Dietary and Lifestyle Changes Associated with High Prevalence of Hyperuricemia and Gout in the Shandong Coastal Cities of Eastern China

ZHIMIN MIAO, CHANGGUI LI, YING CHEN, SHIHUA ZHAO, YANGANG WANG, ZHONGCHAO WANG, XINYAN CHEN, FENG XU, FANG WANG, RUIXIA SUN, JIANXIA HU, WEI SONG, SHENGLI YAN, and CONG-YI WANG

ABSTRACT. ***Objective.*** To demonstrate the prevalence of hyperuricemia and gout associated with dietary and lifestyle changes and evaluate the implication of metabolic disorders to the development of hyperuricemia.

Methods. Data collected from 5,003 subjects randomly recruited from 5 coastal cities (Qingdao, Rizhao, Yantai, Weihai, and Dongying) of Shandong province in Eastern China were analyzed.

Results. Overall, the prevalence for hyperuricemia and gout in the studied populations was 13.19% and 1.14%, respectively. The prevalence was significantly higher in men as compared to women (18.32% vs 8.56% for hyperuricemia, 1.94% vs 0.42% for gout). Hyperuricemia was more common in men over age 30 and in women over age 50. A significant steady increase for the prevalence was noted as compared to the previous published data. Urban residents showed much higher prevalence of hyperuricemia as compared to rural residents (14.9% vs 10.1%, p = 0.004). Similarly, higher prevalence was noted in the developed city compared to the less developed city (18.02 vs 5.3%). These discrepancies were highly correlated with economic development as manifested by the increase of daily consumption of meat and seafood. Additionally, alcohol, overweight or obesity, hypertension, and abnormal triglycerides were highly associated with higher prevalence of hyperuricemia. Moreover, hyperuricemia is likely a risk factor for the development of diabetes mellitus.

Conclusion. There was a remarkable increase for the prevalence of hyperuricemia and gout, which is highly correlated with the development of the economy as manifested by dietary and lifestyle changes. (First Release July 15 2008; J Rheumatol 2008;35:1859–64)

Key Indexing Terms:
GOUT HYPERURICEMIA METABOLIC DISORDERS HYPERTENSION OBESITY

Gout is a metabolic disorder that has been known since ancient times[1,2]. Although the exact etiology of gout is yet to be fully understood, it has been strongly associated with hyperuricemia. Recent studies further suggest that it is also associated with obesity, dyslipidemia, hyperglycemia, and hypertension[3-9]. Gout is considered to be caused by excess storage of uric acid (UA) that accumulates in tissues, including the synovium. Therefore, it is believed that the formation and reversible deposition of monosodium urate (MSU) crystals in the joints and extraarticular tissues are the essential prerequisite for its pathogenesis.

Gout is one of the most common inflammatory arthritides in Western countries[10]. However, gout was once considered a very rare disease in mainland China. It has recently been found more and more commonly, and is now becoming a serious threat to the health of the general population in China[11-15]. Moreover, there is a significant lack of information about dietary and lifestyle changes associated to the prevalence of hyperuricemia and gout in the general population. We studied the prevalence of hyperuricemia and gout associated with dietary and lifestyle changes such as increased meat and seafood intake and alcohol consumption. The impact of metabolic disorders on the prevalence of hyperuricemia was also investigated. Subjects randomly recruited from 5 coastal cities in Shandong province of Eastern China were included in our study.

From the Department of Endocrinology, Medical School Hospital of Qingdao University, Qingdao, China; and the Center for Biotechnology and Genomic Medicine and Department of Pathology, Medical College of Georgia, Augusta, Georgia, USA.

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Z. Miao, MD; C. Li, MD; Y. Chen, MD; S. Zhao, MD; Y. Wang, MD; Z. Wang, MD; X. Chen, MD; F. Xu, MD; F. Wang, MD; R. Sun, MD; J. Hu, MD; W. Song, MD; S. Yan, MD, Department of Endocrinology, Medical School Hospital of Qingdao University; C-Y. Wang, MD, Center for Biotechnology and Genomic Medicine and Department of Pathology, Medical College of Georgia.

Drs. Miao and Li contributed equally to this work.

