDL-C: an HDL-C level of <40 mg/dL in men and <50 mg/dL in women or the use of medications for reduced HDL-C

^{††} over three of the following “†”

significantly increased with age in women, but not in men, and urban people had higher levels of SUA than rural people. The prevalence of hyperuricemia in men (17.7%) in this study is lower than that reported in 2008 in Taiwan (22.0%)⁴⁰⁾, urban Qingdao, China (25.3%)¹⁸⁾ and Japan (24.4%)⁴¹⁾. In addition, the prevalence of hyperuricemia in women was 5.2%, which is lower than that observed in other developing countries (8.7%)⁴²⁾ and other eastern coastal regions of China, such as Qingdao¹⁸⁾ and Hangzhou⁴³⁾. The relatively lower prevalence of hyperuricemia observed in this study is possibly due to the low consumption of seafood among the study population. Additionally, ethnic diversity may be responsible for this discrepancy. Differences in lifestyle between urban residents, who display higher energy intake and a lower level of physical activity, and rural residents may account for the different results. Younger men had a higher possibility of having hyperuricemia than older men in this population, possibly due to their higher level of alcohol consumption and lack of physical activity. Women over 50 years of age exhibited an increased risk of hyperuricemia, which is possibly related to meno-

pause.

Many studies have shown that a higher SUA level is often accompanied by obesity, hypertension, dyslipidemia and glucose intolerance, all of which play a causal role in the pathogenesis of cardiovascular disease. The clustering of the above metabolic disorders, when found together in the same individual, characterizes so-called MetS. We used the latest definitions²⁾ to evaluate the prevalence of MetS in this population. Our results ultimately showed that the prevalence of MetS was nearly 40% in men, which is much higher than that observed in the male populations of Japan⁶⁾, Korea⁵⁾, Israel⁷⁾ and some other areas of China⁴⁴⁻⁴⁷⁾. In the present study, women also had a higher prevalence of MetS than other similar populations. The prevalence of MetS has been shown to be higher in men than women under 60 years of age and higher in women than men over 60 years of age. Sex hormones, especially estrogen and/or the androgen/estrogen ratio, play crucial roles in this phenomenon. In addition, the particular dietary pattern of consuming foods high in energy and rich in fat along with a lack of vegetables inherited from a nomadic history likely contrib-

uted to the high risk of metabolic disease associated with urbanization in populations consisting of herds-men, farmers and citizens⁴⁸). Moreover, the rate of detection of MetS diagnosed based on the consensus criteria released in 2009 from a joint collaboration between the American Heart Association and other organizations is likely higher than that diagnosed based on other criteria^{7, 25}), as abdominal obesity should not be a prerequisite for diagnosis. Moreover, abdominal obesity was one of the five criteria used in this study in association with the Asian cut-off point proposed by the WHO²¹), which is higher than Chinese medical association recommendations⁴⁹).

Similar to other studies, we found that the subjects with hyperuricemia had an increased risk of MetS compared with those without hyperuricemia and that this association was especially significant in men. The results of the correlations between the SUA level and other metabolic indicators showed that waist circumference and triglycerides were the strongest factors correlated with the SUA level in both sexes. The contribution of a high uric acid level to the development of abdominal obesity, elevated triglycerides and hypertension in both men and women was noted as well. Abdominal obesity exhibited a stronger association with an increased SUA level than the other components of MetS, which is in line with the findings of other studies^{50, 51}). The mechanisms underlying the obesity-linked increase in the SUA level involve two factors: excessive uric acid production and poor uric acid excretion. Matsuura *et al.*⁵²) found that, among individuals with visceral fat obesity, the overproduction of uric acid with a reduction in urinary urate excretion and clearance is the crucial mechanism contributing to an increased SUA level, which may occur because visceral fat accumulation induces excessive uric acid production, which in turns leads to an elevated influx of plasma free fatty acids into the portal vein and liver, stimulation of neutral fat synthesis and a consequent attendant surge in uric acid production in the activated uric acid synthesis pathway^{53, 54}). In addition, Bedir A.⁵⁵) suggested that leptin is a possible candidate for the missing link between obesity and hyperuricemia. In addition to abdominal obesity, the levels of hypertriglycerides were closely associated with the SUA levels in both men and women in this study, which is in accordance with the findings of various other studies demonstrating the serum triglyceride level to be independently and strongly related to the uric acid level. Hyperuricemia and elevated triglycerides are associated with insulin resistance syndrome, and the relationships between these parameters are complicated⁵⁶). In the present study, hyperuricemia

