PREVALENCE OF METABOLIC SYNDROME AND ITS ASSOCIATION WITH SERUM URIC ACID LEVELS IN BANGKOK THAILAND

Jamabhorn Jaipakdee, Wiroj Jiamjarasrangsri, Vitool Lohsoonthorn and Somrat Lertmaharit

Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Abstract. Metabolic syndrome (MetS) and hyperuricemia are important risk factors for cardiovascular disease, hypertension and renal disease. The relationship between serum uric acid (UA) levels and MetS remains unclear. In the present study we determined the presence of MetS and measured UA levels among personnel at the Thai Red Cross Society and Chulalongkorn University to evaluate the possible presence of an association between the two. We conducted this cross sectional study in 2009. A total of 2,804 persons, aged 35-60 years (628 men and 2176 women) filled out questionnaires, had laboratory testing and were included in the study. MetS was defined by criteria harmonized from six international expert groups. The association between MetS and UA levels was determined using multivariable logistic regression. The overall prevalences of MetS were 25.1, 21.1, and 18.2% when a BMI ≥ 23 kg/m^2, a BMI≥ 25 kg/m^2 or waist circumference were used to classify abdominal obesity, respectively. Body mass index, waist circumference, blood pressure, and triglycerides significantly elevated in both men and women with elevated UA levels (all a p-value <0.005). After adjustment for potential confounders, the odds ratio of having MetS in the fourth quartile compared with the first quartile of a UA level was 2.77 times for men (95% CI 1.60-4.79) and 8.04 times for women (95% CI 5.43-11.91). There wes a stronger association between the presence of MetS and UA in women than men. UA levels were associated with the presence of MetS.

Keywords: metabolic syndrome, serum uric acid, Thailand

INTRODUCTION

Metabolic syndrome (MetS) is a major public health problem and is increasing in prevalence worldwide (Alberti *et al*, 2006). Around 20-25% of the world's adult population has MetS (Alberti *et al*, 2006). The prevalence of MetS varies according to geographic location, nationality, population characteristics, and MetS criteria (Huang and Jayakar, 2010; Romaguera *et al*, 2010). Among Europeans, the prevalence has a range of 20-30% (Qiao, 2006; Grundy, 2008). A study found the prevalence of MetS among migrant Asians has a range of 14-49% (Misra and Khurana, 2009). The results of the fourth national

Correspondence: Wiroj Jiamjarasrungsri, Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
Tel: +66 (0) 2256 4000 ext 3700-1; Fax: +66 (0) 2256 4292
E-mail: wjiamja@gmail.com

health examination survey among Thai adults aged ≥20 years is 23.2% (19.5% in men and 26.8% in women) and is higher in urban than rural areas (23.1% *vs* 17.9%, $p < 0.05$) (Aekplakorn *et al*, 2011).

MetS consists of a cluster of risk factors for cardiovascular disease (CVD), chronic kidney disease (CKD), type 2 diabetes mellitus and hypertension (Wang *et al*, 2007). The results of a meta-analysis strongly suggest MetS is associated with an increased incidence of CVA and an increase in mortality (Gami *et al*, 2007; Mottillo *et al*, 2010). Adults with MetS are three times more likely to have a heart attack or stroke compared to those without MetS (Alberti *et al*, 2006). People with MetS have a fivefold greater risk of developing type 2 diabetes mellitus (Stern *et al*, 2004; Sarkar *et al*, 2006).

The relationship between elevated serum uric acid **(**UA) levels and CVD, hypertension, renal disease and MetS has been previously reported (Feig *et al*, 2008; Sui *et al*, 2008; Chiou *et al*, 2010). UA levels are more often elevated in subjects with elevated components of MetS (Sui *et al*, 2008). Some studies suggest elevated UA levels predict the development of hypertension (Heinig and Johnson, 2006; Feig *et al*, 2008). About 25-60% of patients with untreated primary hypertension and 90% of newly diagnosed primary hypertensive adolescents have UA levels greater than 5.5 mg/dl (Feig *et al*, 2008); however, the association remains controversial. Some studies have argued UA levels are not related to the development of MetS (Liou *et al*, 2006; Lim *et al*, 2010).