Address reprint requests to Dr. S. Yan, Department of Endocrinology, Medical School Hospital of Qingdao University, 16 Jiangsu Road, Qingdao, 266003, PR China, E-mail: yansl2001@suhu.com; and Dr. C-Y. Wang, Center for Biotechnology and Genomic Medicine and Department of Pathology, Medical College of Georgia, 1120 15th Street, Augusta, GA 30912, E-mail: cwang@mcg.edu

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MATERIALS AND METHODS

Study area and population. A random, stratified cluster sampling approach was used for our study. All subjects were recruited from coastal cities including Qingdao, Rizhao, Yantai, Weihai, and Dongying, which flank 3,000 km of coastline of Shandong province in Eastern China. We randomly recruited 1,100 subjects from 5 sampling places of each city with an average of 220 subjects from each sampling place using a stratified sampling design. In brief, all sampling places with each representing a district or a county were randomly drawn from all the districts and counties in that city. Subdivisions within the selected districts or villages within the selected counties in a particular city were further randomly drawn from all the subdivisions or villages to serve as clusters for the survey. Once the subdivisions or villages had been selected, families within each selected location were then selected by odd or even family registration numbers in the police station. Physicians and nurses subsequently approached and obtained consent from the selected families. Only those subjects aged 20–80 years and who lived in the same place for more than 5 years were selected for the study. Those subjects without hyperuricemia or gout served as controls for analysis of the prevalence in the general population. The only 2 subjects using diuretics at the time of the survey were excluded from the study. The study was approved by the Human Assurance Committee of Medical School of Qingdao University and informed consent was obtained from all subjects.

Sampling approach. A total of 18 physicians and 18 nurses participated in the sampling process, which lasted from May to October 2004. During home interview and on site sampling, a questionnaire was processed by the attending physicians or nurses. The questionnaire included demographic data, household income, average daily consumption of meat, fish, shrimp, shellfish, and alcohol, as well as personal and family history of diabetes and hyperuricemia/gout. The information was further confirmed at the second visit. The average daily consumption of food was measured with a 7-day dietary record from each participant. We assessed validity of self-reported food consumption by comparing family-based estimates provided by the housewives. Fasting blood was also collected for UA testing during the first visit, and was reexamined at the second visit in those subjects with abnormal UA levels. At the end of the second visit an educational lecture was provided that focused on the prevention and treatment of hyperuricemia and gout. All participants were encouraged to finish the survey.

In addition to the above information included in the questionnaire, examination was performed by the attending physicians. This examination included health history, body weight, height, blood pressure, and body mass index [BMI, calculated by body weight (kg)/body height (m^2)].

Experimental procedures. All the participants fasted for 8–14 h before the blood and urine collections. Fasting serum UA, blood urea nitrogen (BUN), serum creatinine, TG, total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C), and high density lipoprotein-cholesterol (HDL-C) were determined using the Sysmex Chemix-180 automatic biochemical analysis device (Sysmex Infosystems, Kobe, Japan). The fasting blood glucose levels were determined by the OneTouch Ultra blood sugar device (LifeScan, Inc. Milpitas, CA, USA). Individuals with blood sugar > 5.0 mmol/l were instructed to drink 75 g glucose (dissolved in 300 ml water) within 3 min, and blood glucose was determined 2 h later. Blood insulin level was determined by Elecsys 2010 device (Hitachi Ltd., Tokyo, Japan).

Diagnostic standards. Clinical diagnosis for gout was carried out under the guidelines of the American College of Rheumatology (ACR) as originally proposed by Wallace and coworkers[16]. Male subjects and postmenopausal female subjects with serum UA > 416 µmol/l or premenopausal female subjects with > 356 µmol/l were diagnosed with hyperuricemia. Hypertension was diagnosed based on the definition and classification suggested by the World Health Organization (WHO) International Society of Hypertension[17]. Participants with systolic blood pressure (SBP) ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg were defined as hypertensive. Diabetes mellitus was diagnosed according to the guidelines of the American Diabetes Association (ADA). Participants with TG > 1.7 mmol/l, TC > 5.17 mmol/l and HDL-C < 0.9 mmol/l were diagnosed with lipid metabolic disorder. Obesity was diagnosed using the WHO standard. Age- and sex-matched controls were selected from subjects without hyperuricemia, gout, lipid and sugar metabolic disorders, hypertension, heart disease, liver disease, and renal disease.

