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ORIGINAL ARTICLE

Prevalence and Metabolic Factors of Hyperuricemia in an Elderly Agricultural and Fishing Population in Taiwan

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ABSTRACT

Objectives: This study aims to explore the potential condition-related sex differences to understand the overall pathogenesis of hyperuricemia among the elderly agricultural and fishing population in Taipei, Taiwan.

Patients and methods: This study included 4,372 healthy elderly agricultural and fishing professionals (2,766 males, 1,606 females; mean age 74.4±6.6 years; range 65.0 to 90.3 years) voluntarily admitted to a teaching hospital in Taipei, Taiwan for physical exams in 2010. Their fasting blood samples were drawn through venipuncture, and they were administered a structured questionnaire by clinical nurses.

Results: The overall prevalence of hyperuricemia was 30.4%, which increased significantly with increasing age (p<0.001). The prevalence was similar in males (30.2%) and females (30.6%) (p=0.78). Age, obesity, type 2 diabetes, hypercholesterolemia, hypertriglyceridemia as well as low high-density lipoprotein and high blood urea nitrogen, creatinine, and alanine amino transferase levels were significantly associated with hyperuricemia. Hypercholesterolemia (odds ratio [OR]=1.26, 95% confidence interval [CI]: 1.05-2.50) and high creatinine levels (OR=3.75, 95% CI: 2.64-5.33) were significantly associated with hyperuricemia in males, whereas type 2 diabetes (OR=1.54, 95% CI: 1.22–1.93) and high alanine amino transferase levels (OR=1.79, 95% CI: 1.31-2.43) were significantly associated with hyperuricemia in females. Hyperuricemia disparity among age groups was also revealed.

Conclusion: Several sex-related differences with regard to factors including age, obesity, type 2 diabetes, hypercholesterolemia, hypertriglyceridemia, low high-density lipoprotein, high blood urea nitrogen, creatinine, and alanine transferase levels were indicated in the prevalence of hyperuricemia in this specific elderly population.

Keywords: Agricultural and fishing population; elderly; hyperuricemia; prevalence; sex difference.

Uric acid acts as an antioxidant in endothelial cells and maintains vascular dilatation during oxidative stress.[1] Recent data have shown that hyperuricemia prevalence is increasing worldwide.[2] This increase is especially pronounced in developed countries, and the additional benefits of therapeutic intervention for hyperuricemia have recently been indicated. Inefficient excretion by the kidneys associated with the overproduction of urate accounts for <10% of hyperuricemia cases in the general population. By contrast, inefficient excretion of uric acid, accounting for >90% of the cases, results from renal insufficiency or medications that impair renal urate clearance.[3] At least two-thirds of patients with hyperuricemia may remain asymptomatic, and current evidence does not support treating asymptomatic hyperuricemia.[4]

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Because hyperuricemia is a critical health problem, the Wilson criteria are used for its routine screening. This requires a thorough understanding of the course of the disease, because patients may present with either a recognizable latent or early symptomatic stage. The clinical tests used for screening are easy to perform and interpret, and are reliable, accurate, acceptable, sensitive, and specific. After screening, an accepted treatment should be started in the event of positive results. From the viewpoint of preventive medicine, regional awareness of the background morbidity of hyperuricemia as well as exploration of the complete spectrum of demographic and biological markers likely associated with hyperuricemia are essential. Sex differences in the prevalence of and risk factors associated with hyperuricemia among specific elderly occupational populations require clarification. Thus, in this study, we aimed to explore the potential condition-related sex differences to understand the overall pathogenesis of hyperuricemia among the elderly agricultural and fishing population in Taipei, Taiwan.

PATIENTS AND METHODS

This population-based cross-sectional study included a total of 4,372 healthy elderly agricultural and fishing professionals (2,766 males, 1,606 females; mean age 74.4±6.6 years; range 65.0 to 90.3 years) voluntarily admitted to New Taipei City Hospital in Taipei, Northern Taiwan for an annual physical exam between January and December 2010.

Complete details regarding the study design and execution have been described elsewhere.[5] Fasting blood samples were drawn from participants through venipuncture by well-trained clinical nurses. Overnight-fasting serum and plasma samples were frozen (-20 °C) until analysis. Face-to-face interviews along with a structured questionnaire were administered by the nurses during each visit.

