Original Article

High prevalence of hyperuricemia in elderly Taiwanese

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Serum urate status, the prevalence of hyperuricemia and their relationship to the metabolic syndrome in elderly Taiwanese were described using data from the Elderly Nutrition and Health Survey in Taiwan (1999-2000), in which a stratified multi-stage clustered sampling scheme was applied. Complete data from biochemical assays and anthropometric measures for 1225 males and 1167 females were included in the analysis. The mean urate level and 95% confidence interval was 411 (398, 424) μM for males and 357 (347, 367) μM for females. Males had significantly higher serum urate levels than females across all age groups (P <0.05). No significant difference in mean serum urate was found among the four age groups of males. On the other hand, females of 75-79 years had significantly higher serum urate levels (376 μM) than that of the 65-69 and ≥ 80 age groups. The overall prevalence of hyperuricemia (≥ 416.7 μM (7.0 mg/dL) in the elderly was 36% (46% for males and 26% for females). Among the participants, 4.2% of males and 1.1% of females were taking medication to lower uric acid. The elderly (males 455 μM; females 416 μM) of the Mountain areas, mainly indigenes, had the highest mean serum urate overall, however, the highest prevalence of hyperuricemia in males was found in the PengHu islands (62%) and that for females in the Mountain areas (51%). The odds ratio (OR) for hyperuricemia was 2.84 for males in the PengHu islands and 4.33 for females in Mountain areas, compared with their counterparts in the third stratum in the northern areas. Adjusting for obesity, alcohol and other related covariates did not alter the relative rank of the ORs in the various strata. Elderly males (22%) had a significantly lower rate of metabolic syndrome (MS) than females (39%) (P <0.05). For both genders, those with MS had a significantly higher mean serum urate (males 436 μM vs. 405 μM; females 389 μM vs. 338 μM) and prevalence of hyperuricemia (males 56% vs. 43%; females 38% vs. 19%) (P <0.05). The population attributable risk for MS from hyperuricemia was 18.8% in men and 15.5% in women. In conclusion, the mean serum urate and prevalence of hyperuricemia in the elderly in Taiwan were higher than those found in other populations and was significantly associated with MS. Gene-environmental interaction may play a key role since great geo-graphical variation exists within various Han Chinese groups in Taiwan and between Han Chinese and Taiwanese indigenes.

Key Words: serum urate, hyperuricemia, metabolic syndrome (MS), elderly, indigenous, mountainous, Taiwan, Elderly Nutrition and Health Survey in Taiwan (1999-2000)

Introduction

The incidence of gout has been increasing in middle-aged and older people globally during the last two decades and has been related to modernization.[1-6] Hyperuricemia is considered to be the most significant risk factor for gout,[7,8] and may play a role in the development of many degenerative diseases.[9-17] The Kuopio Ischaemic Heart Disease Risk Factor Study,[16] the NHANES I Epidemiologic Follow-up Study,[18,19] and the SHEP study[9] demonstrated that serum urate was an independent predictor of cardiovascular events or mortality in middle-aged men and older persons. The ARIC study, however, did not reach the same conclusion.[20] Therefore, the issue of hyperuricemia as a CVD risk factor is still under debate. Metabolic syndrome (MS), a cluster of coronary heart disease risk factors, has been associated with total mortality, and cardiovascular morbidity and mortality among Westerners[21-23] and has been a topic of much interest in Asia in recent years.[24,25] In Taiwan, it has been observed that both the gender and age specific serum urate levels and prevalence of hyperuricemia are unusually high in both the general[26-29] and indigenous populations[30,31], compared to other ethnic groups and world regions.[2,14,15,32,33] It is unclear whether hyperuricemia increases with aging as does MS. Because previous studies have mostly focused on the middle-aged population[14,16,19,34] or have been limited to a single location,[10,17,27,29,30,35]

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Accepted 30 June 2005

we decided to appraise this issue in a representative elderly population of an affluent society. We presented the status of serum urate and prevalence of hyperuricemia and their relationship to MS in the Taiwanese elderly based on comprehensive national survey data.

