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Serum Uric Acid and Its Correlates in Chinese Adult Populations, Urban and Rural, of Beijing

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Background. Reports on serum uric acid (SUA) levels in Chinese populations are sparse, but there is evidence that hyperuricaemia and gout are not uncommon. This paper characterizes SUA levels, their correlates, and their relationship to blood pressure (BP) and prevalent high blood pressure (HBP) for urban and rural adult population samples in north China.

Methods. In 1987–1988, a cross-sectional study was carried out, using standardized methods, on men and women aged 40–58 in a Beijing area urban steel mill (N = 2013) and on rural farms (1507). Main outcome measures were SUA, systolic and diastolic blood pressure (SBP, DBP), and prevalent HBP (SBP ⩾ 140 or DBP ⩾ 90 mmHg or receiving an antihypertensive drug).

Results. Mean SUA levels for men were 5.75 mg/dl in urban and 5.58 mg/dl in rural settings; for women, 4.67 and 4.48 mg/dl. Mean values were higher with age in women, but not in men. Age-standardized prevalence rates of HBP were significantly higher in upper SUA strata (men ⩾7.00, women ⩾6.00 mg/dl) than lower SUA strata both with and without inclusion of those on antihypertensive drugs. Mean SUA levels were correspondingly higher in hypertensive than non-hypertensive people. In multiple regression analyses, body mass index and serum triglycerides were strongly associated with SUA. Also SBP, DBP, and HBP were generally associated with SUA for the whole population sample, with smaller coefficients after excluding those on antihypertensive drugs. However, in these multivariate analyses the strength of the association was low order.

Conclusion. In addition to its strong association with body mass index, SUA is independently related to serum lipids, particularly triglycerides, and to serum glucose. While some of the univariate relation of SUA to BP is apparently due to the strong relation of body mass to both SUA and BP, a low order significant relation between SUA and BP remains with control for BMI.

Keywords: serum uric acid, China, CVD risk factors

In clinical and epidemiological studies, serum uric acid (SUA) has been found to be related not only to risk of gout, but also to risk of hypertension, coronary heart disease, and diabetes mellitus. However, the role of SUA in the pathogenesis of these latter diseases is still unclear.[1–5] Characteristics and determinants of SUA distribution in populations of several countries have been described. Results suggest that SUA levels are affected by both genetic and environmental factors and related to such biological factors as gender, age, and body mass.[1,3,5–9] Reports of studies on SUA levels and their related factors in Chinese populations are scarce, but there is evidence that cases of hyperuricaemia and gout are not uncommon.[10,11]

The People's Republic of China-United States (PRC-USA) Collaborative Study of Cardiovascular and Cardiopulmonary Epidemiology was initiated in 1981 under the PRC-USA Governmental Cooperation in Science and Technology. Implemented through the Cardiovascular Institute of the Chinese Academy of Medical Sciences and Fu Wai Hospital, Beijing and Guangdong Provincial Cardiovascular Institute, Guangzhou in the PRC and the National Heart, Lung, and

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Blood Institute in the USA, this joint research study focuses on cross-sectional and prospective studies of four PRC population samples. These four were identified from urban and rural populations in, or close to, Beijing in the north and Guangzhou in the south. Selection of these sites was based on previously observed north-south differences in prevalence of major cardiovascular risk factors, particularly blood pressure.

A baseline survey, including data collection on risk factors for the major cardiovascular and cardiopulmonary diseases, was completed during the fall of 1983–1984. Follow-up resurveys were done first in 1987–1988 and again in 1993–1994. In addition, follow-up for morbid and mortal events was initiated in 1987–1988.

Objectives of this report are to describe levels of SUA in the northern Chinese population samples as measured during the second survey in 1987–1988 and to assess correlates of SUA levels, especially blood pressure and other cardiovascular disease (CVD) risk factors. Guangzhou samples are not included because of incompleteness of SUA quality control data.

POPULATION SAMPLES AND METHODS

Population Samples

The four population samples were 'cluster' samples of urban and rural populations in the Beijing area, including 3520 men and women aged 40–58 years. The urban sample was drawn from the Capital Iron and Steel Complex of Beijing, and the rural sample from the Shijingshan Agricultural District in a Beijing suburb. Individuals recruited were mainly workers and farmers; few people with other occupations were included.

Serum uric acid concentrations and other related variables were measured at second survey (1987–1988) of the cohort originally examined in 1983–1984.[12]

Biochemical and Other Methods

Fasting blood specimens were collected for measurement of serum total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), triglycerides (TG), glucose, and SUA. After blood was drawn, specimens were allowed to clot at room temperature for 1 to 3 h and serum was separated. Serum was frozen at –20°C and determination of SUA was done within 6 months. All biochemical assays were performed on an Abbott autoanalyzer.

