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Serum uric acid and metabolic syndrome in Taiwanese adults

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Abstract

A positive association between serum uric acid and metabolic syndrome has been reported, but little information is available about the association between serum uric acid and metabolic syndrome in Taiwanese adults. The purpose of this study was to investigate the association between serum uric acid levels and metabolic syndrome in Taiwanese adults. We performed a cross-sectional study of 2085 men and 1557 women. All of the participants underwent a health screening during the period from January 2005 to December 2005 at a health center of the Shin Kong Wu Ho-Su Memorial Hospital. *Metabolic syndrome* was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria. The results showed that hyperuricemia was significantly associated with increased risk for hypertriglyceridemia, low high-density lipoprotein cholesterol level, and high blood pressure in men and women. The risk of metabolic syndrome was significantly higher in the fourth quartile than in the first quartile of uric acid level in men (odds ratio [OR], 1.50; 95% confidence interval [CI], 1.06-2.14) and women (OR, 2.33; 95% CI, 1.39-3.93). In addition, uric acid level was inversely associated with hyperglycemia in men. The ORs of hyperglycemia for the second, third, and fourth quartile of uric acid were 0.69 (95% CI, 0.46-1.03), 0.55 (95% CI, 0.37-0.83), and 0.45 (95% CI, 0.29-0.69), respectively, compared with the lowest quartile of uric acid. The results demonstrate that there is a positive association between serum uric acid levels and metabolic syndrome and an inverse association between uric acid and fasting plasma glucose in Taiwanese adults.

1. Introduction

Metabolic syndrome is a clustering of multiple risk factors for cardiovascular disease such as central obesity, glucose intolerance or type 2 diabetes mellitus, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), and hypertension [1]. It has been postulated that insulin resistance is a key underlying pathophysiologic abnormality in this condition [2]. A series of studies found that individuals with metabolic syndrome are at much higher risk for cardiovascular disease [1,3,4].

Hyperuricemia reflects insulin resistance [5-8]. Some large epidemiologic studies have suggested that serum uric acid levels should be included in the definition of metabolic syndrome [2,9]. Increased serum uric acid levels are often accompanied by obesity, dyslipidemia, and hypertension [10,11]. The National Health and Nutrition Examination Survey I study found that increased serum uric level is independently and significantly associated with risk of cardiovascular mortality. For example, an increase of 1 mg/dL in serum uric acid levels was shown to predict an increase of 28% in cardiovascular mortality in men and 43% in women aged 45 to 54 years [12].

There is a positive association between serum uric acid level and metabolic syndrome [13-16], but little information is available on the association between serum uric acid levels and metabolic syndrome in Taiwanese adults. The purpose of the present study was to investigate the association between serum uric acid levels and metabolic syndrome and its components in Taiwanese adults.

2. Subjects and methods

2.1. Subjects

We performed a cross-sectional study consisting of 3642 persons (2085 men; mean age, 46.8 years; 1557 women;

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mean age, 47.2 years). Each participant was considered to be healthy and had visited a health center (Shin Kong Wu Ho-Su Memorial Hospital) for health screening during the period from January 2005 to December 2005. Each participant was interviewed by a physician, who obtained a detailed medical history and elicited dietary habits and lifestyle characteristics (including smoking status, exercise status, and alcohol consumption). The study protocol was approved by the ethics committee of the Shin Kong Wu Ho-Su Memorial Hospital.

3. Methods

At the time of the examination, height and body weight measurements were determined with a foot-to-foot bioelectrical impedance analyzer (BF-220; Tanita, Tokyo, Japan). Height was measured to the nearest 0.1 cm, and weight was measured to the nearest 0.1 kg with subjects wearing light clothes. Body mass index (BMI, measured in kilograms per square meter) was computed from measured body weight (in kilograms) and height (in meters). 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 by trained nurses using an anthropometric nonstretchable tape after normal expiration. Blood pressure was measured in the right and left arms using an automated oscillometric blood pressure recorder (Dinamap DPC 100X-EN; GE Medical Systems, Milwaukee, WI) in a sitting position after 5 minutes of rest. The systolic and diastolic blood pressure values of 2 measurements were recorded.