Subjects and methods

Study participants

Data for this paper were obtained from the Elderly Nutrition and Health Survey in Taiwan (1999-2000) (Elderly NAHSIT) that was performed between 1999 and 2000. The Elderly NAHSIT was a national survey aimed at studying the nutrition and health status of free-living people aged 65 and older in Taiwan. We divided 359 townships (or districts) in Taiwan into 13 strata according to the dietary patterns of the residents, urbanization index, and the geographic characteristics of the selected areas. These 13 strata included Hakka areas, Mountain areas, Eastern areas, PengHu islands, and 9 strata from the northern, central and southern areas (3 strata each defined by the degree of urbanization, decreasing from the first to the third stratum). A total of 39 townships (3 from each strata) and 78 villages (or Lis, the smallest administrative unit) (2 from each township) were selected using probability proportional to population size (PPS) methodology. We randomly selected 26 elderly people from each village stratified by gender and age. Therefore, theoretically, there were 52 participants in every township, 156 participants in every stratum, and 2,028 participants nation-wide. However, in actuality a total of 1225 males and 1167 females underwent the physical examination and had available serum urate data or complete questionnaire data making them eligible for inclusion in the present analysis. More details about the study design and sam-pling methodology are provided by Pan *et al.*[36]

Data collection

The survey incorporated face-to-face interviews. Data collected included gender; age; residential location; lifestyle related variables: smoking, alcohol consumption, and physical activity; medical history; and the use of medications. Detailed physical examination included anthropometric measurements and the collection of fasting blood samples. The blood specimens were centrifuged immediately after collection. The serum specimens were aliquoted, frozen in a liquid nitrogen tank, and then delivered to the Academia Sinica where they were stored at -70°C. The frozen serum samples were analyzed in the clinical laboratory of the National Taiwan University Hospital within one month of collection (using the Hitachi 747, Japan). The coefficient of variation was derived from duplication of 5% of the blood samples and was 7.2% for serum urate measurement.

Definition of variables

Because there is no universally accepted definition for hyperuricemia, for the purpose of comparison we used two criteria: (1) serum urate ≥ 416.7 μM (7.0 mg/dL) for both genders[8,26,27] and (2) serum urate ≥ 458.0μM (7.7 mg/dL) for males and ≥ 392.9μM (6.6 mg/dL) for females.[26,27] Current use of urate lowering medication was defined as those who reported having taken such medication within one month prior to the interview. The definition of metabolic syndrome was that defined by the National Cholesterol Education Program – Adult Treatment Panel (NCEP-ATP III)[37-39] with modified central obesity criteria.[24,25] Participants needed to fit 3 or more of the following criteria: (1) waist circumference > 90 cm for men and >80 cm for women; (2) serum triglyceride ≥1.69 mM (150 mg/dL) or on lipid lowering medication; (3) HDL<1.03 mM (40 mg/dL) in men and <1.29 mM (50 mg/dL) in women; (4) SBP/DBP ≥130/85 mm-Hg or on anti-hypertension treatment; (5) fasting blood glucose ≥ 6.1 mM (110 mg/dL) or on treatment for diabetes mellitus. Body mass index (BMI) was used as a measure of general obesity and was calculated as weight (kg)/height^2 (m^2). The waist to hip ratio (WHR) was used as the indicator of central obesity. Both BMI and WHR were significant risk factors for hyperuricemia in this population and were adjusted for in the multivariable analyses. Moreover, the impact of monthly variation in serum urate levels was found to be substantial in this population. Though appraising the causes for this variation was not the purpose of the present study, monthly effect was adjusted for in regression analysis.

Statistical analysis

All data were weighted to represent the population in Taiwan. The population size of each gender/age group in each stratum was obtained from the national household registry system. The sampling weights were calculated by dividing the population by its corresponding sampling weights to represent the people of his or her own gender/age group in the stratum. All the analyses were carried out using SAS version 8.01[40] statistical software and SUDDAN version 8.0[41] was used to account for the sampling design. We used either the t-test or one-way ANOVA to compare mean serum urate levels between or within groups accordingly. The chi-square test was used to test the association between hyperuricemia and MS. Logistic regression analyses were used to examine the effect of location on hyperuricemia with and without adjusting for other related factors. Statistical significance was defined as P <0.05.