Statistical analysis. All of the data were recorded using the Microsoft Excel program. To ensure accuracy, the data were further checked by several investigators. All laboratory tests were carried out 3 times and presented as mean ± standard deviation (SD). All statistical analyses were carried out using the SPSS 10.0 software (Shanghai, China). The prevalence, expressed as percentages, was compared using chi-square tests of homogeneity. Linear trends were tested for significance by using the median value for the intake and treating this value as a continuous variable. Logistic regression model was used to correlate age, sex, BMI, hypertension (yes/no), diabetes (yes/no), intake of alcohol (ml/day), carbohydrates (g/day), meat (g/day), fish (g/day), shrimp (g/day), and shellfish (g/day) to evaluate associations between dietary variables and serum UA. To test the correlations of obesity, diabetes, hypertension, and hyperlipidemia with serum UA, we included multiplicative terms in the linear regression models with adjustment for other potential confounders. Odds ratio (OR) was used to evaluate the risk for the development of hyperuricemia or gout associated with sex, age, meat and seafood intake, and alcohol consumption using the logistic regression model. All other data were analyzed by one-way analysis of variance test. For all measures, we calculated 95% confidence intervals (CI). $p < 0.05$ was considered to be statistically significant.

RESULTS

The prevalence of hyperuricemia and gout. We approached 5,500 subjects in 5 coastal cities of Shandong province in Eastern China, only 5,003 (2,395 men and 2608 women) of whom participated in this investigation. Overall, the prevalence for hyperuricemia in Qingdao, Rizhao, Yantai, Weihai, and Dongying was 16.23%, 15.15%, 18.02%, 10.24%, and 5.30%, respectively. As shown in Table 1, 660 subjects were diagnosed with hyperuricemia indicating a prevalence of 13.19% in the general population. Of these, 435 (66%) were male and 225 (34%) were female. The prevalence of hyperuricemia in men was significantly higher than in women in the general population (18.32% vs 8.56%, OR = 2.5, 95% CI 2.10–2.89, $p < 0.01$), and the average age for the onset of hyperuricemia in men was also much younger than in women (44.6 ± 13.7 vs 52.2 ± 14.2 yrs). After sex stratification, it was shown that the prevalence of hyperuricemia became much higher with age. For example, the prevalence increased significantly in men after age 30 (OR = 2.0, 95% CI 1.32–1.55, $p < 0.01$) and women after age 50 (OR = 5.2, 95% CI 2.32–3.75, $p < 0.001$).

Fifty-seven subjects were diagnosed with gout according to the ACR guidelines, and none of them was taking urate-lowering drugs at the time of investigation. The prevalence of gout in Qingdao, Rizhao, Yantai, Weihai, and Dongying was 0.53%, 0.97%, 2.55%, 0.80% and 0.50%, respectively. By combining the data from all these cities, the prevalence of gout was 1.14% in the general population with a significantly higher prevalence in men than women (1.94% vs 0.42%, OR = 5.3, 95% CI 2.92–9.56, $p < 0.001$). Of note, all gout patients showed hyperuricemia, except for several patients whose serum UA levels were normal during an

Table 1. Age and sex distribution for the prevalence of hyperuricemia and gout.

	Male Subjects							Female Subjects						
		Hyperuricemia			Gout				Hyperuricemia			Gout		
Age, yrs	n	No.	Prev.	Std. Rate	No.	Prev.	Std. Rate	n	No.	Prev.	Std. Rate	No.	Prev.	Std. Rate
20–29	457	45	9.85	11.52	2	0.44	0.79	329	8	2.43	5.74	0	0	0
30–39	617	120	19.02	16.10	9	1.46	1.30	684	21	3.07	7.27	0	0	0
40–49	631	122	19.77	16.48	13	2.06	1.60	645	38	5.89	9.54	2	0.31	0.17
50–59	348	68	19.54	16.28	13	3.73	2.40	620	75	12.10	12.64	4	0.65	0.33
60–69	245	53	21.63	17.41	6	2.45	1.79	243	54	22.22	17.71	3	1.23	0.63
70+	97	27	27.84	20.51	3	3.09	2.12	87	29	33.33	22.46	2	2.30	1.06

No.: number of patients; Prev: Prevalence; Std. Rate: Standardized rate. The prevalence was adjusted by the total populations in Shandong province surveyed in 2000.

acute attack, probably because of the stimulatory effect of the acute phase response on renal urate excretion. These data further suggest that hyperuricemia is a pivotal causative factor for the development of gout, and therefore, development of gout became more prevalent with age in both men and women. The highest prevalence for gout was observed in men between the ages of 50–60 years, while in women it was above age 70 (Table 1). In particular, gout was absent in all premenopausal women. It is notable that 13 out of 57 gouty patients showed family history of hyperuricemia and gout including the 2 gouty patients diagnosed at age 24 and 28, respectively. Of note, the prevalence of gout in Dongying (0.5%) was relatively high compared to its low prevalence for hyperuricemia (5.3%): this was caused by the identification of 3 cases within a family with strong genetic inheritance. All these observations demonstrate that genetic predisposition plays a pivotal role in the pathogenesis of hyperuricemia and gout.