Hyperuricemia was diagnosed when serum uric acid levels were ≥7 mg/dL for males or ≥6 mg/dL for females.[6,7] In addition, participants with ≥40 U/L serum alanine amino transferase (ALT) were classified as those with elevated ALT levels.[5] The definitions of type 2 diabetes and hypertension were based on 1999 World Health Organization criteria and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, respectively.[8,9] Participants with a history of type 2 diabetes or hypertension and regularly receiving medication were classified as known cases. The following clinical conditions were used for defining obesity: high body mass index (≥25 kg/m^2), hypercholesterolemia (total cholesterol ≥200 mg/dL), hypertriglyceridemia (triglycerides ≥200 mg/dL), low high-density lipoprotein (HDL) <35 mg/dL, high blood urea nitrogen (BUN) ≥20 mg/dL, and high creatinine levels (≥1.4 mg/dL).[5] The study protocol was approved by the Fu-Jen Catholic University Ethics Committee. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using SAS (Statistical Analysis System) for Windows version 9.2 (SAS Institute Inc., Cary, NC, USA). A two-sample independent t test was used to assess differences in the mean values of continuous variables. Crude and sex- and age-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated. Multiple logistic regression analysis was used to evaluate the independence of hyperuricemia-related factors. A *p* value of <0.05 was considered statistically significant.

RESULTS

In this study, the overall prevalence of hyperuricemia in the screened population was 30.4%, which significantly increased with increasing participant age according to the chi-square trend test results (p<0.0001). The prevalence of hyperuricemia in males was not significantly higher than that in females (30.2% versus 30.6%; p=0.78, Chi-square test). Data were stratified into four broad age groups; females exhibited a higher prevalence of hyperuricemia than males in all age groups, with the exception of the 65-74-year-old group. The age-specific prevalence of hyperuricemia displayed a significant positive association with age according to the Chi-square trend test results for males (p=0.015) and females (p=0.008) (Table 1).

Table 1. Sex- and age-specific prevalence of hyperuricemia in study population

	Hyperuricemia											
	Male (n=2,766)				Female (n=1,606)				*Total* (n=4,372)			
	Screened No	Cases No	Prevalence %	p-value for χ^2-test for trend	Screened No	Cases No	Prevalence %	p-value for χ^2-test for trend	Screened No	Cases No	Prevalence %	p-value for χ^2-test for trend
65-74	1537	430	28.0	0.015	903	250	27.7	0.008	2440	680	27.9	<0.0001
75-84	1033	343	33.2		575	193	33.6		1608	536	33.3	
≥85	196	63	32.1		128	49	38.3		324	112	34.6	
Total	2766	836	30.2		1606	492	30.6		4372	1328	30.4	

The results of the comparison of various test characteristics and their potential association with specific (serum uric acid) class values (either hyperuricemia or normal) for participants aged ≥65 years are listed in Table 2. According to the results of the two-sample independent t test, the associated factors significantly associated with hyperuricemia included age (yes, 75.1±6.7 years, versus no, 73.0±6.5 years), body mass index (yes, 28.0±6.9 kg/m^2, versus no, 25.9±5.3 kg/m^2), fasting plasma glucose (yes, 102.7±28.6 mg/dL, versus no, 99.5±27.3 mg/dL), triglyceride (yes, 153.1±92.7 mg/dL, versus no, 121.8±80.6 mg/dL), HDL (yes, 50.8±14.3 mg/dL, versus no, 55.8±15.1 mg/dL), BUN (yes, 19.2±7.1 mg/dL, versus no, 17.1±4.7 mg/dL), creatinine (yes, 1.1±0.6 mg/dL, versus no, 0.9±0.3 mg/dL), and ALT (yes, 33.2±26.1 U/L, versus no, 30.6±21.1 U/L) levels. In addition, to examine whether sex-related differences in hyperuricemia are related to differences in clinical parameters, Table 2 also shows that triglyceride, BUN, creatinine, and ALT levels were significant factors associated with hyperuricemia in both males and females.