Results

The overall, gender-specific and gender-age specific distributions of serum urate levels and prevalence of hyperuricemia for Taiwanese people 65 years and older are shown in Table 1. The mean serum urate concentration was calculated from all blood samples excluding 80 samples of individuals taking medication to lower serum urate (5.5% of males and 1.1% of females) and 68 blood samples with a hemolyzed index greater than 1 (3.3% of males and 2.4% of females). The average serum urate level and corresponding 95% confidence interval (95% CI) was 411 (398, 424) μM for males and 357 (347, 367) μM for females. In all age groups, males had significantly higher serum urate levels than females. No apparent pattern of variation in uric acid levels was found among the four age groups in males. The highest uric acid value (421μM) occurred in the 70-74 year group, and

Table 1. Serum urate distribution and prevalence of hyperuricemia in elderly Taiwanese by gender and age groups. (All values are weighted to reflect their representation in the population)

Gender	Age (years)	*N*	Serum urate (μM) [1]				Hyperuricemia				Use of anti-hyperuricemic agents, % [4]
			Median	IQR	Mean	(95% CI)	%	Prevalence[1,2] (95% CI)	%	Prevalence[1,3] (95% CI)	
Male	All elderly	2392	375	143	385	(375, 396)	36	(32.1, 39.9)	32	(28.1, 35.9)	2.7
	65-69	452	393	137	408	(394, 421)	44	(38.1, 49.9)	31	(27.1, 34.9)	3.9
	70-74	430	405	131	421	(404, 438)	48	(42.1, 53.4)	34	(28.1, 40.0)	5.1
	75-79	225	387	143	403	(380, 426)	42	(32.2, 51.8)	28	(20.2, 35.8)	4.5
	≥ 80	118	417	155	407	(376, 437)	50	(42.2, 57.8)	30	(18.2, 41.8)	2.4
	All male	1225	399	131	411	(398, 424)	46	(42.1, 49.9)	31	(27.1, 34.9)	4.2
Female	65-69	474	345	119	353	(339, 368)*,[a]	22	(16.1, 27.9) *	30	(24.1, 35.9)	1.5
	70-74	354	351	137	357	(343, 371)*	28	(22.2, 33.9) *	33	(25.2, 40.8)	0.8
	75-79	215	375	143	376	(360, 392)*,[a,b]	34	(26.2, 41.8) *	41	(33.2, 48.8)	1.6
	≥ 80	124	327	95	346	(323, 368) *,[b]	21	(11.2, 30.8) *	24	(14.2, 33.8)	0
	All female	1167	351	131	357	(347, 367)*	26	(22.1, 29.9) *	32	(28.1, 35.9)	1.1

[1] Those who took antihyperuricemic agents were not included in the calculations. Eligible subjects were 1118 males and 1126 females. [2] Defined as serum urate ≥ 416.7 μM (7.0 mg/dL); [3] Defined as serum urate ≥ 458.0 μM (7.7 mg/dL) for males and ≥ 392.9 μM (6.6 mg/dL) for females; [4] Percentage of subjects using antihyperuricemic agents within one month prior to interview; * Significantly different from males of the same age group, $P < 0.05$; Values with common superscript letters (a, b, c) are significantly different at $P < 0.05$ between age groups in females. IOR: interquartile range; SE: standard error; CI: confidence interval.

in the other three age groups the urate levels ranged from 403 μM to 408 μM. For females, however, the mean value increased from 353 μM (65-69 years) to the peak of 376 μM (75-79 years) then decreased to 346 μM for the oldest group. The mean serum urate in 75-79 year old females was significantly higher than that in the youngest and the oldest age groups. Since the distribution of serum urate was skewed to the right, the corresponding median and interquartile ranges for various gender/age groups were also provided for reference.

When the criteria for hyperuricemia was set at ≥416.7 μM (7.0 mg/dL), the prevalence of hyperuricemia in elderly Taiwanese was 36% (males: 46%; females: 26%). The prevalence of hyperuricemia among the various age groups ranged from 42% (75-79 years) to 50% (80 years or older) in males, and ranged from 21% (80 years or older) to 34% (75-79 years) in females. Similarly, in regards to the serum urate level, males had significantly higher rates of hyperuricemia than females across all age groups. There was no difference in prevalence among different age groups in both genders. When the second criteria (serum urate ≥ 458.0 μM [7.7 mg/dL] for males and ≥ 392.9 μM [6.6 mg/dL] for females) were adopted, the prevalence of hyperuricemia in males decreased from 46% to 31%. In contrast, the prevalence of hyperuricemia in females increased form 26% to 32%. Using these criteria there was no gender differences in the prevalence of hyperuricemia. A total of 2.7% (4.2% of males and 1.1% of females) of participants reported having taken antihyperuricemic agents in the one month prior to the interview.