Fasting blood samples were collected from all participants after an 8t-hour overnight fast. Serum levels of uric acid, glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) were measured by an automated clinical analyzer (Hitachi 7600; Hitachi, Tokyo, Japan).

The diagnostic criteria of metabolic syndrome used in this study were established by the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). We modified the definition of metabolic syndrome to include waist circumference criteria as defined by the World Health Organization Asia-Pacific for obesity. Participants with 3 or more of the following criteria

Table 1
Characteristics of the study population according to quartile of serum uric acid

	Men				
	Quartile of serum uric acid				
	Q1	Q2	Q3	Q4	
Uric acid range (mg/dL)	<5.9	5.9-6.7	6.7-7.7	>7.7	
No. of subjects	513	486	565	521	
Age (y)	47.5 ± 11.6	46.8 ± 11.4	45.8 ± 11.0	47.1 ± 11.6	$P = .07$
BMI (kg/m^2)	23.3 ± 3.1	24.1 ± 3.0	24.7 ± 3.0	25.5 ± 3.0	$P < .0001$
Waist circumference (cm)	83.3 ± 8.1	85.0 ± 8.0	86.1 ± 7.3	87.9 ± 7.6	$P < .0001$
Fasting glucose (mg/dL)	101.6 ± 41.2	96.5 ± 28.3	95.2 ± 25.1	95.0 ± 21.9	$P = .001$
TG (mg/dL)	133.1 ± 102.0	148.2 ± 186.4	161.2 ± 138.9	183.7 ± 125.9	$P < .0001$
Total cholesterol (mg/dL)	189.5 ± 35.9	194.6 ± 37.0	198.0 ± 38.5	202.0 ± 38.8	$P < .0001$
HDL-C (mg/dL)	51.0 ± 13.0	49.3 ± 12.0	47.8 ± 11.2	46.9 ± 12.2	$P < .0001$
LDL-C (mg/dL)	117.0 ± 30.3	121.7 ± 31.6	125.4 ± 33.3	126.6 ± 34.4	$P < .0001$
Systolic blood pressure(mm Hg)	118.4 ± 18.0	121.5 ± 18.6	122.7 ± 17.3	126.4 ± 18.6	$P < .0001$
Diastolic blood pressure(mm Hg)	73.2 ± 10.6	75.4 ± 11.3	76.7 ± 10.8	79.0 ± 10.8	$P < .0001$
	Women				
	Quartile of serum uric acid				
	Q1	Q2	Q3	Q4	
Uric acid range (mg/dL)	<4.2	4.2-4.9	4.9-5.7	>5.7	
No. of subjects	367	385	407	398	
Age (y)	43.9 ± 10.8	45.6 ± 10.9	47.5 ± 12.3	51.6 ± 12.0	$P < .0001$
BMI (kg/m^2)	21.1 ± 2.6	21.6 ± 2.6	22.7 ± 3.1	24.5 ± 3.9	$P < .0001$
Waist circumference(cm)	77.7 ± 8.3	78.9 ± 8.8	80.3 ± 10.0	84.9 ± 10.4	$P < .0001$
Fasting glucose (mg/dL)	91.5 ± 28.3	89.1 ± 23.3	90.3 ± 18.2	94.3 ± 24.8	$P = .01$
TG (mg/dL)	90.0 ± 51.0	90.5 ± 45.3	105.8 ± 54.6	139.4 ± 85.6	$P < .0001$
Total cholesterol (mg/dL)	185.0 ± 32.6	189.1 ± 34.6	196.6 ± 38.3	204.9 ± 38.5	$P < .0001$
HDL-C (mg/dL)	65.1 ± 14.4	63.6 ± 14.6	61.6 ± 15.4	56.8 ± 14.2	$P < .0001$
LDL-C (mg/dL)	105.6 ± 29.3	110.3 ± 29.1	118.0 ± 33.0	125.3 ± 33.5	$P < .0001$
Systolic blood pressure (mm Hg)	108.1 ± 18.5	109.0 ± 18.5	114.0 ± 22.4	121.3 ± 23.8	$P < .0001$
Diastolic blood pressure (mm Hg)	64.7 ± 9.8	64.7 ± 10.0	67.3 ± 10.7	70.1 ± 11.9	$P < .0001$