The crude and age- and sex-adjusted ORs for the association between relevant risk factors and hyperuricemia are presented in Table 3. Compared with individuals who exhibited normal uric acid levels, those with hyperuricemia revealed a more pronounced prevalence of obesity (adjusted OR=1.53, 95% CI: 1.32-1.77), type 2 diabetes (adjusted OR=1.16, 95% CI: 1.01-1.33), hypercholesterolemia (adjusted OR=1.22, 95% CI: 1.06-1.41), hypertriglyceridemia (adjusted OR=1.78, 95% CI: 1.52-2.09), low HDL (adjusted OR=1.54, 95% CI: 1.28-1.86), high BUN (adjusted OR=1.57, 95% CI: 1.34-1.85), high creatinine (adjusted OR=3.09, 95% CI: 2.26-4.23), and high ALT levels (adjusted OR=1.36, 95% CI: 1.14-1.64) after adjustment for sex and age.

The effects of independent associated risk factors on hyperuricemia were further examined using a multiple logistic regression model. After adjusting for confounding factors, age (OR=1.02, 95% CI: 1.01-1.03), obesity (yes versus no, OR=1.53, 95% CI: 1.32-1.77), type 2 diabetes (yes versus no, OR=1.16, 95% CI: 1.01-1.33), hypercholesterolemia

Table 2. Hyperuricemia-related characteristics of study population

	Hyperuricemia											
	All screened subjects				Males screened subjects				Females screened subjects			
	No (n=3,044)	Yes (n=1,328)	*Total* (n=4,372)	p-value for t test	No (n=1,930)	Yes (n=836)	*Total* (n=2,766)	p-value for t test	No (n=1,114)	Yes (n=492)	*Total* (n=1,606)	p-value for t test
	Mean±SD	Mean±SD	Mean±SD		Mean±SD	Mean±SD	Mean±SD		Mean±SD	Mean±SD	Mean±SD	
Age (year)	73.0±6.5	75.1±6.7	74.4±6.6	<0.0001	73.1±6.5	75.0±6.8	74.4±6.6	<0.0001	72.9±6.6	75.3±6.7	74.4±6.7	<0.0001
BMI (kg/m^2)	25.9±5.3	28.0±6.9	26.6±5.8	<0..0001	26.4±6.7	28.7±8.6	27.2±7.4	<0.0001	25.1±4.1	26.9±4.1	25.7±4.2	<0.0001
Fasting plasma glucose (mg/dL)	99.5±27.3	102.7±28.6	100.6±27.8	0.007	99.8±28.4	99.4±24.9	99.6±27.3	0.092	99.1±25.3	108.3±33.3	102.1±28.5	<0.0001
SBP (mmHg)	136.9±37.9	140.8±33.2	138.2±36.4	0.270	136.5±34.6	140.1±38.0	137.7±35.8	0.278	137.6±43.0	142.0±22.7	139.1±37.6	0.632
DBP (mmHg)	78.8±24.2	80.0±17.7	79.1±22.3	0.744	78.5±22.1	80.2±20.2	79.1±21.5	0.898	79.2±27.5	79.6±12.6	79.4±23.6	0.729
Cholesterol (mg/dL)	199.6±35.0	203.1±37.2	200.7±35.8	0.100	194.1±33.0	199.0±34.6	195.4±33.6	0.186	209.2±36.3	211.7±39.8	210.0±34.5	0.264
Triglyceride (mg/dL)	121.8±80.6	153.1±92.7	132.1±86.0	<0.0001	121.1±89.0	148.3±92.0	130.0±90.9	0.001	123.1±63.7	161.2±93.4	135.7±76.9	<0.0001
HDL (mg/dL)	55.8±15.1	50.8±14.3	54.1±15.0	0.020	53.3±14.5	48.8±13.8	51.9±14.4	0.045	60.0±15.2	54.3±14.5	58.1±15.2	0.245
BUN (mg/dL)	17.1±4.7	19.2±7.1	17.8±5.7	<0.0001	17.4±4.8	19.2±6.8	18.0±5.6	<0.0001	16.5±4.5	19.2±7.9	17.4±6.0	<0.0001
Creatinine (mg/dL)	0.9±0.3	1.1±0.6	1.0±0.4	<0.0001	1.0±0.3	1.1±0.5	1.0±0.4	<0.0001	0.8±0.3	1.0±0.7	0.8±0.5	<0.0001
ALT (U/L)	30.6±21.1	33.2±26.1	31.5±22.9	<0.0001	31.7±24.0	33.6±29.2	32.4±25.8	0.029	28.8±14.7	32.3±19.6	29.9±16.5	<0.0001

SD: Standard deviation; BMI: Body mass index; SBP: Systolic blood pressure; DBP: diastolic blood pressure; HDL: High-density lipoprotein; BUN: Blood urea nitrogen; ALT: Alanine amino transferase.