Table 2 presents the mean serum urate levels and the prevalence of hyperuricemia in elderly Taiwanese by gender and geographic location, using criteria of ≥416.7 μM (7.0 mg/dL). The mean serum urate level of participants from the Mountain areas was 455μM in males and 416 μM in females, which was 11% and 17% higher than the national average, respectively. In males, the prevalence of hyperuricemia exceeded 50% in the four strata of the PengHu islands (62%), the second stratum in the northern areas (58%), the Mountain areas (57%) and the second stratum in the central areas (51%). The location-specific prevalence rates of hyperuricemia were much lower in females than males. The only location where the prevalence of hyperuricemia in women exceeded 50% (i.e 51%) was in the Mountain areas. The next highest prevalence of hyperuricemia in women was in the PengHu islands with a prevalence of 39%. The prevalence of hyperuricemia in the elderly from the third stratum in the northern areas and the third stratum in the southern areas was relatively lower than the other strata.

Table 2 also presents the risk of hyperuricemia in relation to stratum for elderly Taiwanese. The third stratum in the northern areas was designated as the reference stratum because of the relatively low prevalence of hyperuricemia for both genders. In males, there was a significantly higher risk of hyperuricemia in six strata compared to the reference stratum according to univariate analysis. The highest risk was in the PengHu islands (odds ratio (OR): 2.8). After adjusting for age, monthly variation, body mass index and waist to hip ratio in the multivariable model, the risk was even higher (OR: 3.6; 95% CI: 1.0-13) in males from the PengHu islands and remained significant when compared to the reference group. The second highest risk of hyperuricemia occurred in males from the Mountain areas and this was also a statistically significant effect when compared to the reference group. Elderly women from Mountain areas had a significantly highest risk of hyperuricemia (OR: 5.1; 95% CI: 3.0-8.9) than those from the reference stratum after controlling for related factors. Including alcohol in the model did not substantially change the magnitude of these effects in either gender (data not shown).

Table 2. Gender-specific risk of hyperuricemia in the Taiwanese elderly in relation to location effects[1]

Gender	Location	Serum urate (μM)	Hyperuricemia[2]				
			%	OR[3]	OR[4]	OR[5]	(95% CI)
Male	Hakka areas	430	49	1.7*	2.1	1.8	(0.5, 5.5)
	Mountain areas	455	57	2.3*	2.2*	2.1*	(1.0, 4.4)
	Eastern areas	422	44	1.5	1.8	1.7	(0.6, 5.0)
	PengHu islands	438	62	2.8**	3.8*	3.6*	(1.0, 13)
	Northern areas: 1st stratum	383	42	1.2	1.7	2.0	(0.6, 6.5)
	Northern areas: 2nd stratum	433	58	2.4**	3.2	3.4	(1.0, 12)
	Northern areas: 3rd stratum (reference)	403	39	1.0	1.0	1.0	
	Central areas: 1st stratum	409	48	1.7	2.5	2.7	(0.8, 9.6)
	Central areas: 2nd stratum	408	48	1.6	2.1	2.3	(0.7, 7.9)
	Central areas: 3rd stratum	418	51	1.9**	2.3	2.3	(0.8, 7.1)
	Southern areas: 1st stratum	432	50	2.1*	2.5	2.4	(0.7, 8.4)
	Southern areas: 2nd stratum	408	40	1.5	1.8	1.7	(0.6, 5.1)
	Southern areas: 3rd stratum	400	37	1.1	1.3	1.3	(0.4, 4.0)
Female	Hakka areas	348	24	1.2	2.1*	2.0	(1.0, 3.9)
	Mountain areas	416	51	4.3*	4.9***	5.1***	(3.0, 8.9)
	Eastern areas	339	25	1.4	1.9	1.8	(0.7, 4.4)
	PengHu islands	374	39	2.6	3.9**	3.1*	(1.2, 8.4)
	Northern areas: 1st stratum	351	25	1.3	2.3*	2.5*	(1.1, 5.4)
	Northern areas: 2nd stratum	375	26	1.5	2.5*	2.5*	(1.0, 5.9)
	Northern areas: 3rd stratum (reference)	345	20	1.0	1.0	1.0	
	Central areas: 1st stratum	376	29	1.6	3.0*	3.3*	(1.3, 8.0)
	Central areas: 2nd stratum	367	28	1.7	2.8*	2.8*	(1.0, 7.6)
	Central areas: 3rd stratum	350	29	1.8	2.2*	2.0*	(1.0, 3.7)
	Southern areas: 1st stratum	362	25	1.5	2.7	2.8	(0.9, 8.0)
	Southern areas: 2nd stratum	350	27	1.5	2.3**	2.1*	(1.1, 3.9)
	Southern areas: 3rd stratum	353	23	1.3	2.1*	2.0*	(1.1, 3.4)