was significantly related to hypertension in women, but insignificantly in men. Kuwahata *et al.*¹⁰) reported that a high concentration of SUA is correlated with coronary endothelial microvascular dysfunction in Japanese women. Therefore, endothelial dysfunction possibly resulting from an increased SUA level directly contributes to the pathogenesis of hypertension⁵⁶).

The positive gradient in the prevalence of MetS across tertiles of the SUA level observed in this study was more robust in men than in women; there was a strong association between hyperuricemia and MetS in men only. This gender difference should receive more attention, as various other studies have concluded that the SUA level is more closely associated with the incidence of MetS in women than in men^{20, 27, 57}). An American⁵⁸) study and Turkish study⁵⁹) both showed that hyperuricemia is associated with MetS much more tightly in women than in men, while a Korean study⁵) demonstrated that the SUA level is closely linked and even independently associated with MetS in women only. The inconsistencies between genders in these studies are likely due to genetic differences between races⁶⁰).

Recently, a relationship between the SUA level and the incidence of MetS has been observed not only in patients with hyperuricemia, but also in those with an SUA level considered to be in the normal range⁵⁹). A high normal level of SUA may also reflect the presence of MetS and its component disorders. Therefore, we further divided the participants into three groups according to the SUA level in order to estimate the effect of a "normal" SUA level on the risk of metabolic disorders. The results of the present study demonstrated that men, but not women, in the middle SUA tertile group (>5.0 and <6.3) exhibited an increased risk of metabolic syndrome, particularly hypertriglyceridemia. The subjects in the middle SUA tertile group exhibited a significant number of risk factors in both men and women; this relationship remained significant even after controlling for other confounding factors, which indicates that the hyperuricemia cut-off points currently widely used for Chinese patients, at least men, are insufficient to identify populations with a high risk of metabolic disorders and that the identification of more cut-off points for pre-hyperuricemia is strongly suggested. Zhang *et al.*⁶¹) suggested the appropriate cut-off points for Chinese individuals to be 4.9 mg/dL for women and 6.3 mg/dL for men, which are similar to the cut-off levels used in the middle and upper tertiles among men in the present study. Further research on the development of more appropriate cut-off values for pre-hyperuricemia or even revision of the criteria for hyperuricemia diagnosis is

expected.

The strengths and limitations of our study deserve comment. This study provided important epidemiological evidence for the association between hyperuricemia and MetS in the Mongolian population. It also applied the latest criteria for MetS diagnosis, which have not been used widely in research conducted in China or other countries. However, the cross-sectional design of this study cannot be used to address the potential temporal relationships between hyperuricemia and MetS, which require further investigation in longitudinal studies.

Conclusions

Our data indicate that an independent relationship exists between hyperuricemia and MetS in men living in the Mongolian region. Moreover, the SUA level was found to be significantly correlated with visceral obesity, hypertriglyceridemia and hypertension in women. The early detection of hyperuricemia is essential for the prevention of MetS.

Acknowledgements

We thank all subjects who participated in the study and the staff at Peking University for their assistance with the study. This study was supported by the Foundation of First Phase Research Programme funded by the Ministry of Health, Inner Mongolia, China (NO.2005015). We are grateful for the support provided by Xilinguole Meng Hospital, Inner Mongolia. We also thank Aping Liu and Peiyu Wang for their participation in the study design, Lili You for her help in writing the manuscript and Gaowa Wuyun and Heping Wu for their help in conducting the investigation.

Conflicts of Interest

No authors have any financial relationships (within the past 12 months) with biotechnology manufacturers, pharmaceutical companies or other commercial entities with an interest in the subject matter or materials discussed in the manuscript.