(yes versus no, OR=1.22, 95% CI: 1.06-1.41), hypertriglyceridemia (yes versus no, OR=1.78, 95% CI: 1.52-2.09), low HDL (yes versus no, OR=1.54, 95% CI: 1.28-1.86), high BUN (yes versus no, OR=1.58, 95% CI: 1.34-1.85), high creatinine (yes versus no, OR=3.09, 95% CI: 2.26-4.23), and high ALT levels (yes versus no, OR=1.36, 95% CI: 1.14-1.64) appeared to be significantly associated with hyperuricemia (Table 4). Data in Table 4 also indicate the considerably different results of multiple logistic regression analysis stratified by sex. Among males, significant risk factors for hyperuricemia included age (OR=1.02, 95% CI: 1.01-1.04), obesity (yes versus no, OR=1.53, 95% CI: 1.28-1.84), hypercholesterolemia (yes versus no, OR=1.26, 95% CI: 1.05-2.50), hypertriglyceridemia (OR=1.70, 95% CI: 1.38-2.08), low HDL (yes versus no, OR=1.52, 95% CI: 1.22-1.89), high BUN (yes versus no, OR=1.35, 95% CI: 1.10-1.65), and high creatinine levels (yes versus no, OR=3.75, 95% CI: 2.64-5.33). Among females, significant risk factors for hyperuricemia included age (OR=1.02, 95% CI: 1.00-1.04), obesity (yes versus no, OR=1.58, 95% CI: 1.23-2.03), type 2 diabetes (yes versus no, OR=1.54, 95% CI: 1.22-1.93), hypertriglyceridemia (OR=1.95, 95% CI: 1.52-2.51), low HDL (OR=1.65, 95% CI: 1.14-2.39), high BUN (OR=2.22, 95% CI: 1.69-2.92), and high ALT levels (OR=1.79, 95% CI: 1.31-2.43).

We next investigated whether age-related differences in hyperuricemia are associated with differences in the risk factors for hyperuricemia. Age-group disparities associated with hyperuricemia were also examined using the multiple logistic regression model. After adjustment for confounding factors, obesity and hypertension were the common factors associated with hyperuricemia (Table 5).

DISCUSSION

Hyperuricemia is considered to be the major etiological factor in gout. In addition to an inflammatory state triggered by urate crystal deposition in the joints, hyperuricemia has additional pathophysiological consequences causing tissue inflammation, mainly in the vascular wall.[10] Epidemiological studies have also

Table 3. Crude and adjusted odds ratios of hyperuricemia-related factors among study population

	Hyperuricemia		Crude OR		Adjusted OR*	
	Yes (n=1,328)	No (n=3,044)	(95% CI)	*p*	(95% CI)	*p*
Sex						
Female	492	1,114	1.00	-	-	-
Male	836	1,930	0.98 (0.86-1.12)	0.78	-	-
Age (year)						
65-74	680	1,760	1.00	-	-	-
75-84	536	1,072	1.29 (1.10-1.47)	0.01	-	-
≥85	112	212	1.37 (1.19-2.27)	<0.001	-	-
Obesity						
No	672	2,002	1.00	-	1.00	-
Yes	656	1042	1.88 (1.64-2.14)	<0.001	1.53 (1.321.77)	<0.001
Type 2 diabetes						
No	1,143	1,901	1.00	-	1.00	-
Yes	623	705	1.47 (1.29-1.67)	<0.001	1.16 (1.01-133)	0.037
Hypertension						
No	2,270	774	1.00	-	1.00	-
Yes	1049	279	1.28 (1.10-1.50)	0.002	1.13 (0.96-1.33)	0.143
Hypercholesterolemia						
No	664	1,634	1.00	-	1.00	-
Yes	664	1,401	1.17 (1.08-1.33)	0.016	1.22 (1.06-1.41)	0.005
Hypertriglyceridemia						
No	786	2,351	1.00	-	1.00	-
Yes	542	693	2.34 (2.04-2.69)	<0.001	1.78 (1.52-2.09)	<0.001
Low HDL						
No	983	2,619	1.00	-	1.00	-
Yes	345	425	2.16 (1.84-2.54)	<0.001	1.54 (1.28-1.86)	<0.001
High BUN						
No	906	2,437	1.00	-	1.00	-
Yes	422	607	1.87 (1.62-2.16)	<0.001	1.57 (1.34-1.85)	<0.001
High creatinine						
No	1,185	2,970	1.00	-	1.00	-
Yes	143	74	4.84 (3.63-6.46)	<0.001	3.09 (2.26-4.23)	<0.001
High ALT						
No	1,071	2,637	1.00	-	1.00	-
Yes	257	407	1.55 (1.31-1.85)	<0.001	1.36 (1.14-1.64)	0.001