[1] Eligible subjects were those who had blood samples and completed anthropometric measures but did not take uric acid medications (1213 males and 1170 females); [2]Defined as serum urate ≥ 416.7 μM (7.0 mg/dL); [3]Results of univariate logistic regression analysis; [4]Adjusted for age (65-69, 70-74, 75-79, ≥80, in year) and monthly variation; [5]Adjusted for age (65-69, 70-74, 75-79, ≥80, in year), monthly variation, BMI and waist-hip ratio (quartiles); OR: odds ratio; CI: confidence interval; *P<0.05, **P<0.01, ***P<0.001.

The prevalence of MS in the study population was 21.8% in males and 39.2% in females based on the modified NCEP-ATP III definition. The mean serum urate levels for those with and without MS were 436μM and 405μM in males and 389μM and 338μM in females, respectively. The difference in serum urate between those with and without MS was significant in both genders. The prevalence of individual criteria for MS in order were: raised triglyceride (men 20.9%, women 31.4%), decreased HDL (men 20.1%, women 38.1%), raised blood glucose (men 29.3%, women 32.8%), abdominal obesity (men 29.3%, 55.8%) and raised blood pressure (men 56.0%, women 61.1%) (data not shown). For all of these five measures, the prevalence of abnormal results were higher in females than in males. The biggest difference in these abnormalities was found in abdominal obesity, where the prevalence in females was nearly double that of males. Similarly, a significantly higher prevalence of hyperuricemia was found in elderly men with MS compared to men without MS (56% vs. 43%). The difference in prevalence of hyperuricemia between women with and without MS was also pronounced as the prevalence of hyperuricemia in women with MS was double the rate in non-MS women (38% vs. 19%) (P<0.01) (Fig. 1). In addition, we calculated the gender-specific attributable risk measures of hyperuricemia in relation to MS. From our calculations of those elderly Taiwanese with MS, an estimated 18.8% of men and 15.5% of women would not have MS if hyperuricemia was eliminated (Table 3).

Discussion

This paper describes the distribution of serum urate and the prevalence of hyperuricemia in the Taiwanese population aged 65 years and older. The average serum urate level was 411 μM (6.9 mg/dL) for males and 357 μM (6.0 mg/dL) for females. Females were found to have lower uric acid levels than males across all age groups.[26,32,42]

Epidemiologic studies have suggested that age-related increases in serum urate in women are due to menopause.[43] This hypothesis has been further confirmed by the reduction of serum urate after using hormone replacement therapy in postmenopausal women.[44] Among the Taiwanese elderly however, the difference in serum uric acid levels between genders decreased along with aging, 33% in the 19-44 year age group and 22% in the 45-64 year age group, compared to 9.3% (data from the Nutrition and Health Survey in Taiwan 1993-1996; NAHSIT