Metabolic disorders and the prevalence of hyperuricemia/gout. We next analyzed the differences of biomedical indexes between the hyperuricemic/gouty and control subjects. The control subjects (1,729 in total) were selected from all participants without evidence for hyperuricemia/gout, hypertension, lipid and sugar metabolic disorders, heart disease, liver disease, and renal disease. As can be seen in Table 2, in general, hyperuricemic and gouty patients showed

Table 2. Demographic, clinical and laboratory characteristics of the study population.

Groups	HUA (n = 660)	Gout (n = 57)	Normal (n = 1729)	p
Age, mean ± SD	47.3 ± 14.3	49.3 ± 12.1	46.7 ± 12.8	NS
Sex, female n (%)	225 (34)*	11 (19.3)*	931 (53.8)	< 0.01
BMI, kg/m^2	25.8 ± 3.5*	26.1 ± 3.00*	20.5 ± 1.6	< 0.01
WHR	0.90 ± 0.07*	0.92 ± 0.06*	0.81 ± 0.06	< 0.01
SBP, mm Hg	134 ± 24*	134 ± 19*	114 ± 11	< 0.01
DBP, mm Hg	86.0 ± 13	51.0 ± 12	75.0 ± 7	NS
BUN, mmol/l	5.51 ± 1.66	5.66 ± 1.74	4.94 ± 1.11	NS
Cr, mmol/l	62.0 ± 19	63.0 ± 21	50.0 ± 11	NS
TG, mmol/l	1.86 ± 1.80*	2.98 ± 7.96*	0.71 ± 0.30	< 0.001
TC, mmol/l	4.91 ± 1.08	4.77 ± 0.96	3.94 ± 0.66	NS
UA, μmol/l	481 ± 113*	446 ± 58*	259 ± 64	< 0.001
LDL-C, mmol/l	2.95 ± 0.94	2.30 ± 0.64	2.30 ± 0.58	NS
HDL-C, mmol/l	1.11 ± 0.31	1.12 ± 0.44	1.30 ± 0.26	NS
Daily food consumption				
Carbohydrates, g/day	398.6 ± 164.2	394.7 ± 147.2	391.54 ± 156.9	NS
Meat, g/day	52.90 ± 23.4	57.10 ± 55.1	42.50 ± 42.6	< 0.04
Fish, g/day	63.40 ± 35.1*	79.80 ± 55.7*	43.50 ± 69.0	< 0.001
Shrimp, g/day	15.10 ± 33.4	17.20 ± 33.7	11.50 ± 29.2	NS
Shellfish, g/day	37.80 ± 85.6*	58.70 ± 47.9*	21.50 ± 40.0	< 0.001
Wine, ml/day	194.0 ± 147	204.0 ± 103	147.0 ± 108	NS
Beer, ml/day	843.0 ± 956	750.0 ± 830	460.0 ± 560	NS

* Significant difference vs control subjects. HUA: hyperuricemia; Normal: control subjects without hyperuricemia, gout, hypertension, lipid and sugar metabolic disorders, heart disease, liver disease and renal disease; BMI: body mass index; WHR: waist to hip ratio; SBP: systolic blood pressure (1 mm Hg = 0.133 kPa); DBP: diastolic blood pressure; BUN: blood urea nitrogen; Cr: serum creatinine; TG: triglycerides; TC: total cholesterol; UA: uric acid; LDL-C: low density lipoprotein-cholesterol; HDL-C: High density lipoprotein-cholesterol; NS: not significant.