We conducted the present study to: 1) estimate the prevalence of MetS among personnel using a harmonized definition of MetS and, 2) determine the association between MetS and UA levels after adjusting for potential confounders. There is no general consensus of what constitutes abdominal obesity in the Thai population. Body mass index (BMI) and waist circumference (WC) norms for Asian populations were used to define abdominal obesity in this study. A BMI of ≥25 kg/m^2 was considered as overweight. Cut-off point of ≥23 kg/m^2 was also added since this level has been considered as increased risk (WHO expert consulation, 2004). In practice, WC is more difficult to measure and tends to result in more errors than BMI. Consequently, we determined the prevalence of MetS using a BMI ≥23, ≥25 kg/m^2 and using WC as a measure of abdominal obesity.

MATERIALS AND METHODS

Participants and data collection

This cross sectional study, part of a Chulalongkorn University and Thai Red Cross (CU-TRC) Cohort project, was carried out in 2009. The study was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University. Three thousand three hundred ninety-three professionals and office workers at the Thai Red Cross Society and Chulalongkorn University, aged 35-60 years agreed to participate in this study after giving written informed consent. Data were gathered through self reported questionnaires, anthropometry and biochemistry tests conducted by Thai Red Cross nurses and trained staff. Participants previously treated for hyperuricemia or gout were excluded. A total of 2,804 persons, (628 men and 2,176 women) completed the questionnaires and laboratory tests.

Participants provided information about their demographics, personal and family medical and medication histories

using a standard questionnaire. A medical history of diabetes mellitus (DM), hypertension (HT) and dyslipidemia was recorded if the participant was previously diagnosed by a physician or was taking medications. Data regarding smoking status (never versus ever, frequency and amount per day), depression (never versus ever been diagnosed), and regular physical activity (never versus ever; type, frequency and duration) were also collected.

Anthropometric measurement taken were: weight, height, blood pressure (BP) and WC using standard procedures. Standing height was determined without shoes and measured to the nearest 0.5 centimeter. Weight was determined without shoes and with participants lightly clothed. Weight was measured using an automatic electronic scale (Seca, Hamburg, Germany) to the nearest 100 grams. BMI was calculated as the weight (kg) divided by the square of the height (m). WC was measured with a heavy-duty inelastic plastic fiber tape measure to the nearest 0.5 centimeter while the subject stood on both feet, with the feet touching each other and both arms hanging down freely. The measurement was taken midway between the inferior margin of the last rib and the iliac crest at the end of expiration (Wang *et al*, 2003). Blood pressure was measured using an automatic sphygmomanometer (UDEX-IIa, UEDA, Tokyo, Japan), in a seated position after each subject had rested for at least 5 minutes.

Laboratory measurements

Ten milliliters (ml) venous blood sample was collected from each participant after a 12-hour overnight fast. Serum samples were used to determine lipid profiles. Serum triglyceride (TG) levels were determined with a standardized enzymatic procedure using a glycerol phosphate oxidase assay. High-density lipoprotein–cholesterol (HDL-C) was measured with a chemical precipitation technique using dextran sulfate. UA concentrations were measured using the Uricase EMST method. Plasma samples were used to determine fasting plasma glucose (FPG) using the hexokinase enzyme method. Serum creatinine (sCr) levels were measured using a Roche Diagnostics (Indianapolis, IN) CREA plus (11775642) enzymatic assay (CrEnz) on a COBAS INTEGRA 400 plus analyzer. All laboratory tests were conducted without knowledge of the participants' medical history. Lipid profile results, FPG, UA, and sCr concentrations were reported in mg/dl.

Definition of MetS

MetS was defined by harmonizing six international expert groups (Alberti *et al*, 2009) using four out of five components: 1) elevated TG (≥ 150 mg/dl) or treatment for this lipid abnormality, 2) a low HDL-C (<40 mg/dl in men and <50 mg/dl in women), 3) an elevated BP defined by a systolic BP (SBP) ≥130 or a diastolic BP (DBP) ≥85 mmHg, or history of HT, 4) an elevated FPG level (≥100 mg/dl) or having previously been diagnosed with DM. The fifth component was abdominal obesity, defined by three different measures: a) a BMI ≥23 kg/m^2 following the Western Pacific Regional Office, World Health Organization (WPRO) criteria (Anuurad *et al*, 2003), b) a BMI ≥25 kg/m^2 normal international standards for BMI classification, and c) a WC with a cut-off point for Asian populations (≥90 cm in men and ≥80 cm in women). The presence of any combination of three of five components was considered MetS. The prevalences of MetS using the definitions including a

BMI ≥23 kg/m^2, a BMI ≥25 kg/m^2 or WC were compared to determine these factors in the overall diagnosis of MetS.