Table 2
Prevalence of each metabolic syndrome–associated abnormality according to quartile of serum uric acid

	Men				
	Quartile of serum uric acid				
	Q1	Q2	Q3	Q4	
Uric acid range (mg/dL)	<5.9	5.9-6.7	6.7-7.7	>7.7	
No. of subjects	513	486	565	521	
Ever smoking	215 (41.9%)	169 (34.8%)	250 (44.2%)	185 (35.5%)	$P = .01$
Ever drinker	126 (24.6%)	114 (23.5%)	137 (24.2%)	138 (26.5%)	$P = .25$
Physical inactivity	274 (53.4%)	258 (53.1%)	314 (55.6%)	267 (51.2%)	$P = .80$
Central obesity	94 (18.3%)	107 (22.0%)	139 (24.6%)	158 (30.3%)	$P < .0001$
Hyperglycemia	78 (15.2%)	55 (11.3%)	54 (9.6%)	59 (11.3%)	$P = .03$
Hypertriglyceridemia	131 (25.5%)	152 (31.3%)	218 (38.6%)	253 (48.6%)	$P < .0001$
Low HDL-C	88 (17.2%)	90 (18.5%)	144 (25.5%)	147 (28.2%)	$P < .0001$
High blood pressure	156 (30.4%)	177 (36.4%)	221 (39.1%)	243 (46.6%)	$P < .0001$
	Women				
	Quartile of serum uric acid				
	Q1	Q2	Q3	Q4	
Uric acid range (mg/dL)	<4.2	4.2-4.9	4.9-5.7	>5.7	
No. of subjects	367	385	407	398	
Ever smoking	39 (10.6%)	38 (9.9%)	43 (10.6%)	25 (6.3%)	$P = .27$
Ever drinker	25 (6.8%)	18 (4.7%)	22 (5.4%)	22 (5.5%)	$P = .63$
Physical inactivity	230 (62.7%)	241 (62.6%)	264 (64.9%)	203 (51.0%)	$P = .07$
Central obesity	129 (35.1%)	170 (44.2%)	190 (46.7%)	239 (60.1%)	$P < .0001$
Hyperglycemia	21 (5.7%)	17 (4.4%)	26 (6.4%)	40 (10.1%)	$P = .01$
Hypertriglyceridemia	39 (10.6%)	40 (10.4%)	74 (18.2%)	124 (31.2%)	$P < .0001$
Low HDL-C	61 (16.6%)	66 (17.1%)	87 (21.4%)	138 (34.7%)	$P < .0001$
High blood pressure	54 (14.7%)	62 (16.1%)	97 (23.8%)	152 (38.2%)	$P < .0001$

were defined as having metabolic syndrome: (1) high blood pressure, with systolic blood pressure of at least 130 mm Hg or diastolic blood pressure of at least 85 mm Hg; (2) hypertriglyceridemia, with TG levels of at least 150 mg/dL (1.69 mmol/L); (3) low HDL-C, with HDL cholesterol level less than 40 mg/dL (1.03 mmol/L) for men and less than 50 mg/dL (1.29 mmol/L) for women; (4) hyperglycemia, with fasting plasma glucose of at least 110 mg/dL (6.1 mmol/L); and (5) abdominal obesity (waist circumference ≥90 cm for men and ≥80 cm for women).