almost 2-fold higher UA than that of control subjects ($p < 0.001$). It was found that 58.6% of the hyperuricemic subjects were overweight or obese, while only 18.2% of the normal subjects showed overweight or obesity (OR = 2.53, 95% CI 2.14–2.98, $p < 0.001$). As expected, the average BMI and waist to hip ratio (WHR) for all hyperuricemic subjects were significantly higher than that of the control subjects (OR = 1.290, 95% CI 1.062–1.119 for BMI, OR = 1.273, 95% CI 1.058–1.088 for WHR, $p < 0.01$), suggesting that obesity is probably a risk factor for the development of hyperuricemia and gout. Similarly, hypertension is probably another independent risk factor for the disorder. Forty-five percent of the hyperuricemic subjects were diagnosed with hypertension, and the average SBP for all hyperuricemic subjects was marginal to be hypertensive. In contrast, only 26% of the control subjects were hypertensive (OR = 1.38, 95% CI 1.01–1.62, $p < 0.001$). It was also found that hyperuricemia and gout were positively associated with serum TG levels. In 53% of the hyperuricemic subjects, abnormal TG levels were noted, and the average TG levels for all hyperuricemic subjects were out of normal range. In contrast, only 23% of the control subjects were noted with abnormal TG levels (OR = 2.63, 95% CI 2.21–3.14, $p < 0.001$). Interestingly, although we observed higher levels of TC/LDL-C or lower levels of HDL-C in the hyperuricemic/gouty subjects compared to that of the control subjects, all of these biomedical indexes were within the normal range. Unexpectedly, all hyperuricemic/gouty subjects showed normal BUN and serum creatinine.

Dietary and lifestyle changes and the prevalence of hyperuricemia/gout. In general, the prevalence of hyperuricemia and gout is highly associated with meat and seafood consumption (Table 2). We also observed a strong correlation between the prevalence of hyperuricemia and dietary/lifestyle changes corresponding to economic development. We first noticed that urban residents had much higher prevalence of hyperuricemia than rural residents (14.9% vs 10.1%, $p < 0.01$). To determine whether dietary factors are responsible for this discrepancy, we investigated dietary differences between the 2 groups of subjects shown in Table 3. It was found that urban residents consume much more meat, fish, and shrimp daily compared to rural residents. On the other hand, rural residents consume more carbohydrates than the urban residents. Similar phenomena were observed between the urban residents with household income differences. For example, the economically developed and seafood-rich city of Yantai, where daily consumption of meat, fish, shrimp, and shellfish for the residents was the highest among the cities, we found the highest prevalence for hyperuricemia (18.8%) and gout (2.55%). By contrast, the less developed city of Dongying, where the average daily consumption of meat and seafood was the lowest compared to other cities, we found a significantly lower prevalence for hyperuricemia (5.4%) and gout (0.5%) (Table 3). Next, 670 sex- and age-matched controls were selected to further confirm this observation. As shown in Table 4, hyperuricemic patients showed significantly higher daily consumption of meat (OR = 1.26, 95% CI 1.10–1.33, $p < 0.05$), fish (OR = 1.28, 95% CI 1.16–1.19, $p < 0.01$), and shellfish (OR = 1.34, 95% CI 1.20–1.27, $p < 0.01$), but lower carbohydrates compared to control subjects. Altogether, with economic development, there were significant dietary and lifestyle changes in residents in this area, characterized by the increased consumption of meat and seafood, which could then predispose to development of hyperuricemia.

Alcohol consumption and the prevalence for hyperuricemia. Although we observed higher consumption of alcohol in the hyperuricemic/gouty subjects compared to the control subjects in the studied population (Tables 2 and 3), this finding was not statistically significant because of variations between the studied subjects. After stratification for sex and age differences (Table 4), it was found that the average daily consumption of alcohol for the hyperuricemic patients was significantly higher than that of the control subjects (OR = 1.23, 95% CI 1.11–1.15, $p < 0.01$). We then selected 949 subjects recruited from Qingdao city to further confirm the observation, as those subjects did not show significant differences in dietary consumption. Among these, 183 were alcohol consumers, while the remaining 766 subjects were non-alcohol consumers. Consistently, the prevalence of hyperuricemia in alcohol consumers (53 out of 183, 29%) was more than 2-fold higher than that of non-alcohol consumers (105 out of 766, 13.7%, OR = 2.6, 95% CI 1.75–3.75, $p < 0.001$), indicating the importance of alcohol consumption in the development of hyperuricemia.

Table 3. Comparison of daily food consumption between residents in different living locations.