Statistical analysis

Prevalences of MetS by age, gender, health behavior, depression status, medical history, sCr level, and UA level were examined. Comparisons between the prevalences of MetS were analyzed using a chi-square (χ^2) test. We divided UA concentration into quartiles within each gender [in men: Quartile 1 (Q1): UA level ≤ 5.2 mg/dl, Quartile 2 (Q2): UA levels of 5.3-6.1 mg/dl, Quartile 3 (Q3): UA level of 6.2-7.0 mg/dl, and Quartile 4 (Q4): UA level >7.0 mg/dl; in women: Q1: UA level ≤ 3.9 mg/dl, Q2: UA level of 4.0-4.5 mg/dl, Q3: UA level of 4.6-5.2 mg/dl, and Q4: UA level >5.2 mg/dl]. UA quartile distribution by age, smoking status, regular physical activity, and MetS components were examined. We used a chi-square test for categorical variables and ANOVA for continuous variables.

Multivariable logistic regression was used to predict the association between MetS and UA levels, adjusted for potential confounding factors. We considered the following covariates as possible confounders: age, smoking status, regular physical activity, depression status, and sCr levels. Analyses were conducted separately for men and women. The UA quartile was treated as an ordinal score to test for a significant linear trend with UA and MetS association. A p-value <0.05 were considered statistically significant. Confidence intervals were calculated at the 95% level. All statistical analyses were performed with STATA software, version 11.0 (Stata, College Station, TX).

RESULTS

After excluding participants with incomplete data, 2,804 persons, (628 men and 2,176 women) were included in the analysis. The mean age of participants was 46.0 ± 7.0 years (46.4 ± 7.0 years in men and 45.9 ± 7.0 years in women). Four point four percent had DM, 14.7% had HT and 37.1% had dyslipidemia.

The overall prevalences of MetS were 25.1% (38.9% in men *vs* 21.1% in women, p-<0.001), 21.1% (31.7% in men *vs* 18.1% in women, p<0.001) and 18.2% (25.2% in men *vs* 16.2% in women, p<0.001) using a BMI ≥ 23 kg/m^2, BMI ≥ 25 kg/m^2 and a WC to classify abdominal obesity, respectively. The highest prevalences of MetS were seen in participants with DM, HT, current smokers, and participants with a high sCr. However, no significant differences were seen in the prevalences of MetS in regard to physical activity, depression or family history of HT or dyslipidemia (Table 1).

The various characteristics studied in women and men and their association with UA quartiles are shown in Table 2. A higher prevalence of MetS was significantly related to the higher quartiles of UA in both men and women (p<0.001). The mean UA level was 4.9±1.3 mg/dl. The mean UA level was significantly higher in men than women (6.2±1.3 mg/dl in men *vs* 4.6±1.0 mg/dl in women, p<0.001). Participants with higher UA quartiles had significantly higher BMI, WC, SBP, DBP and serum TG levels (p<0.005) and significantly lower HDL-C levels in both genders (p<0.001). Among men, there were no significant associations between age (p=0.717), FPG (p=0.366) or total cholesterol level (p=0.572) and UA quartiles.

Associations between UA levels and MetS are shown in Table 3. Multivariable logistic regression analysis was used to quantify the strength of the association between the UA quartile and MetS by

Table 1
Prevalence of metabolic syndrome (MetS) among study participants.