The SUA was determined in a single laboratory in Beijing by the uricase method with Abbott uric acid enzymatic reagent kits. Commercial lyophilyzed serum samples were used for internal quality control. The monthly coefficient of variation (CV, %) of measurement averaged 4.2% and 2.2% during 1987 and 1988 respectively. Serum glucose was determined using enzymatic reagent kits and calibration with Gilford Optimate standards.

The laboratory was standardized for TC, TG, and HDL-C by the Lipid Standardization Program of the US National Heart, Lung, and Blood Institute and Centers for Disease Control. Serum TC was measured with the Boehringer-Mannheim Diagnostic (BMD) high-performance enzymatic reagent and calibrated with BMD Preciset standards. Serum HDL-C was measured by the same enzymatic serum cholesterol method after precipitation of other lipoprotein fractions with dextran sulfate (MW 50 000)–Mg++. Serum TG was determined with use of an enzymatic reagent from Abbott Laboratories; total and free glycerols were assayed separately and then TG values were obtained by subtracting free glycerol from total glycerol. Low density lipoprotein (LDL-C) was estimated according to the formula, LDL-C = TC – HDL-C – (TG/5), when TG was $<$400 mg/dl.

Physical examinations, including measurement of height, weight, and blood pressure, were performed following the same protocol in urban and rural populations. Smoking, alcohol intake, and antihypertensive medication status were determined using standard questionnaires. The participant was classified as a smoker if he/she was currently smoking at least one cigarette per day. When leaf tobacco was smoked, cigarette equivalents were calculated as 1 g of tobacco per commercial cigarette. A participant was classified as 'drinker' if a yes was given to the question, 'During the past year, have you drunk beer or any other alcoholic beverage?' Alcohol intake was calculated by converting the alcohol consumption of the past week into grams per day. Antihypertensive medication was determined by the question, 'Have you taken antihypertensive drugs in the last two weeks?' Methods of this study have been reported in detail.[12]

Statistical Methods

Analysis of covariance was employed to compare mean SUA levels among groups (urban and rural, men and women) with adjustment for age. Age-adjusted prevalence rates of hypertension were calculated according to levels of dichotomized SUA (cut points 7.00 and 6.00 mg/dl for men and women respectively). Relationships of SUA to blood pressure (BP) and high blood pressure (HBP) were analysed with and without inclusion of those reporting use of antihypertensive medication in the last 2 weeks.

Relationship between SUA and several variables was evaluated separately for men and women, first by univariate and then by multivariate analysis. A simple correlation technique was used for univariate assessment.

TABLE 1 *Serum uric acid levels (mg/dl) by gender, age, and setting, Beijing participants, 1987–1988*

Setting	Age	Men			Women		
		N	Mean	SD	N	Mean	SD
Urban	40–44	163	5.69	1.30	111	4.37	0.92
	45–49	325	5.72	1.34	282	4.48	1.04
	50–54	296	5.66	1.29	329	4.75	0.99
	55–58	278	5.90	1.27	229	4.92	1.03
	Total	1062	5.75	1.30	951	4.67	1.02
	Age-adjusted mean[a]		5.75*			4.60	
Rural	40–44	115	5.56	1.16	352	4.30	1.04
	45–49	103	5.35	1.30	279	4.33	0.94
	50–54	180	5.64	1.46	193	4.68	1.27
	55–58	160	5.68	1.19	125	5.01	1.36
	Total	558	5.58	1.30	949	4.48	1.14
	Age-adjusted mean		5.58			4.55	

[a] Age-adjusted by analysis of covariance.
* Significantly different ($P < 0.05$) between urban and rural settings.

For multivariable analysis, multiple linear regression was performed separately for men and women, for the whole population sample and after exclusion of people on antihypertensive medication during the last 2 weeks. The independent variables included in the multiple regression model were setting (urban/rural), age, BMI, TG, TC, HDL-C, glucose, cigarette use (0 = no, 1 = yes), alcohol use (0 = no, 1 = yes) and SBP or DBP. Analyses were done separately for SBP and DBP. Regression results were summarized by presenting estimated difference associated with a one standard deviation difference for each continuous variable and with dichotomization (no/yes = 0/1) of cigarette and alcohol use.

RESULTS

SUA by Age, Gender, and Setting

Table 1 shows the number of participants and their mean SUA levels by age for each of the four gender-setting subgroups. Levels of SUA were significantly higher in the urban than rural setting for men but not for women. Age-adjusted mean SUA was 5.75 mg/dl for urban men and 5.58 mg/dl for rural men; 4.60 and 4.55 mg/dl for urban and rural women. Within the age range of 40–58 years, SUA was higher stepwise with age in women but not in men. After exclusion of 285 antihypertensive medication users, mean SUA values were slightly lower (data not shown).