References

- 1) Yu L, Liu X, Gao X: Investigation on prevalence of metabolic syndrome and its risk factors in mongolian people of tongliao city. *Chin J Public Health*, 2008; 24: 1186-1188
- 2) Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JJ, Donato KA, Fruchart JC, James WP, Loria CM, Smith SJ: Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; National heart, lung, and blood institute; American heart association; World heart federation; International atherosclerosis society; And international association for the study of obesity. *Circulation*, 2009; 120: 1640-1645
- 3) Kojima C, Takei T, Ogawa T, Nitta K: Serum complement c3 predicts renal arteriolosclerosis in non-diabetic chronic kidney disease. *J Atheroscler Thromb*, 2012; 19: 854-861
- 4) Xiong Z, Zhu C, Zheng Z, Wang M, Wu Z, Chen L, Chen Y: Relationship between arterial stiffness assessed by brachial-ankle pulse wave velocity and coronary artery disease severity assessed by the syntax score. *J Atheroscler Thromb*, 2012; 19: 970-976
- 5) Rho YH, Woo JH, Choi SJ, Lee YH, Ji JD, Song GG: Association between serum uric acid and the adult treatment panel iii-defined metabolic syndrome: results from a single hospital database. *Metabolism*, 2008; 57: 71-76
- 6) Numata T, Miyatake N, Wada J, Makino H: Comparison of serum uric acid levels between japanese with and without metabolic syndrome. *Diabetes Res Clin Pract*, 2008; 80: e1-e5
- 7) Cohen E, Krause I, Fraser A, Goldberg E, Garty M: Hyperuricemia and metabolic syndrome: lessons from a large cohort from israel. *Isr Med Assoc J*, 2012; 14: 676-680
- 8) Grassi D, Ferri L, Desideri G, Di Giosia P, Cheli P, Del PR, Properzi G, Ferri C: Chronic hyperuricemia, uric acid deposit and cardiovascular risk. *Curr Pharm Des*, 2012; 33: 429-432
- 9) Wu YQ, Li J, Xu YX, Wang YL, Luo YY, Hu DY, Liu WJ, Yang M, Pi L, Wang MS, Wang JY, Zhao SM, Li MJ: Predictive value of serum uric acid on cardiovascular disease and all-cause mortality in urban chinese patients. *Chin Med J (Engl)*, 2010; 123: 1387-1391
- 10) Kuwahata S, Hamasaki S, Ishida S, Kataoka T, Yoshikawa A, Orihara K, Ogawa M, Oketani N, Saihara K, Okui H, Shinsato T, Kubozono T, Ichiki H, Fujita S, Takumi T, Yoshino S, Nakazaki M, Miyata M, Tei C: Effect of uric acid on coronary microvascular endothelial function in women: association with egfr and adma. *J Atheroscler Thromb*, 2010; 17: 259-269
- 11) Chang CH, Chen YM, Chuang YW, Liao SC, Lin CS, Tang YJ, Sheu WH, Chen DY: Relationship between hyperuricemia (huc) and metabolic syndrome (ms) in institutionalized elderly men. *Arch Gerontol Geriatr*, 2009; 49 Suppl 2: S46-S49
- 12) Chen JH, Chuang SY, Chen HJ, Yeh WT, Pan WH: Serum uric acid level as an independent risk factor for all-cause, cardiovascular, and ischemic stroke mortality: a chinese cohort study. *Arthritis Rheum*, 2009; 61: 225-232
- 13) Chu NF, Wang DJ, Liou SH, Shieh SM: Relationship between hyperuricemia and other cardiovascular disease risk factors among adult males in taiwan. *Eur J Epidemiol*, 2000; 16: 13-17
- 14) Chuang SY, Chen JH, Yeh WT, Wu CC, Pan WH:

- Hyperuricemia and increased risk of ischemic heart disease in a large chinese cohort. *Int J Cardiol*, 2012; 154: 316-321
- 15) Lin JD, Chiou WK, Chang HY, Liu FH, Weng HF: Serum uric acid and leptin levels in metabolic syndrome: a quandary over the role of uric acid. *Metabolism*, 2007; 56: 751-756
 - 16) Yeh TK, Yeh TC, Weng CF, Shih BF, Tsao HJ, Hsiao CH, Chuang FT, Hu CY, Chang CY: Association of polymorphisms in genes involved in the dopaminergic pathway with blood pressure and uric acid levels in chinese females. *J Neural Transm*, 2010; 117: 1371-1376
 - 17) Cai Z, Xu X, Wu X, Zhou C, Li D: Hyperuricemia and the metabolic syndrome in hangzhou. *Asia Pac J Clin Nutr*, 2009; 18: 81-87
 - 18) Nan H, Qiao Q, Dong Y, Gao W, Tang B, Qian R, Tuomilehto J: The prevalence of hyperuricemia in a population of the coastal city of qingdao, china. *J Rheumatol*, 2006; 33: 1346-1350
 - 19) Fang J, Alderman MH: Serum uric acid and cardiovascular mortality the nhanes i epidemiologic follow-up study, 1971-1992. *National health and nutrition examination survey. JAMA*, 2000; 283: 2404-2410
 - 20) Sui X, Church TS, Meriwether RA, Lobelo F, Blair SN: Uric acid and the development of metabolic syndrome in women and men. *Metabolism*, 2008; 57: 845-852
 - 21) Choo V: Who reassesses appropriate body-mass index for asian populations. *Lancet*, 2002; 360: 235
 - 22) Lu ZS, Lu ZH, Lu H, Yan SG, Wang JA, Li L, You W: Association between hyperuricemia and hypertension in a chinese population at a high risk of hypertension. *Blood Press*, 2009; 18: 268-272
 - 23) Woo J, Swaminathan R, Cockram C, Lau E, Chan A: Association between serum uric acid and some cardiovascular risk factors in a chinese population. *Postgrad Med J*, 1994; 70: 486-491
 - 24) Zhao LJ, Zhao D, Liu J, Wang W, Wu GX, Qin LP, Liu J, Liu S, Wang WH, Zeng ZC: [association between serum uric acid and triglyceride in a chinese community]. *Zhonghua Nei Ke Za Zhi*, 2005; 44: 664-667
 - 25) Zhang Q, Lou S, Meng Z, Ren X: Gender and age impacts on the correlations between hyperuricemia and metabolic syndrome in chinese. *Clin Rheumatol*, 2011; 30: 777-787
 - 26) Lin WY, Liu CS, Li TC, Lin T, Chen W, Chen CC, Li CI, Lin CC: In addition to insulin resistance and obesity, hyperuricemia is strongly associated with metabolic syndrome using different definitions in chinese populations: a population-based study (taichung community health study). *Ann Rheum Dis*, 2008; 67: 432-433
 - 27) Nan H, Qiao Q, Soderberg S, Gao W, Zimmet P, Shaw J, Alberti G, Dong Y, Uusitalo U, Pavaday V, Chitson P, Tuomilehto J: Serum uric acid and components of the metabolic syndrome in non-diabetic populations in mauritian indians and creoles and in chinese in qingdao, china. *Metab Syndr Relat Disord*, 2008; 6: 47-57
 - 28) Li Y, Stamler J, Xiao Z, Folsom A, Tao S, Zhang H: Serum uric acid and its correlates in chinese adult populations, urban and rural, of beijing. The prc-usa collaborative study in cardiovascular and cardiopulmonary epidemiology. *Int J Epidemiol*, 1997; 26: 288-296