Characteristics	No. of subjects	Prevalence of metabolic syndrome		
		BMI ≥ 23[a]	BMI ≥ 25[b]	WC[c]
		Cases (%)	Cases (%)	Cases (%)
Age (years)				
35-45	1,357	232 (17.1)	196 (14.4)	158 (11.6)
46-60	1,447	471 (32.6)	397 (27.4)	353 (24.4)
Gender				
Men	628	244 (38.9)	199 (31.7)	158 (25.2)
Women	2,176	459 (21.1)	394 (18.1)	353 (16.2)
Smoking status				
Never smoker	2,516	586 (23.3)	492 (19.6)	430 (17.1)
Former smoker	155	59 (38.1)	48 (31.0)	40 (25.8)
Current smoker	111	50 (45.0)	46 (41.4)	36 (32.4)
Regular physical activity				
Yes	913	237 (26.0)[e]	190 (20.8)[e]	162 (17.7)[e]
No	1,867	460 (24.6)	398 (21.3)	347 (18.6)
Medical history				
Diabetes mellitus				
Yes	124	89 (71.8)	82 (66.1)	76 (61.3)
No	2,680	614 (22.9)	511 (19.1)	435 (16.2)
Hypertension				
Yes	410	238 (58.0)	218 (53.2)	197 (48.1)
No	2,389	461 (19.3)	371 (15.5)	311 (13.0)
Dyslipidemia				
Yes	1,037	346 (33.4)	302 (29.1)	258 (24.9)
No	1,755	353 (20.1)	287 (16.4)	252 (14.4)
Family history				
Diabetes mellitus				
Yes	1,070	323 (30.2)	272 (25.4)	237 (22.2)
No	1,729	377 (21.8)	318 (18.4)	272 (15.7)
Hypertension				
Yes	1,573	405 (25.7)[e]	346 (22.0)[e]	295 (18.8)[e]
No	1,228	297 (24.2)	247 (20.1)	216 (17.6)
Dyslipidemia				
Yes	1,211	284 (23.5)[e]	247 (20.4)[e]	208 (17.2)[e]
No	1,570	411 (26.2)	339 (21.6)	298 (19.0)
Depression status				
No depressionn	2,650	659 (24.9)[e]	552 (20.8)[e]	478 (18.0)[e]
Yes, no antidepressant	93	26 (28.0)	25 (26.9)	22 (23.7)
Yes, antidepressant	59	17 (28.0)	15 (25.4)	11 (18.6)
Serum creatinine[d]				
Normal	2,744	674 (24.6)	569 (20.7)	492 (17.9)
High	59	29 (49.2)	24 (40.7)	19 (32.2)

[a]The overall prevalence of MetS when a BMI ≥23 kg/m^2 defined abdominal obesity.
[b]The overall prevalence of MetS when a BMI ≥25 kg/m^2 defined abdominal obesity.
[c]The overall prevalence of MetS when WC defined abdominal obesity.
[d]Elevated serum creatinine was defined as >1.2 mg/dl in men and >1.0 mg/dl in women.
[e]p-value > 0.05 (χ^2 test for the difference between MetS and non-MetS group).

Table 2
Characteristics of study participants according to uric acid level quartile.

Characteristics	Quartile of serum uric acid				*p*-value
	Q1	Q2	Q3	Q4	
Men					
Uric acid range (mg/dl)	≤ 5.2	5.3-6.1	6.2-7.0	>7.0	
No. of subjects	160	161	159	148	
Age (years; mean ± SD)	46.4 ± 7.1	46.2 ± 6.9	46.0 ± 6.5	46.9 ± 7.5	0.717
Current smoker (%)	10.0	20.5	16.9	16.4	0.150
Physical activity (%)	43.1	44.0	38.6	46.9	0.526
BMI (kg/m^2; mean ± SD)	23.5 ± 3.1	25.0 ± 3.8	25.1 ± 3.2	26.5 ± 3.7	<0.001
WC (cm; mean ± SD)	82.3 ± 9.0	85.6 ± 9.7	85.6 ± 8.3	89.4 ± 9.2	<0.001
SBP (mm Hg; mean ± SD)	123.1 ± 13.9	126.3 ± 15.3	127.7 ± 14.8	129.8 ± 15.4	0.001
DBP (mm Hg; mean ± SD)	78.9 ± 9.7	80.0 ± 10.4	81.5 ± 9.9	83.5 ± 10.2	0.001
FPG (mg/dl; mean ± SD)	99.2 ± 35.3	95.8 ± 26.5	94.4 ± 20.5	95.4 ± 23.0	0.366
TC (mg/dl; mean ± SD)	209.4 ± 38.1	212.1 ± 37.9	213.2 ± 39.6	215.5 ± 38.6	0.572
HDL-C (mg/dl; mean ± SD)	54.5 ± 12.9	49.5 ± 11.0	48.7 ± 12.3	48.7 ± 11.4	<0.001
TG (mg/dl; mean ± SD)	118.4 ± 64.5	139.1 ± 109.9	157.5 ± 112.6	173.2 ± 103.4	<0.001
MetS ; BMI ≥ 23[a] (%)	23.1	35.4	43.4	54.7	<0.001
MetS ; BMI ≥ 25[b] (%)	18.1	26.7	36.5	46.6	<0.001
MetS ; WC[c] (%)	18.1	21.7	24.5	37.2	0.001
Women					
Uric acid range (mg/dl)	≤3.9	4.0-4.5	4.6-5.2	>5.2	
No. of subjects	618	554	501	503	
Age (years; mean ± SD)	44.6 ± 6.5	45.1 ± 6.9	46.5 ± 7.2	47.8 ± 7.1	<0.001
Current smoker (%)	0.5	0.2	0.6	1.0	0.090
Physical activity (%)	27.9	30.9	31.1	30.1	0.629
BMI (kg/m^2; mean ± SD)	22.4 ± 3.2	23.0 ± 3.5	24.1 ± 3.8	26.1 ± 4.5	<0.001
WC (cm; mean ± SD)	72.1 ± 7.4	73.4 ± 8.2	76.1 ± 9.1	80.6 ± 10.2	<0.001
SBP (mm Hg; mean ± SD)	114.1 ± 13.6	116.1 ± 13.4	118.5 ± 13.8	124.3 ± 16.5	<0.001
DBP (mm Hg; mean ± SD)	73.2 ± 9.5	74.7 ± 9.6	76.1 ± 9.4	79.7 ± 10.4	<0.001
FPG (mg/dl; mean ± SD)	88.3 ± 19.5	87.8 ± 13.4	91.3 ± 20.1	94.6 ± 19.2	<0.001
TC (mg/dl; mean ± SD)	208.1 ± 35.9	208.6 ± 35.4	208.8 ± 35.0	217.2 ± 39.5	<0.001
HDL-C (mg/dl; mean ± SD)	66.3 ± 15.3	64.2 ± 15.7	60.3 ± 15.2	56.8 ± 14.1	<0.001
TG (mg/dl; mean ± SD)	81.7 ± 43.5	93.0 ± 46.4	103.8 ± 56.1	128.4 ± 66.4	<0.001
MetS; BMI ≥ 23[a] (%)	9.2	14.3	21.8	42.5	<0.001
MetS; BMI ≥ 25[b] (%)	6.5	12.3	19.4	37.6	<0.001
MetS; WC[c] (%)	5.7	9.6	17.4	35.4	<0.001