Subjects were stratified by sex into quartiles of baseline serum uric acid levels. The baseline characteristics of continuous variables were measured and divided into quartiles of serum uric acid level, and the differences across quartiles were tested with analysis of variance separately for men and women.

3.1. Statistical analysis

Categorical data were analyzed by the χ^2 test. Differences in continuous variables between quartiles were compared by analysis of variance. A P value < .05 was taken to be statistically significant. Multiple logistic regression was used to examine the association between quartiles of uric acid and metabolic syndrome. All statistical analyses were performed using SAS statistical software (SAS program for Windows, version 8.02; SAS institute, Cary, NC).

4. Results

The mean serum uric acid level was 6.9 ± 1.4 mg/dL in men and 5.0 ± 1.2 mg/dL in women. Mean uric acid level was significantly higher in men than in women. Men and women were each divided into quartiles based on fasting serum uric acid concentration (men: first quartile <5.9 mg/dL, second quartile 5.9-6.7 mg/dL, third quartile 6.7-7.7 mg/dL, and fourth quartile >7.7 mg/dL; women: first quartile <4.2 mg/dL, second quartile 4.2-4.9 mg/dL, third quartile 4.9-5.7 mg/dL, and fourth quartile >5.7 mg/dL). The baseline characteristics of the study population according to quartile of serum uric acid are shown in Table 1. Overall, higher quartiles of serum uric acid levels were associated with increasing BMI, waist circumference, serum TG, total cholesterol level, LDL, and blood pressure in men and in women ($P < .0001$). There was a graded decrease in HDL-C level with uric acid quartile ($P < .0001$). In men, there were no significant differences in age between quartiles; but in women, age increased from the lowest to the highest quartile ($P < .0001$).

Table 2 shows the prevalence of each metabolic syndrome–associated abnormality in each quartile of serum uric acid. Of the 5 components evaluated, the most common abnormalities in the fourth quartile of serum uric acid concentration were hypertriglyceridemia in men (48.6%) and central obesity in women (60.1%). The

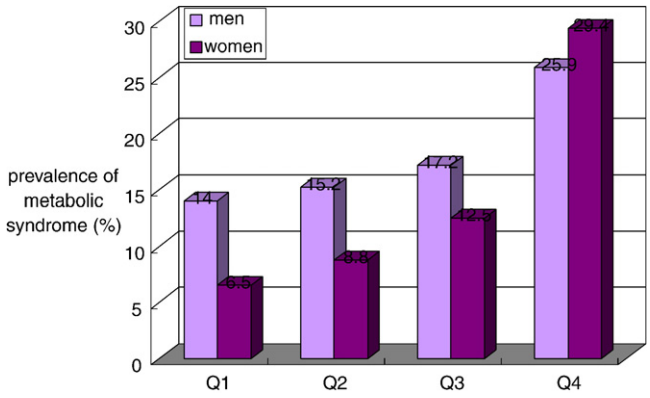

Fig. 1. The prevalence of metabolic syndrome increased according to the quartile of serum uric acid.

prevalence of abdominal obesity, low HDL-C level, hypertriglyceridemia, and high blood pressure increased as the level of serum uric acid increased ($P < .0001$).

The prevalence of metabolic syndrome increased in men and in women according to the quartile of serum uric acid ($P < .0001$) (Fig. 1). The prevalence of metabolic syndrome in the fourth quartile of uric acid concentration in men (25.9%) and in women (29.4%) was significantly higher than that in the first quartile (14.0% in men and 6.5% in women), second quartile (15.2% in men and 8.8% in women), and third quartile (17.2% in men and 12.5% in women). In the first, second, and third quartiles, the prevalence of metabolic syndrome in men was higher than that in women; however, in the fourth quartile, the prevalence of metabolic syndrome was higher in women than in men.