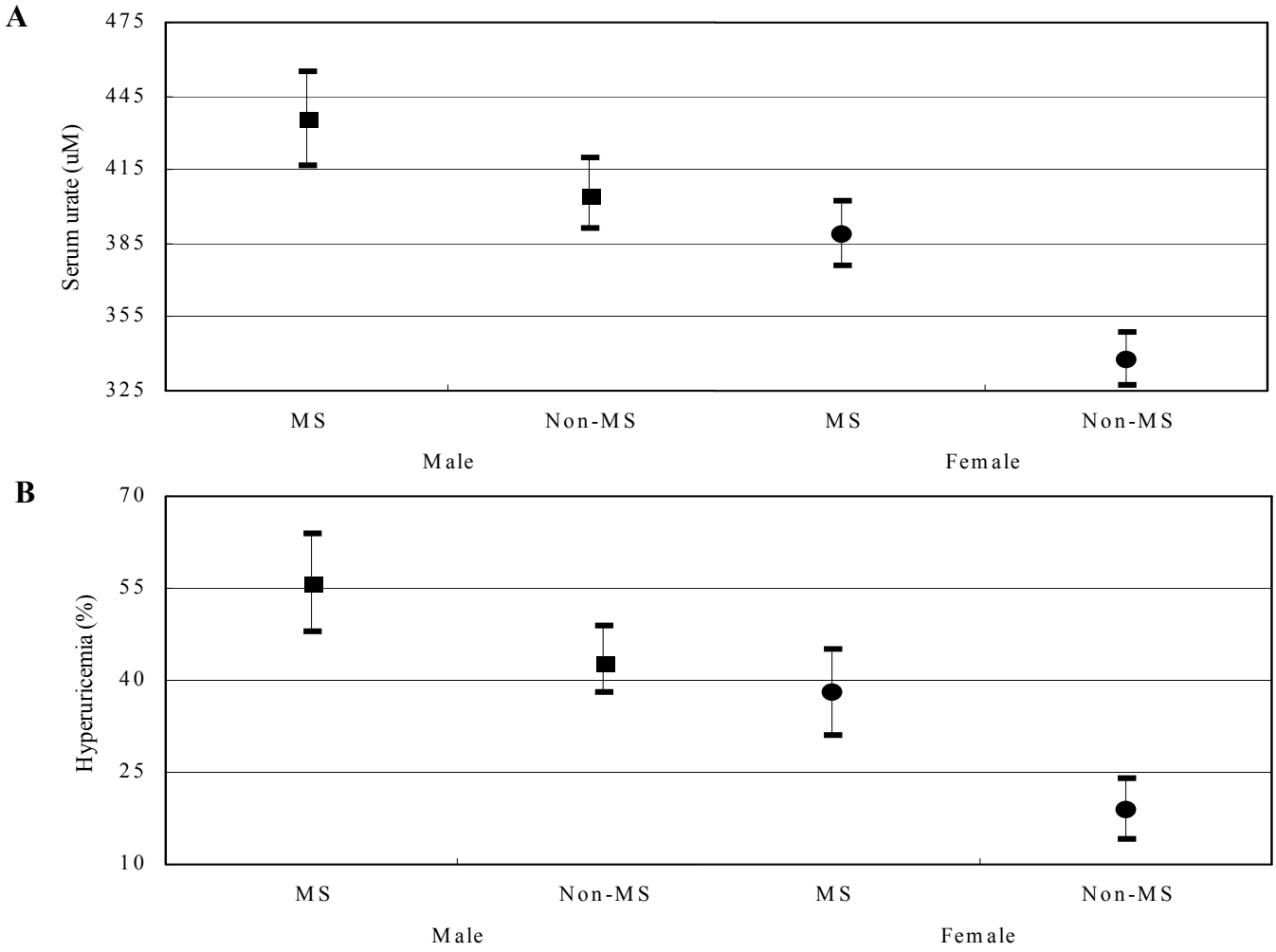

Figure 1. Gender and metabolic syndrome (MS) status specific (A) mean serum urate (μM) and (B) prevalence of hyperuricemia in the Taiwanese elderly. Hyperuricemia was defined as serum urate ≥416.7 μM (7.0 mg/dL). The corresponding 95% confidence intervals are also shown. All values are weighted to reflect their representation in the population. MS was defined by the presence of 3 or more of the following: (1) waist circumference >90 cm for men and > 80 cm for women; (2) serum triglyceride ≥1.69 mM (150 mg/dL) or on lipid lowering medication; (3) HDL <1.03 mM (40 mg/dL) in men and <1.29 mM (50 mg/dL) in women; (4) SBP/DBP ≥ 130/85 mmHg or on anti-hypertension treatment; (5) fasting blood glucose ≥6.1 mM (110 mg/dL) or on treatment for diabetes mellitus. The gender specific differences between MS groups were significant (P<0.01) by the t-test and chi-square test.