Frequency Distribution of SUA by Gender and Setting

Frequency distribution histograms of SUA are shown for all urban and rural men and women in Figure 1. Skewness to the right was observed for all four gender-setting subgroups.

Prevalence of Hyperuricaemia

The criteria used for hyperuricaemia, $\geqslant$7.0 mg/dl for men and $\geqslant$6.0 mg/dl for women, are those commonly adopted in population studies. Prevalence rates of hyperuricaemia were 15.4% for urban men, 11.3% for rural men, 11.0% for urban women, and 8.4% for rural women.

Other Variables

Means or per cents for other variables by gender and setting are shown in Table 2. For both men and women, mean body mass index (BMI, kg/m^2), serum TC, and LDL-C values were higher in urban than in rural participants. Urban women had the highest mean BMI of 25.0 kg/m^2 and rural men had the lowest mean of 23.0 kg/m^2. For the four subgroups, mean serum TC ranged from 174 mg/dl in rural men to 188 mg/dl in urban women. Mean serum HDL-C was about 50 mg/dl in men and 2–3 mg higher in women, with similar urban-rural values. Blood pressure levels were higher in men than women with small urban-rural differences. Cigarette smoking was reported in 64–65% of men and 19–26% of women. Similarly, prevalence of alcohol

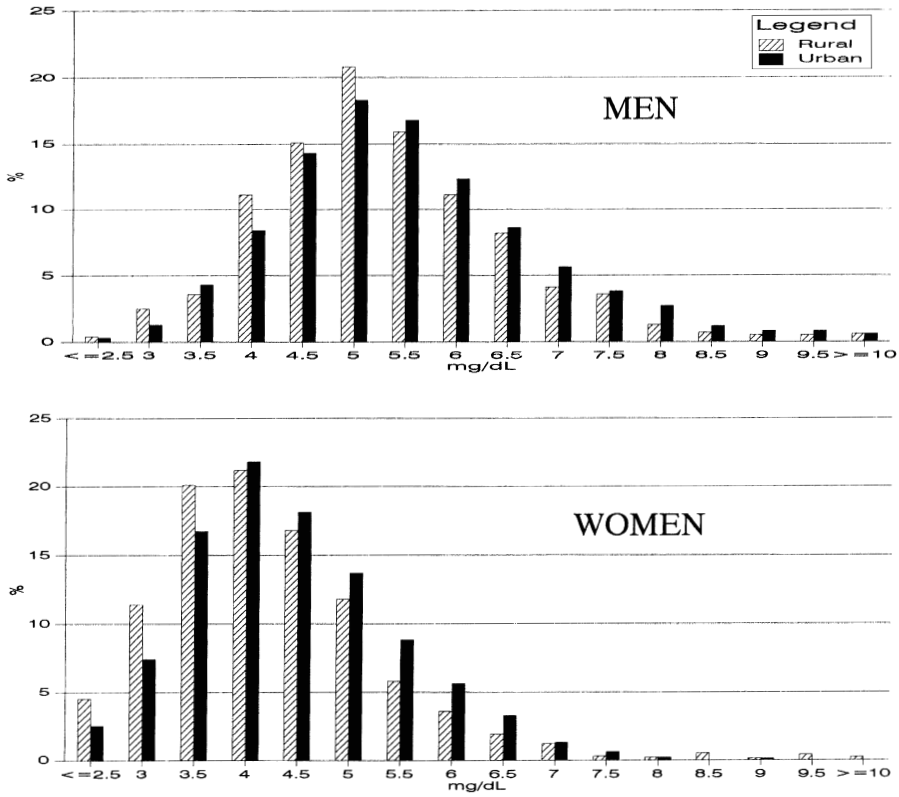

FIGURE 1 *Distribution of serum uric acid (mg/dl) by gender and setting (rural, urban)*

drinking was relatively high in men (58–69%) and low in women (11–12%). Use of antihypertensive medication was reported by 9–11% of the urban and 5% of the rural population, with little or no gender difference.

Simple Correlation Analyses

Simple correlation analyses, done separately for the four subgroups, yielded similar results for urban and rural setting. Analyses were therefore done for all men and all women (Table 3). Age, BMI, SBP, DBP, serum TC, TG, and LDL-C showed statistically significant positive correlations with SUA in both men and women. Glucose was significantly correlated with SUA in women. There was a significant inverse correlation of HDL-C and SUA in men and women. Cigarette smoking was inversely associated with SUA in men. In analyses excluding users of antihypertensive medication, correlations of variables with SUA remained at the same levels of significance, with reduction in size of coefficients for SUA and blood pressure (data not shown).