* Adjustment for sex and age; OR: Odds ratio; CI: Confidence interval; HDL: High-density lipoprotein; BUN: Blood urea nitrogen; ALT: Alanine amino transferase.

demonstrated that high serum uric acid levels are associated with type 2 diabetes, hypertension, stroke, atherosclerosis, cardiovascular disease, and metabolic syndrome; a large-scale investigation indicated that elevated serum uric acid levels are associated with an increased mortality rate.[1,11-14] Hyperuricemia appears to increase the risk of coronary heart disease events in the general population, mainly adult females.[14]

Social problems resulting from the division between rich and poor have led to the coexistence of unsustainable lifestyles among approximately one billion people in the developed world and unacceptable poverty in another one billion people, largely from developing countries.[5] In this study, we used an age- and sex-based approach to estimate the morbidity of hyperuricemia in an elderly agricultural and fishing population. The prevalence of hyperuricemia in males and females was 30.2% and 30.6%, respectively. In multiple logistic regression analysis, age, obesity, type 2 diabetes, hypercholesterolemia, hypertriglyceridemia, low HDL level, and high BUN, creatinine, and ALT levels were independent predictors of hyperuricemia. A crucial benefit of a uric acid screening program is that gout and other chronic complications are often detected in apparently healthy individuals through elevated serum uric acid levels because the related screening tests are commonly included in serum chemistry panels.[5] The relative significance of these results is often overlooked when the serum uric acid levels are deemed slightly abnormal. In addition, the differences observed in factors associated with hyperuricemia in each age subgroup imply that multiple strategies for the health promotion of elderly people are necessary for reducing the risk of elevated serum uric acid levels.

Table 4. Multiple logistic regression of hyperuricemia-related factors among study population

	Hyperuricemia (yes versus no)					
	Male		Female		*Total*	
	OR	95% CI	OR	95% CI	OR	95% CI
Age (year)	1.02	1.01-1.04	1.02	1.00-1.04	1.02	1.01-1.03
Sex (female versus male)	-	-	-	-	0.83	0.72-1.27
Obesity (yes versus no)	1.53	1.28-1.84	1.58	1.23-2.03	1.53	1.32-1.77
Type 2 diabetes (yes versus no)	0.98	0.82-1.17	1.54	1.22-1.93	1.16	1.01-1.33
Hypertension (yes versus no)	1.09	0.89-1.34	1.20	0.91-1.57	1.13	0.96-1.33
Hypercholesterolemia (yes versus no)	1.26	1.05-2.50	1.20	0.95-1.53	1.22	1.06-1.41
Hypertriglyceridemia (yes versus no)	1.70	1.38-2.08	1.95	1.52-2.51	1.78	1.52-2.09
Low HDL (yes versus no)	1.52	1.22-1.89	1.65	1.14-2.39	1.54	1.28-1.86
High BUN (yes versus no)	1.35	1.10-1.65	2.22	1.69-2.92	1.58	1.34-1.85
High creatinine (yes versus no)	3.75	2.64-5.33	1.68	0.82-3.40	3.09	2.26-4.23
High ALT (yes versus no)	1.20	0.96-1.51	1.79	1.31-2.43	1.36	1.14-1.64

OR: Odds ratio; CI: Confidence interval; HDL: High-density lipoprotein; BUN: Blood urea nitrogen; ALT: Alanine amino transferase.