Table 3. Gender-specific attributable risks measures of hyperuricemia in relation to metabolic syndrome in the Taiwanese elderly[1]

	Male N=1110	Female N=1105
Metabolic syndrome (MS)[2] (%)	21.8	39.2
MS with hyperuricemia[3] (%)	26.7	56.4
MS with non-hyperuricemia (%)	17.7	3.1
Attributable risk (%)	9.0	23.3
Attributable risk percent (%)	33.7	41.3
Population attributable risk (%)	4.1	6.1
Population attributable risk percent (%)	18.8	15.5

[1]Those who had serum urate data and completed metabolic syndrome measures but did not take antihyperuricemic agents were eligible for the analysis. All values were weighted to reflect their representation in the population. [2]Defined by a modified ATP III clinical definition. It requires the presence of 3 or more of the following: (1) waist circumference >90 cm for men and >80 cm for women; (2) serum triglyceride ≥1.69 mM (150 mg/dL) or on lipid lowering medication; (3) HDL <1.03 mM (40 mg/dL) in men and <1.29 mM (50 mg/dL) in women; (4) SBP/DBP ≥130/85 mmHg or on anti-hypertension treatment; (5) fasting blood glucose ≥6.1 mM (110 mg/dL) or on treatment for diabetes mellitus. [3]Defined as serum urate ≥ 416.7 μM (7.0 mg/dL).

1993-1996)[26] and 15% (present survey) in the elderly population.

The criteria for hyperuricemia is based on the solubility of sodium urate in body fluids.[8] Because there has been no international agreement on the definition of hyperuricemia to date, we have used a variety of definitions for comparison purposes. In general, males had a higher rate of hyperuricemia than females no matter which definition was adopted. For elderly Taiwanese, the prevalence of hyperuricemia was 36% based on a definition of serum urate ≥416.7μM (7.0mg/dl). This means that more than one third of the elderly were hyperuricemic, which is quite high compared to global figures.[45] When the cut-offs were dropped to ≥416.4 μM (7.0mg/dl) for males and ≥356.9μM (6.0 mg/dl) for females, which is a definition commonly used in epidemiologic studies,[14,15,31,33] almost half of our participants were classified as hyperuricemic.

The serum urate levels and prevalence of hyperuricemia found in the present survey were higher than those reported in the previous national nutrition survey, other local studies in Taiwan and studies in other countries (Table 4). For example, compared to the elderly in the NAHSIT 1993-1996,[26] the mean serum urate increased 4.6%, from 393μM to 411μM in males. In particular,

when 458.0 μM (7.7mg/dL) was used as the cut point, the prevalence of hyperuricemia in elderly men rose from 19% to 31%. Similarly, when 416.7μM (7.0 mg/dL) was used as the cut point the prevalence rose from 36.8% to 46%. Urate levels in other countries showed a median serum urate of 345 μM for men and 285 μM for women aged 60 and older in the SHEP study [9] and a mean value of 351 μM for men and 286 μM for women aged 65-74 among CHS participants.[46] It is unclear whether this rise is an inevitable change over time due to modernization. Some may argue that this is a self-selective effect, as people who are more unwell would be more willing to attend screening, and as a result would raise the values. However, this does not seem to be a major issue in this population for serum urate, as only a few people reported having a history of gout and only 2.7% of participants reported taking medicines to treat hyperuricemia. In addition, respondents and non-respondents did not differ significantly in their education levels and occupation.[36]

As per other published data from Taiwan, the present study found an apparent geographic difference in serum urate status. Regardless of the criteria used, the prevalence of hyperuricemia was highest in the elderly from the Mountain areas and the PengHu islands in both genders. The prevalence of gout in Taiwanese indigenes was as high as 16.2% for males and 4.8% for females compared to only 0.3% among non-indigenes.[31] This has been attributed in the past to heavier drinking among aboriginal people. Serum urate level is not the most reliable or solitary criteria for the diagnosis of gout,[7,8] the prevalence of hyperuricemia is affected by a variety of factors according to the literature including alcohol consumption. However, in the current analysis we found that the higher prevalence of hyperuricemia in the elderly of the Mountain areas who were predominantly of aboriginal origin (77%), was not due to obesity or alcohol consumption, in contrast to what has been reported for other age groups.[26,30,47] In this population, 57% of males and 94% of females were non-drinkers, and only 13.9% of males and 0.9% of females reported having ≥1 drink per week. The mean BMI in different areas ranged from 22.1 to 23.9 in men and 23.0 to 25.2 in women (data not shown). Cheng *et al.,* has reported a significant linkage for gout in chromosome 4q25 in Taiwanese indigenes[48] suggesting that genetic factors may contribute to the prevalence of hyperuricemia. Obesity and alcohol consumption also cannot explain the higher level of urate in the elderly of the PengHu islands where fish consumption is extremely high. Choi *et al*., found that higher intake of meat and seafood was related to higher serum urate in NHANES III subjects.[49] Further study is required to evaluate the effect of diet on uric acid metabolism.