Hyperuricaemia and Prevalence of Hypertension

For hypertension, two sets of criteria were used: (i) SBP $\geqslant$140 or DBP $\geqslant$90 mmHg or use of antihypertensive medication in the last 2 weeks; (ii) SBP $\geqslant$160 or DBP $\geqslant$95 or use of antihypertensive medication in the last 2 weeks. For all four gender-setting groups, age-adjusted prevalence rates of hypertension were higher in higher SUA than in lower SUA groups (Table 4). As expected, when antihypertensive medication users were excluded, prevalence rates of hypertension became lower, but differences in rates remained between the two SUA strata (data not shown). Correspondingly, in age-gender-specific analyses, mean levels of SUA were higher in hypertensives than nonhypertensives, including untreated hypertensives compared to non-hypertensives (data not shown).

Multiple Regression Analyses

The results of multiple linear regression analysis are summarized in Table 5 showing estimated difference in SUA for one standard deviation difference in several

TABLE 2 *Means or per cents for other variables by gender and setting*

Variable	Men		Women	
	Urban	Rural	Urban	Rural
Age (years)	50.2	50.4	50.5	47.4
BMI (kg/m^2)	24.3	23.0	25.0	23.6
SBP (mmHg)	129.1	129.5	127.2	125.3
DBP (mmHg)	84.4	85.1	78.9	80.2
TC (mg/dl)	179.0	174.2	188.4	176.0
TG (mg/dl)	106.8	120.4	119.4	112.1
HDL-C (mg/dl)	50.3	49.6	53.7	52.4
LDL-C (mg/dl)	107.4	101.3	111.1	101.3
Glucose (mg/dl)	87.9	85.7	92.3	85.4
Smoker (%)	64.9	64.0	19.3	26.2
Cigarettes/day				
for all	9.7	9.9	1.4	2.2
for smokers	14.9	15.5	7.2	8.3
Drinker (%)	58.2	68.8	11.5	11.0
Alcohol (g/day)				
for all	16.4	32.5	0.7	1.1
for drinkers	28.2	47.3	5.8	10.3
Antihypertensive				
medication (%)	11.3	4.8	9.7	4.8

BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = serum total cholesterol, TG = triglycerides, LDL-C = low density lipoprotein cholesterol, HDL-C = high density lipoprotein cholesterol.

TABLE 3 *Simple Pearson correlation coefficients of several variables with serum uric acid, by gender*

Variable	Men		Women	
	r		r	
Age (years)	0.05	*	0.22	***
BMI (kg/m^2)	0.30	***	0.26	***
SBP (mmHg)	0.18	***	0.19	***
DBP (mmHg)	0.21	***	0.17	***
TC (mg/dl)	0.14	***	0.17	***
TG (mg/dl)	0.22	***	0.26	***
HDL-C (mg/dl)	–0.10	***	–0.16	***
LDL-C (mg/dl)	0.11	***	0.13	***
Glucose (mg/dl)	–0.02	NS	0.05	*
Cigarettes/day for all	-0.08	**	0.04	NS
Alcohol (g/day) for all	0.03	NS	-0.02	NS

BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = serum total cholesterol, TG = triglycerides, LDL-C = low density lipoprotein cholesterol, HDL-C = high density lipoprotein cholesterol.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, NS $P \geqslant 0.05$.

continuous variables including SBP. Cigarette and alcohol use were taken as dichotomous (no/yes = 0/1) variables as was setting (urban = 0/rural = 1). Age was significantly positively related to SUA in women but not in men. The BMI and serum TG showed strong positive associations with SUA for both genders for the whole population sample and after exclusion of antihypertensive medication use. Serum TC was positively and HDL-C negatively associated with SUA for both men and women, significantly so in women. There was an inverse association between serum glucose and SUA which was statistically significant for men. Cigarette use by men was inversely related to SUA. The SBP was significantly related to SUA in both genders for the whole population sample and after exclusion of antihypertensive medication users.

Multiple regression analyses were done in a similar way with inclusion in the independent variables of DBP instead of SBP (data not shown). In this DBP

TABLE 4 *Age standardized[a] prevalence (%) of hypertension[b] by level of serum uric acid (SUA) and gender*

Setting	SUA (mg/dl)	N	Men				SUA (mg/dl)	N	Women			
			BP ⩾ 140/90 (mmHg)		BP ⩾ 160/95 (mmHg)				BP ⩾ 140/90 (mmHg)		BP ⩾ 160/95 (mmHg)	
			n	%	n	%			n	%	n	%
Urban	<7	898	323	34.1	158	17.4	<6	846	217	23.8	114	11.9
	⩾7	164	79	49.2	55	35.5	⩾6	105	45	38.2	22	14.8
Rural	<7	495	160	30.7	89	17.1	<6	869	203	25.2	103	12.5
	⩾7	63	35	53.0	23	33.4	⩾6	80	30	37.7	21	26.6

[a]Age-standardized to WHO standard population.
[b] According to two sets of BP criteria: (i) SBP ⩾ 140 or DBP ⩾ 90 or antihypertensive drug treatment in the last 2 weeks; (ii) SBP ⩾ 160 or DBP ⩾ 95 or antihypertensive drug treatment in the last 2 weeks.