Agriculture includes both crop and animal husbandry and fisheries to produce the food requirements of humankind.[15] Good health and appropriate training programs are essential for agricultural and fishing professionals. Their long or irregular working hours may cause adverse health effects. To the best of our knowledge, however, few clinical evidence-based studies have determined the prevalence and possible etiology of hyperuricemia among the elderly agricultural and fishing population in Taiwan. The prevalence of hyperuricemia in various populations are presented in Table 6. The prevalence of hyperuricemia among different screened populations seems to vary between countries.[16-25] This disparity is likely due to differences among various populations with regard to participant characteristics (e.g., age, socioeconomic status, and abnormal associated factors), study period, and different diagnostic definitions for elevated serum uric acid levels. The prevalence of hyperuricemia in our study population (30.4%) was higher than that reported in previous population-based studies conducted in general Chinese populations.[11,16,20-22,25] The agricultural and fishing population endures strenuous working conditions, job stress, and reversed working and resting times compared to those of the general population.[5] Irregular lifestyles and carelessness regarding personal health are also major problems in this population. These factors might partially explain the apparently high prevalence of hyperuricemia observed in our study. Another reason for the discrepancy between the results for the general population and our results may be the differences in the populations studied.

Table 5. Multiple logistic regression of hyperuricemia-related factors for stratified by age group

	65-74 years (n=2,456)		75-84 years (n=1,613)		≥85 years (n=326)	
	OR	95% CI	OR	95% CI	OR	95% CI
Sex (male versus female)	0.80	0.65-0.98	0.92	0.72-1.16	0.61	0.35-1.07
Obesity (yes versus no)	1.57	1.29-1.92	1.42	1.13-1.79	1.83	1.03-3.24
Type 2 diabetes (yes versus no)	1.17	0.96-1.42	1.20	0.96-1.50	0.85	0.49-1.48
Hypertension (yes versus no)	1.24	0.99-1.55	0.93	0.71-1.21	1.52	0.79-2.95
Hypercholesterolemia (yes versus no)	1.04	0.85-1.26	1.43	1.14-1.85	1.91	1.10-3.30
Hypertriglyceridemia (yes versus no)	1.99	1.61-2.46	1.58	1.21-2.05	1.66	0.86-3.21
Low HDL (yes versus no)	1.36	1.05-1.76	1.70	1.26-2.28	2.41	1.20-4.83
High BUN (yes versus no)	1.47	1.16-1.86	1.66	1.29-2.12	1.93	1.11-3.33
High creatinine (yes versus no)	2.66	1.56-4.54	2.83	1.83-4.38	7.72	3.05-19.57
High ALT (yes versus no)	1.55	1.23-1.96	1.18	0.86-1.61	0.45	0.15-1.31

OR: Odds ratio; CI: Confidence interval; HDL: High-density lipoprotein; BUN: Blood urea nitrogen; ALT: Alanine amino transferase.

Table 6. Prevalence of hyperuricemia among various populations

Author	Study year	Screened number	Setting	Prevalence of hyperuricemia (%)	Associated factors
Yu et al.[16]	2012	11,576	Northeast China	Overall: 10.9 Male: 15.0 Female: 7.3	Abdominal obesity, general obesity, hypertriglyceridemia, hypertension, hypercholesterolemia, low HDL-C, ethnic minority, physical activity, current smoking, drinking
Zhu et al.[17]	2007	5,707	United States	Overall: 3.9 Male: 5.9 Female: 2.0	Adiposity, hypertension
You et al.[18]	2009	1,426	Mongolia	Male: 17.7 Female: 5.2	Waist circumference, the level of triglycerides
Alikor et al.[19]	2013	500	Nigeria	Overall: 17.2 Male: 25 Female: 13.7	Waist circumference, total cholesterol, LDL, sex
Qu et al.[20]	2007	9,354	Three Gorges, China	Male: 5.6 Female: 3.3	Alcohol drinking, low intake of green vegetables and fruits
Qiu et al.[21]	2008	13,141	Northern China	Overall: 13.7 Male: 21 Female: 7.9	Age, sex, residence, obesity hypertension, abdominal obesity impaired fasting glucose, CKD, drinking and sleeping, hypercholesterolemia, hypertriglyceridemia,
Yang et al.[22]	2012	4,218	Jinan, China	Male: 6.4 Female: 2.1 Urban: 6.7% Rural areas: 1.7%	Male sex, urban residence, obesity, hypertension, high serum creatinine level, hyper triglyceridemia,hypercholeste rolemia,
Conen et al.[23]	2004	1,011	The Seychelles, Indian Ocean, population mainly of African origin	Male: 35.2 Female: 8.7	Serum triglycerides, age, BMI, blood pressure, alcohol, the use of antihypertensive therapy
Nakamura et al.[24]	2011	3,310	Japan	21.6	Habitual alcohol intake
Lin et al.[25]	2010	2,145	Taiwan	Given thiazides: 44% Given loop diuretics: 56% Given aldosterone receptor blockers: 57%	Impaired renal function, diuretic use

HDL-C: High-density lipoprotein C; LDL: Low density lipoprotein; CKD: Chronic kidney disease; BMI: Body mass index.