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; and TG, triglycerides.

[a]The prevalence of MetS when a BMI ≥ 23 kg/m^2 defined abdominal obesity.

[b]The prevalence of MetS when a BMI ≥ 25 kg/m^2 defined abdominal obesity.

[c]The prevalence of MetS when WC defined abdominal obesity.

Table 3
Multivariable analysis results for uric acid level and MetS association.

Uric acid levels (mg/dl)	Crude OR (95% CI)	*p* for trend	aOR[a] (95% CI)	*p* for trend
Model 1				
Men				
≤ 5.2	1.00 (reference)	<0.001	1.00 (reference)	<0.001
5.3-6.1	1.82 (1.12-2.97)		1.85 (1.12-3.06)	
6.2-7.0	2.55 (1.57-4.13)		2.56 (1.56-4.22)	
> 7.0	4.02 (2.46-6.56)		3.86 (2.33-6.41)	
Women				
≤ 3.9	1.00 (reference)	<0.001	1.00 (reference)	<0.001
4.0-4.5	1.64 (1.14-2.35)		1.57 (1.10-2.27)	
4.6-5.2	2.74 (1.94-3.87)		2.48 (1.75-3.53)	
> 5.2	7.29 (5.27-10.08)		6.46 (4.64-8.99)	
Model 2				
Men				
≤ 5.2	1.00 (reference)	<0.001	1.00 (reference)	<0.001
5.3-6.1	1.65 (0.97-2.83)		1.62 (0.94-2.80)	
6.2-7.0	2.59 (1.55-4.35)		2.59 (1.53-4.41)	
> 7.0	3.95 (2.36-6.61)		3.85 (2.23-6.50)	
Women				
≤ 3.9	1.00 (reference)	<0.001	1.00 (reference)	<0.001
4.0-4.5	2.02 (1.34-3.04)		1.95 (1.29-2.94)	
4.6-5.2	3.47 (2.35-5.12)		3.15 (2.12-4.68)	
> 5.2	8.70 (6.02-12.56)		7.73 (5.32-11.23)	
Model 3				
Men				
≤ 5.2	1.00 (reference)	<0.001	1.00 (reference)	<0.001
5.3-6.1	1.25 (0.72-2.17)		1.25 (0.71-2.21)	
6.2-7.0	1.47 (0.85-2.52)		1.48 (0.85-2.59)	
> 7.0	2.67 (1.58-4.50)		2.77 (1.60-4.79)	
Women				
≤ 3.9	1.00 (reference)	<0.001	1.00 (reference)	<0.001
4.0-4.5	1.76 (1.13-2.75)		1.69 (1.08-2.66)	
4.6-5.2	3.50 (2.32-5.29)		3.25 (2.14-4.93)	
> 5.2	9.12 (6.20-13.43)		8.04 (5.43-11.91)	