TABLE 5 *Estimated difference[a] in serum uric acid (SUA) (in mg/dl) for one standard deviation difference in several continuous variables, including systolic blood pressure (SBP), and for cigarette and alcohol use as dichotomous (no,yes) variables, by gender—multiple linear regression analyses*

Independent variables (SD: Men, Women)	Men (N = 1620)	Women (N = 1900)
Setting (Urban = 0, Rural = 1)	–0.130	0.008
Age (years) (5.1, 5.1)	0.033	0.173 ***
BMI (kg/m^2) (3.2, 3.8)	0.281 ***	0.195 ***
TG (mg/dl) (71.6, 70.7)	0.190 ***	0.151 ***
TC (mg/dl) (32.7, 35.0)	0.059	0.074 **
HDL-C (mg/dl) (11.6, 11.6)	–0.012	–0.078 **
Glucose (mg/dl) (21.3, 28.0)	–0.086 **	–0.033
Cigarette/use (0 = No, 1 = Yes)	–0.182 **	0.079
Alcohol use (0 = No, 1 = Yes)	0.107	–0.096
SBP (mmHg) (20.1, 22.2)	0.090 **	0.055 *
R^2	0.13	0.15

BMI = body mass index, TG = triglycerides, TC = total cholesterol, HDL-C = high density lipoprotein cholesterol, DBP = diastolic blood pressure.

[a] Estimated difference was derived from multiple linear regression of SUA on several variables adjusted for setting (Urban = 0, Rural = 1), and computed by multiplying the regression coefficient times 1SD for each continuous variable and by 1.0 for cigarette and alcohol use.

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

was significantly related to SUA for both genders in the whole population sample and after exclusion of antihypertensive medication users. For all other variables the results were similar to those shown in Table 5.

In view of the inverse association between SUA and glucose in the above analyses, cross classification analyses were done for these two variables. They showed that SUA was lower in men and women with fasting serum glucose ⩾120 mg/dl, a finding reported by other investigators.[3,5,13] Therefore, the multiple regression analyses were repeated after exclusion of individuals with serum glucose ⩾120 mg/dl (62 men and 94 women). The result was a positive association between glucose and SUA for men and women, with regression coefficients of 0.071 ($P < 0.05$) and 0.079 ($P < 0.01$). Coefficients for other variables were similar to those in Table 5. Corresponding results were found when DBP was included in this further analysis instead of SBP.

To assess further relationships of SUA with BP and HBP, additional multiple regression analyses were done with SBP, DBP, and HBP as dependent variables. In these SUA was significantly related to SBP for men and women for the whole population, and for men and women combined for those not using antihypertensive drugs (data not shown). With SUA higher by 1 standard deviation (1.3 and 1.1 mg/dl for men and women respectively), SBP was higher by 1.3 and 1.1 mmHg; for those not receiving antihypertensive drugs, by 0.8 mmHg. Results were similar with DBP as the dependent variable. With prevalent HBP as the dependent variable (no, yes) in multiple logistic regression analyses, SUA was significantly related as independent variable, for men, and for men and women combined, without and with exclusion of people on antihypertensive drugs.

DISCUSSION

Interpopulation Differences in SUA

In this study mean SUA levels and prevalence of hyperuricaemia were found to be higher in urban than rural population samples of Beijing. The male to female ratio of mean SUA level was about 1.2; similar to findings of other studies.[6–8,14]

Mean SUA levels were higher than the mean of 4.4 ± 0.9 mg/dl for men and 3.4 ± 0.9 mg/dl for women reported in a previous study of middle-aged Chinese populations by Fang *et al.* in 1983.[11] This difference could be partly due to differences in the populations sampled. Participants in the previous study included men and women 20 years and older of various occupational groups among urban residents of Beijing and three cities in southern China. A difference in methods for SUA may also be a factor. Reported mean levels of SUA in US adult population samples also have varied from 5 to >6 mg/dl in men, about 1 mg/dl lower in women.[6,7,14–16] Unusually high values of 7.0–7.4 mg/d for men and 5.8–6.4 for women were reported by Prior[17] among Polynesians, who had high prevalence rates of obesity, diabetes, and gout. Cut points used for hyperuricaemia varied in different studies, limiting the ability to compare findings.[6,7,17–18]

Previous studies have indicated that SUA levels of individuals are affected by both genetic and environmental factors. In comparative epidemiological studies on Japanese men in Japan, Hawaii, and California, Kagan[19] reported that serum uric acid (as well as serum cholesterol, triglycerides, and glucose), were all significantly higher in Japanese immigrants to Hawaii and California than in Japanese living in Japan. As pointed out by Yano,[1] differences in the SUA levels between Japanese immigrants and indigenous population samples are attributable mainly to environmental changes since the genetic background of these Japanese population samples was essentially the same. As previously reported,[12] among the Beijing population samples under study, baseline levels of several CVD risk factors were higher for urban than rural samples, e.g. for BMI, DBP, prevalence rate of hypertension, serum TC for both men

and women, and TG for women. The patterns of the urban-rural differences in mean SUA levels and prevalence of hyperuricaemia conform with those found for these risk factors.