Serum urate and hyperuricemia have been found to be associated with various CVD risk factors in different population or age groups.[9-15] MS, a cluster of CVD risk factors, has been associated with total mortality, and cardiovascular morbidity and mortality in Western countries.[21-23] To evaluate the relationship between serum urate and these metabolic disorders collectively, we chose to use MS defined by ATP III as a surrogate measure. For elderly Taiwanese, both serum urate level and the prevalence of hyperuricemia were significantly higher in MS subjects than non-MS subjects. As hyperuricemia is not a commonly used criterion for MS, the significant association between hyperuricemia and MS indicate the possibility that both share common risk factor(s).

Table 4. Serum urate level in elderly people from different countries

Study	Time of Study	Location (or ethnic group)	Age (year)	Gender	Mean serum urate (μM)
Elderly NAHSIT	1999-2000	Taiwan	≥ 65	M	411
				F	357
NAHSIT	1993-1996 [26]	Taiwan	≥ 65	M	393
				F	359
	1987 [27]	Pu-Li, Taiwan	≥ 60	M	376
				F	331
	1978 [32]	Nagano, Japan	60-69	M	340
				F	277
		Nagano, Japan	≥ 70	M	343
				F	295
CHS	1989 [46]	USA	65-74	M	351
				F	286
			≥ 75	M	339
				F	280
SHEP	1985 [9]	USA	≥ 60	M	345[1]
				F	285[1]
	2004 [52]	Papua New Guinea (Kitavans)	≥ 75	M	305
				F	253
		Sweden	≥ 75	M	343
				F	280
	1992 [4]	New Zealand (Maoris)	65-74	B	365
			≥ 75	B	360
		New Zealand (Europeans)	65-74	M	325
			≥ 75	F	335

[1] Median. M: males; F: females; B: both.

Theoretically, from the population attributable risk percent, if hyperuricemia could be eliminated from the population, around 20% of MS could be prevented. Although a significant association between serum urate and MS was found, we do not know the mechanism of this relationship and whether urate via MS affects the risk of CVD or vice versa. Due to its antioxidant properties, uric acid may protect the body from oxidative stress, which has been linked to cardiovascular disease. Hence, it has been proposed that hyperuricemia is an early marker of CVD.[16] It is also worth noting that over half of Taiwanese elderly women were centrally obese. It is considered by ATP III that the rising prevalence of MS is mainly due to obesity.[50] Takahashi *et al*., has also reported that the size of intra-abdominal visceral fat is positively correlated with serum urate and negatively correlated with uric acid clearance.[51] Therefore, it would be valuable to use our results to evaluate the effect of change in serum urate on CVD risk via central obesity modification.

Consistent with the results of other age groups in Taiwan,[26] we found a relatively high serum uric acid level and prevalence of hyperuricemia in the elderly Han Chinese without the associated risk factors of alcohol consumption and obesity. In addition, the mean uric acid level and prevalence of hyperuricemia in people from the Mountain areas, mainly indigenes, were even higher, which may be due to a gene-environment interaction. Our data show that the metabolic disorders of MS were significantly associated with hyperuricemia in the Taiwanese elderly.

Acknowledgements

We express our thanks to Dr. Su-Chien Chang, Ms. I-Chen Huang, Wan-Yuan Chou, and Su-Chuan Wang for their valuable assistance in the preparation of this manuscript. We would like to thank all of the interviewers, local health department dietitians and all of those who assisted with the survey in local areas. We are particularly grateful for financial assistance from the Department of Health, Executive Yuan (Project name: Elderly Nutrition and Health Survey in Taiwan 1997-2002).

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