 - 29) Liang J, Xue Y, Zou C, Zhang T, Song H, Qi L: Serum uric acid and prehypertension among chinese adults. *J Hypertens*, 2009; 27: 1761-1765
 - 30) Yang T, Chu CH, Bai CH, You SL, Chou YC, Chou WY, Chien KL, Hwang LC, Su TC, Tseng CH, Sun CA: Uric acid level as a risk marker for metabolic syndrome: a chinese cohort study. *Atherosclerosis*, 2012; 220: 525-531
 - 31) Villegas R, Xiang YB, Cai Q, Fazio S, Linton M, Li H, Elasy T, Zheng W, Shu XO: Prevalence and determinants of hyperuricemia in middle-aged, urban chinese men. *Metab Syndr Relat Disord*, 2010; 8: 263-270
 - 32) Hara S, Tsuji H, Ohmoto Y, Amakawa K, Hsieh SD, Arase Y, Nakajima H: High serum uric acid level and low urine ph as predictors of metabolic syndrome: a retrospective cohort study in a japanese urban population. *Metabolism*, 2012; 61: 281-288
 - 33) Zhang Z, Bian L, Choi Y: Serum uric acid: a marker of metabolic syndrome and subclinical atherosclerosis in korean men. *Angiology*, 2012; 63: 420-428
 - 34) Tomiyama H, Higashi Y, Takase B, Node K, Sata M, Inoue T, Ishibashi Y, Ueda S, Shimada K, Yamashina A: Relationships among hyperuricemia, metabolic syndrome, and endothelial function. *Am J Hypertens*, 2011; 24: 770-774
 - 35) Li Q, Yang Z, Lu B, Wen J, Ye Z, Chen L, He M, Tao X, Zhang W, Huang Y, Zhang Z, Qu S, Hu R: Serum uric acid level and its association with metabolic syndrome and carotid atherosclerosis in patients with type 2 diabetes. *Cardiovasc Diabetol*, 2011; 10: 72
 - 36) Pacifico L, Cantisani V, Anania C, Bonaiuto E, Martino F, Pascone R, Chiesa C: Serum uric acid and its association with metabolic syndrome and carotid atherosclerosis in obese children. *Eur J Endocrinol*, 2009; 160: 45-52
 - 37) Lu Z, Dong B, Wu H, Chen T, Zhang Y, Wu J, Xiao H: Serum uric acid level in primary hypertension among chinese nonagenarians/centenarians. *J Hum Hypertens*, 2009; 23: 113-121
 - 38) Sumino H, Ichikawa S, Kanda T, Nakamura T, Sakamaki T: Reduction of serum uric acid by hormone replacement therapy in postmenopausal women with hyperuricaemia. *Lancet* 1999; 354: 650
 - 39) Anton FM, Garcia PJ, Ramos T, Gonzalez P, Ordas J: Sex differences in uric acid metabolism in adults: evidence for a lack of influence of estradiol-17 beta (e2) on the renal handling of urate. *Metabolism*, 1986; 35: 343-348
 - 40) Chuang SY, Lee SC, Hsieh YT, Pan WH: Trends in hyperuricemia and gout prevalence: nutrition and health survey in taiwan from 1993-1996 to 2005-2008. *Asia Pac J Clin Nutr*, 2011; 20: 301-308
 - 41) Nagahama K, Iseki K, Inoue T, Touma T, Ikemiya Y, Takishita S: Hyperuricemia and cardiovascular risk factor clustering in a screened cohort in okinawa, japan. *Hypertens Res*, 2004; 27: 227-233
 - 42) Conen D, Wietlisbach V, Bovet P, Shamlaye C, Riesen W, Paccaud F, Burnier M: Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. *Bmc Public Health*, 2004; 4: 9
 - 43) Yin JH, Song ZY, Shan PF, Xu J, Ye ZM, Xu XH, Zhang SZ, Liang Q, Zhao Y, Ren Z, Yu YP: Age- and gender-