Relationship of Age and Sex to SUA

In 1965, Mikkelsen [7] described the differences in SUA levels with age for Americans, and found that in men SUA level became higher between 10 and 16 years of age and reached a peak at about 20, while in women, mean SUA level began to become higher at around age 50. In our study mean levels of SUA in men were about 1 mg/dl higher than those in women. For the age groups studied, in women age was highly significantly correlated with SUA in both univariate and multivariate analyses, while in men, a weak correlation was found only in univariate analyses. These findings are in accordance with the observations made by Mikkelsen[7] and by others on middle-aged people.[6,8] Sex differences in SUA were interpreted to be related to endocrine function. Mikkelsen pointed out that oestrogens may have a urate depressing action, as did Prior,[17] but Bengtson *et al.*[20] found no difference in SUA levels in women; pre- and post-menopausal.

Relationship of Other Variables to SUA

Body mass index. A consistent positive association between BMI and SUA was reported in several previous population studies.[1,5,8,10,13,17] Our data also indicate a strong association between BMI and SUA. In addition, a significant relationship between weight loss by diet or exercise and decrease in SUA was reported by Nicholls and Scott.[21] All these data indicate that BMI has an important influence on SUA level.

Alcohol consumption. The present study indicated an independent association between alcohol intake and SUA level, in accordance with other reports.[1,22]

Blood lipids. In summarizing published findings from population studies[14,23,24] on relationships between SUA and blood lipids, Yano[1] concluded that there was no significant correlation between SUA and serum total cholesterol (TC). However, unpublished data from several large studies show a low-order significant association independent of age and body mass index. Thus, for 2237 employed men aged 35–59 at baseline in the Chicago Peoples Gas Company Study, the partial correlation coefficient was 0.056 ($P = 0.008$). For 7898 employed men and 6872 employed women aged 35–59 at baseline in the Chicago Heart Association Detection Project in Industry (CHA) Study, partial r values were 0.090 ($P < 0.001$) and 0.066 ($P < 0.001$). For 12 851 men from 18 US cities, aged 35–57 at baseline when randomized into the Multiple Risk Factor Intervention Trial (MRFIT), partial 4 was 0.116 ($P < 0.001$); partial 4 values for SUA and other plasma lipids were 0.207 ($P < 0.001$) for triglycerides (TG) (hence also for VLDL-C), –0.035 for LDL-C, and –0.002 for HDL-C. For 2223 men aged 17–35 at baseline in the US national cooperative Coronary Artery Risk Development in Young Adults Study (CARDIA) partial r values for SUA and serum lipids were: TC 0.077 ($P < 0.001$); TG 0.204 ($P < 0.001$); LDL-C 0.051 ($P = 0.016$); HDL-C –0.103 ($P < 0.001$). For 2674 women aged 17–35 at baseline in the CARDIA Study, these partial r values were 0.033, 0.179 ($P < 0.001$), 0.026, and –0.082 ($P < 0.001$). These data from MRFIT and CARDIA on SUA and triglycerides are consistent with reported results showing a stronger association between SUA and TG than between SUA and TC, as was found also in the present study of northern Chinese adults aged 40–58. Possibly, from the data available here, the low-order SUA-TC association is attributable largely to the higher-order VLDL-C (TG) association. While overweight is known to be related to higher levels of both SUA and TG, all the significant correlations between SUA and serum lipids noted here were with control for body mass (as well as age), hence they are independent of overweight. Moreover, they are present in the Chinese cohorts reported on here, all of them on average lean. These findings pose intriguing questions concerning possible metabolic pathways and mechanisms accounting for these associations, and concerning possible interdigitating influences of SUA and lipids on long-term health and disease.