[a]aOR = adjusted for age, smoking status, regular activity, depression status, and serum creatinine.
Model 1: BMI ≥23 kg/m^2 defined abdominal obesity.
Model 2: BMI ≥25 kg/m^2 defined abdominal obesity.
Model 3: WC defined abdominal obesity.

gender. After adjusting for potential confounders, UA levels were significantly associated with increasing prevalence of MetS (p <0.001). The association was stronger in women than men. The adjusted odds ratio (aOR) for the association between MetS and the UA fourth quartile compared with the first quartile was 2.77 times (95% CI 1.60-4.79) in men and 8.04 times (95% CI 5.43-11.91) in women.

Since some antihypertensive drugs can affect UA concentration, we also reanalyzed the data by excluding participants with a history of antihypertensive drug

use. The results were similar but with slightly lower magnitudes of odds ratios (OR) (results not shown). We report only the analysis with all participants.

DISCUSSION

In the present study the prevalence of MetS was higher than previous reports for Thailand (Lohsoonthorn *et al*, 2007; Pongchaiyakul *et al*, 2007). This was partly due to a difference in the FPG cut-off point (Lohsoonthorn *et al*, 2007) and the BMI cut-off levels used to define abdominal obesity which differed between men and women, as ≥27 kg/m^2 and ≥25 kg/m^2, respectively (Pongchaiyakul *et al*, 2007). However the overall prevalence of MetS in our study was lower than the prevalence reported by the fourth national health examination survey (18.2% *vs* 23.2%) using similar difinitions. That study reported the prevalence of MetS was higher among Thai women than Thai men (26.8% *vs* 19.5%) (Aekplakorn *et al*, 2011).

MetS was more prevalent among men than women and the prevalence increased with aged in our study, similar to findings in other populations (Ervin, 2006; Qiao, 2006; Kuzaya *et al*, 2007; Hwang *et al*, 2009; Moy and Bulgiba, 2010). Previous studies have found the prevalence of MetS was higher among men than women in Americans (35.1% *vs* 32.6%) (Ervin, 2009), Europeans (32.2% *vs* 28.5%) (Qiao, 2006), Malaysian (54.7% *vs* 45.3%) (Moy and Bulgiba, 2010), Koreans (21.7% *vs* 11.4%) (Hwang *et al*, 2009), and Japanese (11.6% *vs* 4.0%) (Kuzuya *et al*, 2007). The above studies also show that MetS prevalence increase with age.

Our results suggest that UA concentration is associated with MetS, especially in women. This finding persisted even when excluding participants with a history of antihypertensive drug use. The UA level forth quartile was associated with a 6-8 times higher prevalence of MetS than the first quartile. We also found the components of MetS were significantly related to an elevated UA level and the association between MetS and UA levels was stronger in women than in men. The UA level was found to be associated with MetS using all three different measures of abdominal obesity. The finding that gender had an influence on the association between UA levels and MetS is supported by several studies (Choi and Ford, 2007; Ebrahimpour *et al*, 2008; Sui *et al*, 2008; Zhang *et al*, 2011).

A Chinese cohort study found an association between MetS and UA levels (Yang *et al*, 2012). In that study higher levels of UA were significantly associated with a higher BMI, WC, BP, TC, LDL-C, and serum TG levels in both men and women (p<0.001) (Liu *et al*, 2010; Yang *et al*, 2012). A cohort study also showed hyperuricemia was a stronger predictor MetS in women than men (Sui *et al*, 2008). Among women, the risk for MetS is at least two times higher when the serum UA≥4.6 mg/dl (Sui *et al*, 2008). Another study among adults reported the prevalence of MetS was significantly higher among those with an elevated UA level in both genders but especially in women (Ebrahimpour *et al*, 2008). Choi and Ford (2007) found 70% of US adults with MetS had hyperuricemia; this was true for both genders, but more common among women than men, especially among those with UA levels ≥6 mg/dl. However, Zhang *et al* (2011) found the prevalence of high UA levels was more common among men than women, but UA levels were more related to MetS among women than among men. After adjusting for BMI, young women (≤44 years old) with a high UA level had a three times

greater risk of developing MetS than those with a normal UA.