Older age was a significant risk factor for hyperuricemia even in our elderly study population. This finding is consistent with the results of previous hospital- and community-based studies for general and occupational populations.[11,21-23] The mechanism underlying the slightly lower prevalence of hyperuricemia in males aged ≥85 than in those aged 75-84 years remains unclear; nevertheless, in females, the increase in hyperuricemia prevalence with increasing age may be explained by postmenopausal changes in the endocrine system and estrogen levels.[22]

Consistent with other studies,[21,22,25] we observed a positive association between hyperuricemia and metabolic disorders in our Chinese population. Epidemiological studies have also reported an association between hyperuricemia and metabolic disorders such as metabolic syndrome, hyperlipidemia, obesity, and type 2 diabetes.[11,22,25] Metabolic syndrome is a cluster of three diseases-hypertension, hyperglycemia, and gout,[11] Although metabolic syndrome is clearly associated with obesity, insulin resistance, and abnormal blood lipids, which lead to the three diseases, the etiological mechanisms of this syndrome remain unknown.[26] Previous studies have indicated that serum uric acid level can be used as a crucial predictor of metabolic syndrome and that the number of metabolic syndrome components increases the prevalence and OR for significantly increased uric acid activity.[11,27,28]

Among patients with chronic hepatitis, fructose load may cause a substantial increase in serum uric acid levels.[5,7] Furthermore, serum uric acid levels are high in patients with chronic liver lesions. Our results regarding the significant association between high serum ALT level and hyperuricemia are similar to those reported in other studies.[5,29] However, because of the cross-sectional design of our study, we could not determine the extent to which the increase in serum ALT level occurs before hyperuricemia development.

Uric acid levels are high among renal failure patients because of decreased renal clearance.[1] A decrease in the glomerular filtration rate contributes to hyperuricemia, frequently observed in patients with chronic kidney disease.[30] Here, we observed a positive association between serum creatinine level and hyperuricemia, consistent with other studies.[11,31] Although evidence-based studies have indicated that serum uric acid itself may harm patients with chronic kidney disease by increasing inflammation and progression, the topic remains controversial.[31] In addition, we observed that BUN is strongly associated with hyperuricemia after adjustment for confounding factors. This suggests that BUN is an indicator of deterioration caused by hyperuricemia. A study indicated that despite significantly influencing serum uric acid, creatinine, and BUN levels, diuretic dose failed to emerge as the strongest predictor of serum uric acid in multiple regression analyses. This implied that increased diuretic dose may indirectly reflect the deterioration of renal function and clinical status.[32]

A major limitation of this study was potential selection bias because the screened elderly population was selected from only one area; this bias may have affected the estimated prevalence of and risk factors for hyperuricemia. Nevertheless, given our relatively large sample size, the statistical power was sufficient to effectively evaluate the presence of any sex differences between the various associated risk factors for hyperuricemia after adjusting for confounding factors. Second, we evaluated only elderly participants, who might have characteristics differing from those of the general population. This subpopulation is more susceptible to hyperuricemia than other populations in Taiwan. Third, some nonrespondents, who did not return for biochemical examination, may have had more prevalent hyperuricemia; thus, the prevalence may have been underestimated. Finally, our measurements were conducted at a single time point; hence, they cannot be used to reflect the effects of long-term exposure to the various risk factors, which may critically affect hyperuricemia. Thus, prospective longitudinal analogous studies are required, the results of which may complement the cross-sectional findings of this study.

In conclusion, in this study for prevalence of and risk factors for hyperuricemia in our elderly agricultural and fishing population, we noted several sex differences with regard to factors including age, obesity, type 2 diabetes, hypercholesterolemia, hypertriglyceridemia, low HDL level, and high BUN, creatinine, and ALT levels. Future studies are required to elucidate the temporal sequence of events typically leading to hyperuricemia and further explore the sex differences in the factors causing hyperuricemia among the elderly agricultural and fishing population.

Declaration of conflicting interests

The authors certify full disclosure of all affiliations or financial involvements with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in this manuscript, within the past five years and in the foreseeable future (e.g., employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, and royalties).

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