Blood glucose. The association of serum fasting glucose with SUA, tested in this study by both simple correlation and multiple linear regression analyses, was inverse in both men and women. To further evaluate this result we stratified SUA according to different glucose levels and found that SUA was progressively higher with higher glucose up to a level of 120 mg/dl. The relationship of glucose with SUA was positive in simple correlation and multiple linear regression analyses after excluding people having elevated glucose levels of $\geqslant$120 mg/dl. This result suggests that blood glucose is positively related to SUA in those without hyperglycaemia. This interpretation receives support from the finding of lower SUA with overt diabetes in several other studies.[3–5,7,13,14]

Relationship of SUA with Blood Pressure

Significant association of hyperuricaemia with BP and HBP has been reported in many clinical and epidemiological studies.[1,2,14,16,23,25] In multivariate analyses,

the relationship of SUA with blood pressure has been confirmed in most studies.[1,5,8,20,26] The issue of antihypertensive medication as a confounding factor of the relationship between SUA and hypertension has been noted in most of these studies. Yano[1] reported that there was a striking association between an increased level of SUA and hypertension, which persisted even after excluding men on medication. Shelby *et al.* demonstrated that SUA remained independently predictive of incident cases of hypertension after adjusting for known risk factors.[26] In Okada's report,[8] however, SBP and DBP were not selected in stepwise multiple linear regression analyses as variables related to SUA.

In the present study an association of high SUA with HBP was also observed. Multiple regression analyses showed that SBP and DBP were related significantly to SUA in both men and women but the relationship was weaker than in the univariate ones. This finding suggests that the relation of SUA to blood pressure may at least in part be explained by the strong relationship of BMI to both SUA and BP. This interpretation receives support from similar results of a cohort study on baseline SUA and incidence of hypertension in a Beijing population sample.[27]

The associations shown here between SUA and other variables, independent of BMI, pose intriguing questions as to metabolic interrelationships and factors possibly accounting for them, environmental (e.g. dietary) and genetic. They also pose questions as to their combined impact on long-term risks of cardiovascular and other chronic diseases. High SUA is hypothesized to be a component of the obesity-insulin resistance syndrome, implicated as associated with increased risk of coronary heart disease (CHD).[3,28] Long-term prospective studies have produced inconsistent findings as to whether SUA is an independent risk factor for CHD in men and women.[6,14–17,28–31] Evidence from a large Chicago prospective study indicates it is a significant independent risk factor for mortality from both cardiovascular and neoplastic disease in older women, especially older women with hypertension and/or diabetes.[16,29,30] A recent study reported SUA to be a predictor of mortality from all causes and from ischaemic heart disease among women.[32] In the present cross-sectional analysis of these northern Chinese data, prevalence rates of clinical gout, diabetes, and CHD were too low in both men and women to provide meaningful multivariate cross-sectional assessment of possible independent relationships of SUA and other traits to these diseases. However, the finding of strong positive association of BP and serum TG, and negative association of SUA with HDL-C, can be viewed as broadly concordant with the concept that high SUA is a risk factor for CHD.

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REFERENCES

[1] Yano K, Rhoads G G, Kagan A. Epidemiology of serum uric acid among 8000 Japanese-American men in Hawaii. *J Chron Dis* 1977; **30:** 171–84.

[2] Breckenridge A. Hypertension and hyperuricaemia. *Lancet* 1966; **i:** 15–18.

[3] Tuomilehto J, Zimmet P, Wolf E, Taylor R, Ram P, King H. Plasma uric acid level and its association with diabetes mellitus and some biological parameters in a biracial population of Fiji. *Am J Epidemiol* 1988; **127:** 321–36.

[4] Herman J B, Goldbourt U. Uric acid and diabetes: observations in population study. *Lancet* 1982; **ii:** 240–43.

[5] Goldbourt U, Medalie J H, Herman J B, Neufeld H N. Serum uric acid: correlation with biochemical, anthropometric, clinical and behavioral parameters in 10 000 Israeli men. *J Chron Dis* 1980; **33:** 435–43.

[6] Hall A P, Barry P E, Dawber T R, McNamara P M. Epidemiology of gout and hyperuricemia. A long term population study. *Am J Med* 1967; **42:** 27–37.

[7] Mikkelsen W M, Dodge H J, Valkenburg H. The distribution of serum uric acid values in a population unselected as to gout or hyperuricaemia, Tecumseh, Michigan 1959–1960. *Am J Med* 1965; **39:** 242–51.

[8] Okada M, Takeshita M, Ueda K, Omae T, Hirota Y. Factors influencing the serum uric acid level. A study based on a population survey in Hisayama town, Kyushu, Japan. *J Chron Dis* 1980; **33:** 607–12.

[9] Acheson R M, Chan Y K. New Haven survey of joint diseases. The prediction of serum uric acid in a general population. *J Chron Dis* 1969; **21:** 543–53.

[10] Meng S T, Yun K. A report of 44 cases with acute secondary gouty arthritis. *Chin J Intern Med* (In Chinese) 1981; **20:** 25–27.

[11] Fang Q, You K, Lin Q C *et al.* The level of uric acid in Chinese normal populations and the association with blood lipids. *Chin J Intern Med* (In Chinese) 1983; **22:** 434–38.