Some studies found no effect of gender on the association between UA and MetS. In a study from Taipei, Taiwan among 393 men aged 45-60 years, hyperuricemia was not associated with MetS (Liou *et al*, 2006). Lim *et al* (2010) found, after adjusting for age, smoking status, total cholesterol (TC), and creatinine, there was no significant effect of gender on UA and MetS. These results may be due to differences in study subjects, variations in UA cut-of points and difference in potential confounders.

Two mechanisms have been proposed to explain the association between hyperuricemia and MetS. The first mechanism, suggested by Fieg *et al* (2008) is related to the fact that glucose uptake in skeletal muscle depends in part on increases in blood flow mediated by insulin-stimulated release of nitric oxide from endothelial cells. Hyperuricemia can induce endothelial dysfunction by reducing nitric oxide production, resulting in decreased blood flow and impaired glucose uptake by skeletal muscle and resultant insulin resistance (Zoccali *et al*, 2006; Feig *et al*, 2008). The second mechanism, proposed by Sautin *et al* (2007) concerns the inflammatory and oxidative changes uric acid induces in adipocytes. Increased reactive oxygen species (ROS) secretion into peripheral blood from adipocytes involves induction of insulin resistance in skeletal muscle and adipose tissue, impaired insulin secretion by β cells, and the pathogenesis of various vascular diseases, such as atherosclerosis and hypertension.

Although the present study was carried out in a large number of participants, the results should be interpreted cautiously because of limitations. First, misclassification of MetS status may have occurred as the result of errors in WC measurement. However, this error tended to be non-differential and was biased toward the null. Second, in our study, women (77.6%) had a higher proportion than men (22.4%); the study population may differ from the general population. Third, the cross sectional nature of our study leaves uncertainty regarding the temporal sequence in the relationship between UA levels and MetS. Finally, participant dietary habits, frequency and duration of physical activity and other medications may have affects UA levels, these data were not obtained as a part of this study. These factors could confound the association between UA levels and MetS.

In conclusion, the overall prevalences of MetS were 25.1, 21.1, and 18.2% when BMI≥ 23 kg/m^2, BMI ≥25 kg/m^2 or WC were used to classify abdominal obesity, respectively. The prevalence of MetS increased with increasing age, UA levels and was more common among men than women. UA levels and MetS had a stronger association among women than men. UA levels are associated with the presence of MetS.

ACKNOWLEDGEMENTS

This project was supported by the Ratchadapisek Sompoj Fund of Chulalongkorn University, contract numbers CU-CLUSTER-Emerging H-41-101-53 and RD-47-53-30. We would like to thank the executives of the Thai Red Cross and Chulalongkorn University for their cooperation with data collection.

REFERENCES

Aekplakorn W, Kessomboon P, Sangthong R, *et al*. Urban and rural variation in cluster-

ing of metabolic syndrome components in the Thai population: results from the fourth National Health Examination Survey 2009. *BMC Public Health* 2011; 11: 2-9.

Alberti KG, Zimmer P, Shaw J, Grundy SM. The IDF consensus worldwide definition of the metabolic syndrome. Brussels: International Diabetes Federation, 2006: 1-23.

Alberti KG, Eckel RH, Grundy SM, *et al*. 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: 1640-5.

Anuurad E, Shiwaku K, Nogi A, *et al*. The new BMI criteria for Asians by the Regional Office for the Western Pacific Region of WHO are suitable for screening of overweight to prevent metabolic syndrome in elder Japanese workers. *J Occup Health* 2003; 45: 335-43.

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: 219-24.

Choi HK, Ford ES. Prevalence of the metabolic syndrome in individuals with hyperuricemia. *Am J Med* 2007; 120: 4 42-7.

Ebrahimpour P, Fakhrzadeh H, Heshmat R, Bandarian F, Larijani B. Serum uric acid levels and risk of metabolic syndrome in healthy adults. *Endocrine Pract* 2008; 14: 298-304.

Ervin RB. Prevalence of metabolic syndrome among adults 20 years of age and over, by sex, age, race and ethnicity, and body mass index: United States, 2003-2006. *Natl Health Stat Rep* 2009; 5: 1-7.

Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. *N Engl J Med* 2008; 359: 1811-21.

Gami AS, Witt BJ, Howard DE, *et al*. Metabolic syndrome and risk of incident cardiovascular events and death: A systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol* 2007; 49: 403-14.

Grundy SM. Metabolic syndrome pandemic. *Arterioscl Thromb Vasc Biol* 2008; 28: 629-36.