We also assessed the odds ratios (ORs) and 95% confidence intervals (CIs) of serum uric acid levels and each metabolic syndrome–associated abnormality. After adjusting for age, smoking status, alcohol consumption, and exercise status, there was a positive association between uric acid concentration and hypertriglyceridemia, low HDL-C, and high blood pressure in both men and women (Table 3). Uric acid was negatively associated with hyperglycemia in men. There was a positive association between serum uric acid levels and central obesity in women, but not in men.

After adjusting for age, smoking status, alcohol consumption, and exercise status, multivariate logistic regression analysis revealed that there was a significant association between fourth-quartile uric acid levels and prevalence of metabolic syndrome in men and in women (Table 4). Women with fourth-quartile uric acid concentrations had a significantly greater risk of metabolic syndrome than men with fourth-quartile uric acid concentrations (OR, 2.33; 95% CI, 1.39-3.93 vs OR, 1.50; 95% CI, 1.06-2.14).

5. Discussion

In the present study, we found that the risk for metabolic syndrome, hypertriglyceridemia, low HDL-C level, and high blood pressure was significantly greater in men and in women with serum uric acid concentrations in the fourth quartile. In addition, we found that uric acid was negatively associated with hyperglycemia in men; the ORs of hyperglycemia in the second, third, and fourth quartiles of uric acid were 0.69 (95% CI, 0.46-1.03), 0.55 (95% CI, 0.37-0.83), and 0.45 (95% CI, 0.29-0.69), respectively. The mean serum uric acid level of men (6.9 ± 1.4 mg/dL) in this study was higher than that of the other studies in Asian areas [17]. Different ethnic genes and dietary habits may partly explain this discrepancy.

Our results showed that there was a negative association between uric acid level and hyperglycemia in men, but not in women. Previous studies have reported a positive association between hyperuricemia and the risk for type 2 diabetes mellitus [7,18,19]. Cook et al [20] showed that there was a positive association between serum glucose and serum uric acid concentrations up to serum glucose of about 134 mg/dL in middle-aged British men; at higher levels of glucose, the association with serum uric acid decreased. Choi and Ford [18] also showed a bell-shaped association

Table 3
Multivariate analysis of the OR and 95% CIs between uric acid and each component of metabolic syndrome

	Quartile of serum uric acid			
	Q1	Q2	Q3	Q4
Men				
Central obesity	1 (reference)	1.13 (0.78-1.65)	1.10 (0.77-1.58)	1.27 (0.88-1.83)
Hyperglycemia	1 (reference)	0.69 (0.46-1.03)	0.55 (0.37-0.83)	0.45 (0.29-0.69)
Hypertriglyceridemia	1 (reference)	1.36 (1.03-1.81)	1.74 (1.33-2.27)	2.52 (1.91-3.33)
Low HDL-C	1 (reference)	1.10 (0.79-1.53)	1.52 (1.12-2.06)	1.68 (1.23-2.30)
High blood pressure	1 (reference)	1.34 (1.00-1.78)	1.60 (1.22-2.11)	2.18 (1.64-2.90)
Women				
Central obesity	1 (reference)	1.37 (1.01-1.86)	1.27 (0.94-1.73)	2.07 (1.49-2.88)
Hyperglycemia	1 (reference)	0.50 (0.24-1.04)	0.58 (0.29-1.13)	0.65 (0.34-1.24)
Hypertriglyceridemia	1 (reference)	0.87 (0.54-1.39)	1.41 (0.92-2.18)	2.47 (1.62-3.78)
Low HDL-C	1 (reference)	0.95 (0.65-1.40)	1.11 (0.76-1.61)	1.96 (1.35-2.86)
High blood pressure	1 (reference)	0.91 (0.58-1.43)	1.22 (0.80-1.87)	1.96 (1.29-3.00)

Odds ratios and 95% CIs adjusted for age, smoking status, alcohol consumption, and exercise status.