[12] People's Republic of China-United States Cardiovascular and Cardiopulmonary Epidemiology Research Group. An epidemiological study of cardiovascular and cardiopulmonary disease risk factors in four populations in the People's Republic of China. *Circulation* 1992; **85:** 1083–96.

[13] Mikkelsen W M. The possible association of hyperuricemia and/or gout with diabetes mellitus. *Arth Rheum* 1965; **8:** 853–59.

[14] Klein R, Klein B E, Cornoni J C, Maready J, Cassel J C, Tyroler H A. Serum uric acid: Its relationship to coronary heart disease risk factors and cardiovascular disease, Evans County, Georgia. *Arch Intern Med* 1973; **132:** 401–10.

[15] Brand F N, McGee D L, Kannel W B, Stokes J, Castelli W P. Hyperuricemia as a risk factor of coronary heart disease: The Framingham Study. *Am J Epidemiol* 1985; **121:** 11–18.

[16] Levine W, Dyer A R, Shekelle R B, Schoenberger J A, Stamler J. Serum uric acid and 11.5-year mortality of middle-aged women: Findings of the Chicago Heart Association Detection Project in Industry. *J Clin Epidemiol* 1989; **42:** 257–67.

[17] Prior I A M, Rose B S, Harvey H P B, Davidson F. Hyperuricaemia, gout and diabetic abnormality in Polynesian people. *Lancet* 1966; **i:** 333–38.

[18] Zalokar J, Lellouch J, Claude J R, Kuntz D. Serum uric acid in 23,922 men and gout in a subsample of 4257 men in France. *J Chron Dis* 1972; **25:** 305–12.

[19] Kagan A, Harris B R, Winkelstein W Jr *et al.* Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: demographic, physical, dietary and biochemical characteristics. *J Chron Dis* 1974; **27:** 345–64.

[20] Bengtson C, Tibblin E. Serum uric acid levels in women. An epidemiological survey with special reference to women with high serum uric acid values. *Acta Med Scand* 1974; **196:** 93–102.

[21] Nicholls A, Scott J T. Effect of weight-loss on plasma and urinary levels of uric acid. *Lancet* 1972; **ii:** 1223–24.

[22] Gordon T, Kannel W B. Drinking and its relation to smoking, blood pressure, blood lipids, and uric acid. The Framingham Study. *Arch Intern Med* 1983; **143:** 1366–74.

[23] Myers A R, Epstein F H, Dodge H J, Mikkelsen W M. The relationship of serum uric acid to risk factors in coronary heart disease. *Am J Med* 1968; **45:** 520–28.

[24] Hagerup L M. Coronary heart disease risk factors in men and women. From the population study in Glostrup, Denmark. *Acta Med Scand* 1974; **557 (Suppl.):** 1–116.

[25] Stamler J, Rhomberg P, Schoenberger J A *et al.* Multivariate analysis of the relationship of seven variables to blood pressure: Findings of the Chicago Heart Association Detection Project in Industry, 1967–1972. *J Chron Dis* 1975; **28:** 527–48.

[26] Selby J V, Friedman G D, Quesenberry C P. Precursors of essential hypertension: pulmonary function, heart rate, uric acid, serum cholesterol, and other serum chemistries. *Am J Epidemiol* 1990; **131:** 1017–27.

[27] Zhang H Y, Li Y, Wu X G, Tao S C, Warnick G, Stamler J. A prospective study of serum uric acid and incidence of high blood pressure. 3rd International Conference on Preventive Cardiology. Oslo, Norway, 27 June–1 July 1993.

[28] Lee J, Sparrow D, Vokonas P S, Landsberg L, Weiss S T. Uric acid and coronary heart disease risk: evidence for a role of uric acid in the obesity-insulin distance syndrome. The Normative Aging Study. *Am J Epidemiol* 1995; **142:** 288–94.

[29] Dyer A R, Stamler R, Stamler J, Garside D. Serum Uric Acid: 18-year cardiovascular mortality in the Chicago Heart Association Detection Project in Industry. In: Gotto A M Jr *et al.* (eds). *Multiple Risk Factors in Cardiovascular Disease.* Dordrecht Kleever Academic Publisher, 1995, pp. 365–372. Medical Science Symposia Series, Vol. 8.

[30] Dyer A R, Stamler R, Stamler J, Garside D. Serum uric acid and 21.5 year cardiovascular mortality in the Chicago Heart Association Detection Project in Industry. *Circulation* 1996; **93:** 626 (abstract).

[31] Defronzo R A, Ferrannini E. Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 1991; **14:** 173–94.

[32] Freedman D S, Williamson D F, Gunter E W, Byers T. Relation of serum uric acid to mortality and ischemic heart disease. The NHANES I Epidemiologic Follow-up Study. *Am J Epidemiol* 1995; **141:** 637–44.

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