- specific prevalence of carotid atherosclerosis and its association with metabolic syndrome in hangzhou, china. *Clin Endocrinol (Oxf)*, 2012; 76: 802-809
- 44) Chen B, Yang D, Chen Y, Xu W, Ye B, Ni Z: The prevalence of microalbuminuria and its relationships with the components of metabolic syndrome in the general population of china. *Clin Chim Acta*, 2010; 411: 705-709
- 45) Li SL, Yang Q, Lv SY, Zhang YL, Zhang JA: Prevalence of the metabolic syndrome in the yan-an region of northwest china. *J Int Med Res*, 2012; 40: 673-680
- 46) Li JB, Wang X, Zhang JX, Gu P, Zhang X, Chen CX, Guo R, Wu M: Metabolic syndrome: prevalence and risk factors in southern china. *J Int Med Res*, 2010; 38: 1142-1148
- 47) Lao XQ, Zhang YH, Wong MC, Xu YJ, Xu HF, Nie SP, Ma WJ, Thomas GN, Yu IT: The prevalence of metabolic syndrome and cardiovascular risk factors in adults in southern china. *Bmc Public Health*, 2012; 12: 64
- 48) Wuyun GW, Huang YX, Wu HP, Su XL, Wang PY, You LL, Liu AP: Survey on the Prevalence of Common Chronic Diseases among the Mongolian Nomads and Farmers in the Inner Mongolia. *Chinese J of Preventive and Control of Chronic Diseases*, 2011; 19: 448-451
- 49) Zhou BF: 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
- 50) Bonora E, Targher G, Zenere MB, Saggiani F, Cacciatori V, Tosi F, Travia D, Zenti MG, Branzi P, Santi L, Muggeo M: Relationship of uric acid concentration to cardiovascular risk factors in young men. Role of obesity and central fat distribution. The verona young men atherosclerosis risk factors study. *Int J Obes Relat Metab Disord*, 1996; 20: 975-980
- 51) Lee J, Sparrow D, Vokonas PS, Landsberg L, Weiss ST: Uric acid and coronary heart disease risk: evidence for a role of uric acid in the obesity-insulin resistance syndrome. The normative aging study. *Am J Epidemiol*, 1995; 142: 288-294
- 52) Matsuura F, Yamashita S, Nakamura T, Nishida M, Nozaki S, Funahashi T, Matsuzawa Y: 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
- 53) Fox IH: Metabolic basis for disorders of purine nucleotide degradation. *Metabolism*, 1981; 30: 616-634
- 54) Fabregat I, Revilla E, Machado A: Short-term control of the pentose phosphate cycle by insulin could be modulated by the nadph/nadp ratio in rat adipocytes and hepatocytes. *Biochem Biophys Res Commun*, 1987; 146: 920-925
- 55) Bedir A, Topbas M, Tanyeri F, Alvur M, Arik N: Leptin might be a regulator of serum uric acid concentrations in humans. *Jpn Heart J*, 2003; 44: 527-536
- 56) Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C, Mu W, Krotova K, Block ER, Prabhakar S, Johnson RJ: Hyperuricemia induces endothelial dysfunction. *Kidney Int*, 2005; 67: 1739-1742
- 57) Chiou WK, Wang MH, Huang DH, Chiu HT, Lee YJ, Lin JD: The relationship between serum uric acid level and metabolic syndrome: differences by sex and age in taiwanese. *J Epidemiol*, 2010; 20: 219-224
- 58) Onat A, Uyarel H, Hergenc G, Karabulut A, Albayrak S, Sari I, Yazici M, Keles I: Serum uric acid is a determinant of metabolic syndrome in a population-based study. *Am J Hypertens*, 2006; 19: 1055-1062
- 59) Strassak A, Ruttman E, Brant L, Kelleher C, Klenk J, Concin H, Diem G, Pfeiffer K, Ulmer H: Serum uric acid and risk of cardiovascular mortality: a prospective long-term study of 83,683 austrian men. *Clin Chem*, 2008; 54: 273-284
- 60) Takeuchi F, Yamamoto K, Isono M, Katsuya T, Akiyama K, Ohnaka K, Rakugi H, Yamori Y, Ogihara T, Takayanagi R, Kato N: Genetic impact on uric acid concentration and hyperuricemia in the Japanese population. *J Atheroscler Thromb*, 2013; 20: 351-367
- 61) Zhang ML, Gao YX, Wang X, Chang H, Huang GW: Serum uric acid and appropriate cutoff value for prediction of metabolic syndrome among chinese adults. *J Clin Biochem Nutr*, 2013; 52: 38-42