Table 4
Multivariate analysis of the OR and 95% CIs between uric acid and metabolic syndrome

	Quartile of serum uric acid			
	Q1	Q2	Q3	Q4
Whole	1 (reference)	1.05 (0.77-1.45)	1.17 (0.87-1.58)	1.87 (1.41-2.47)
Men	1 (reference)	1.00 (0.68-1.47)	1.08 (0.75-1.56)	1.50 (1.06-2.14)
Women	1 (reference)	1.14 (0.64-2.04)	1.16 (0.67-2.03)	2.33 (1.39-3.93)

Odds ratios and 95% CIs adjusted for age, smoking status, alcohol consumption, and exercise status.

between serum uric acid levels and plasma glucose levels. It has also been shown that hyperglycemia enhances uric acid excretion, possibly by impairing tubular reabsorption of uric acid [21,22]. Most of the aforementioned studies were based on diabetic patients in Western populations. Few studies have assessed the association between uric acid levels and plasma glucose in nondiabetic populations, especially Asian populations. One study in Taiwan found an inverse association between serum uric acid levels and diabetes in men (OR, 0.451; 95% CI, 0.349-0.583; $P < .001$) [23], a finding similar to that in our study. A study in Japan showed a negative association between hyperuricemia and diabetes mellitus in men (OR, 0.61; 95% CI, 0.49-0.75; $P < .05$) [17]. Chou et al [24] and Lin et al [25] investigated the sex difference in the relationship of serum uric acid with fasting plasma glucose in nondiabetic Chinese populations. They reported that the fasting plasma glucose level increased significantly with increasing uric acid level in women but not in men. The inconsistent results in these studies may be due to ethnic and sex differences; we suggest that more studies of different populations be conducted to investigate the association between serum uric acid and hyperglycemia.

The present study found that women with uric acid concentrations in the fourth quartile (>5.7 mg/dL) had a significantly increased risk for metabolic syndrome (OR, 2.33; 95% CI, 1.39-3.93). Studies have reported that the association between serum uric acid levels and metabolic syndrome is stronger in women than in men. Ishizaka et al [26] reported that the ORs for metabolic syndrome increased across successive quartiles of serum uric acid concentrations. Lohsoonthorn et al [13] investigated the association between metabolic syndrome and hyperuricemia in Thai adults and reported similar results. The findings in the present study are consistent with the findings reported in the aforementioned studies, and we recommend that women with serum uric acid levels exceeding 5.7 mg/dL undergo a systemic workup to rule out metabolic syndrome.

A few studies have demonstrated a sex-dependent association between hyperuricemia and cardiovascular risk factors. The National Health and Nutrition Examination Survey I epidemiologic follow-up study demonstrated a stronger association between hyperuricemia and cardiovascular mortality among women than among men [12]. The association between insulin resistance and hyperuricemia has also been shown to be higher in women than in men [24]. The interaction between estrogen and other hormones has been suggested as a possible cause of the difference in risk for metabolic syndrome between men and women.

In the present study, hyperuricemia was significantly related to central obesity in women. A positive association was also found in men, but did not reach statistical significance. The positive association between serum uric acid levels and obesity has been recognized for more than 2 decades [27,28]. Yamashita et al [29] indicated that increases in serum uric acid levels in obese subjects might be due to decreases in uric acid clearance. They also showed that uric acid clearance was higher in subjects with lower BMI values [29]. Our study also revealed that hypertriglyceridemia, hypo-HDL-cholesterolemia, and high blood pressure were significantly associated with serum uric acid levels. The results were similar to previous studies [30-33].

In summary, there is a significant association between serum uric acid levels and metabolic syndrome in Taiwanese adults, especially women. Women with serum uric acid levels in the fourth quartile (>5.7 mg/dL) had the highest OR (2.33) of developing metabolic syndrome. In addition, to the best of our knowledge, this is the first study to find an inverse association between serum uric acid levels and fasting plasma glucose level in an Asian nondiabetic population. We suggest that a longitudinal study be conducted to clarify the clinical significance of this inverse association between uric acid and fasting plasma glucose.

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