Heinig M, Johnson RJ. Role of uric acid in hypertension, renal disease, and metabolic syndrome. *Cleveland Clin J Med* 2006; 73: 1059-64.

Huang J, Jayakar J. Metabolic syndrome. *Spring* 2010; 79: 8-10.

Hwang YC, Jee JH, Oh EY, *et al*. Metabolic syndrome as a predictor of cardiovascular diseases and type 2 diabetes in Koreans. *Int J Cardiol* 2009; 134: 313-21.

Kuzuya M, Ando F, Iguchi A, Shimokata H. Age-specific change of prevalence of metabolic syndrome: Longitudinal observation of large Japanese cohort. *Atherosclerosis* 2007; 191: 305-12.

Lim JH, Kim YK, Kim YS, Na SH, Rhee MY, Lee MM. Relationship between serum uric acid levels, metabolic syndrome, and arterial stiffness in Korean. *Korean Circulat J* 2010; 40: 314-20.

Liou TL, Lin MW, Hsiao LC, *et al*. Is hyperuricemia another facet of the metabolic syndrome? *J Chin Med Assoc* 2006; 69: 104-9.

Liu PW, Chang TY, Chen JD. Serum uric acid and metabolic syndrome in Taiwanese adults. *Metab Clin Exp* 2010; 59: 802-7.

Lohsoonthorn V, Lertmaharit S, Williams MA. Prevalence of metabolic syndrome among professional and office workers in Bangkok, Thailand. *J Med Assoc Thai* 2007; 90: 1908-15.

Misra A, Khurana L. The metabolic syndrome in South Asians: Epidemiology, determinants, and prevention. *Metab Syndr Related Disord* 2009; 7: 497-514.

Mottillo S, Filion KB, Genest J, *et al*. The metabolic syndrome and cardiovascular risk: A systematic review and meta-analysis. *J Am Coll Cardiol* 2010; 56: 1113-32.

Moy FM, Bulgiba A. The modified NCEP ATP

III criteria may be better than the IDF criteria in diagnosing Metabolic Syndrome among Malays in Kuala Lumpur. *BMC Public Health* 2010; 10: 678-84.

Pongchaiyakul C, Nguyen TV, Wanothayaroj E, Krusun N, Klungboonkrong V. Prevalence of metabolic syndrome and its relationship to weight in the Thai population. *J Med Assoc Thai* 2007; 90: 459-67.

Qiao Q. Comparison of different definitions of the metabolic syndrome in relation to cardiovascular mortality in European men and women. *Diabetologia* 2006; 49: 2837-46.

Romaguera J, Ortiz P, Roca FJ, Colon G, Suarez E. Factors associated with metabolic syndrome in a sample of women in Puerto Rico. *J North Am Menop Soc* 2010; 17: 388-92.

Sarkar S, Das M, Mukhopadhyay B, Chakrabarti CS, Majumder PP. High prevalence of metabolic syndrome & its correlates in two tribal populations of India & the impact of urbanization. *Indian J Med Res* 2006; 123: 679-86.

Sautin YY, Nakagawa T, Zharikov S, Johnson RJ. Adverse effects of the classic antioxidant uric acid in adipocytes: NADPH oxidase-mediated oxidative/nitrosative stress. *Am J Physiol Cell Physiol* 2007; 293: C584-96.

Stern MP, Williams K, Gonz·lez-Villalpando C, Hunt KJ, Haffner SM. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? *Diabetes Care* 2004; 27: 2676-81.

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: 845-52.

Wang J, Ruotsalainen S, Moilanen, L, Lepisto P, Laakso M, Kuusisto J. The metabolic syndrome predicts cardiovascular mortality: a 13-year follow-up study in elderly non-diabetic Finns. *Eur Heart J* 2007; 28: 857-64.

Wang J, Thornton JC, Bari S, *et al*. Comparisons of waist circumferences measured at 4 sites. *Am J Clin Nutr* 2003; 77: 379-84.

WHO expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004; 363: 157-63.

Yang T, Chu CH, Bai CH, *et al*. Uric acid level as a risk marker for metabolic syndrome: A Chinese cohort study. *Atherosclerosis* 2012; 220: 525-31.

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: 777-87.

Zoccali C, Maio R, Mallamaci F, Sesti G, Perticone F. Uric acid and endothelial dysfunction in essential hypertension. *J Am Soc Nephrol* 2006; 17: 1466-71.