Group	n	HUA Prevalence, %	Carbohydrates, g/day	Meat, g/day	Fish, g/day	Shrimp, g/day	Shellfish, g/day	Wine, ml/day	Beer, ml/day
City vs countryside									
City residents	2480	14.19%	394 ± 165	49 ± 113	42 ± 60	12.27 ± 25.03	22 ± 42	151 ± 122	662 ± 924
Countryside residents	2523	10.1%*	414 ± 170*	40 ± 72*	50 ± 102*	9.06 ± 27.43*	23 ± 58	759 ± 824	653 ± 650
Developed vs less developed									
Yantai residents	1060	18.8%	380 ± 160	45 ± 49	37 ± 94	7.74 ± 18.07	23 ± 48	159 ± 132	749 ± 885
Dongying residents	1000	5.4%	455 ± 191*	32 ± 36*	17 ± 21*	4.95 ± 11.09*	8 ± 15*	162 ± 123	1069 ± 733

* $p < 0.01$ for the comparison between the 2 groups of subjects (city residents vs countryside residents or residents in Yantai vs residents in Dongying).

Table 4. Comparison of daily food consumption between the hyperuricemic subjects and age- and sex-matched controls.

Group	n	Carbohydrates, g/day	Meat, g/day	Fish, g/day	Shrimp, g/day	Shellfish, g/day	Wine, ml/day	Beer, ml/day
Control	670	423 ± 199	43 ± 53	42 ± 68	10.93 ± 24.05	20.29 ± 36.29	150 ± 119	552 ± 628
HUA	660	398 ± 164*	53 ± 23*	63 ± 35**	15.06 ± 33.47	37.78 ± 85.57**	194 ± 147**	843 ± 956**

* $p < 0.05$ for the comparison between the 2 groups of subjects. ** $p < 0.01$ for the comparison between the 2 groups of subjects. HUA: hyperuricemic subjects.

Hyperuricemia and the development of glucose metabolic disorder. In our investigation of the impact of hyperuricemia on the development of glucose metabolic disorder, based on fasting blood glucose (FBG) and postprandial blood glucose (PBG) levels as well as insulin levels for all participants, diabetes was diagnosed based on the ADA guidelines after repetitive FBG and PBG tests. Out of the 5,003 participants, 419 subjects were diagnosed with diabetes mellitus, with a prevalence of 8.4% in the studied population. However, hyperuricemic subjects showed a higher prevalence (10.8%) for diabetes. We then analyzed diabetes prevalence in men and women (Table 5). Consistently, diabetes prevalence in the female hyperuricemic subjects (16.4%) was about 2-fold higher than that of the control subjects (8.4%, OR = 2.15, 95% CI 1.47–3.14, $p < 0.001$). To our surprise, we failed to observe a significant difference for the diabetes prevalence between the male hyperuricemic subjects (7.8%) and their corresponding controls (8.3%). Overall, our results suggest that hyperuricemia is probably a risk factor for the development of diabetes mellitus in women.

DISCUSSION

In the early 1980s, gout was absent in all populations studied in China[18]. For the past 2 decades, there was a remarkable steady increase in the prevalence of gout in China[15,19,20]. Our current data indicate that the prevalence of hyperuricemia (13.19%) and gout (1.14%) in the studied population of coastal cities of Eastern China has actually reached similar levels to Western countries. Although the significant increase for gout prevalence is probably also associated with increased awareness of this disorder, it is particularly alarming for the health of the general population, especially for the rapidly increasing numbers of senior citizens because of enhanced average life expectancy. We further noted that early onset of gout is usually accompanied by family history, indicating a role for genetic factors in disease development.

With economic development in China, significant dietary and lifestyle changes have resulted for all citizens. These changes are strongly associated with increased prevalence of hyperuricemia and gout. For example, urban residents consume much more meat, fish, and shrimp compared to rural residents and, as a result, the prevalence of hyperuricemia was significantly higher in the urban residents versus rural residents (Table 3). In contrast, in the developed cities such as Qingdao, there was no significant difference in the consumption of daily foods, and consequently, the prevalence of hyperuricemia was almost the same between urban and rural residents (data not shown). Of note, the establishment of this correlation is based on a 7-day dietary record, and therefore, a longitudinal dietary survey would be more accurate to demonstrate the relationship between dietary changes and the development of hyperuricemia.

The implication of alcohol intake in the development of gout has long been suspected[3]. Choi and coworkers convincingly demonstrated that alcohol consumption, especially consumption of purine-rich alcoholic beverages such as beer, significantly increases the risk for the development of hyperuricemia or gout[21]. Our data further show that consumption of beer is a high risk factor for hyperuricemia (Table 4). However, unlike previous data for the effect of moderate wine consumption (1–2 glasses/day) on the risk of hyperuricemia[21], our data suggest that consumption of wine is also a risk factor for hyperuricemia. This discrepancy was probably caused by excessive consumption of wine (> 2 glasses/day) in many of the subjects or combination of consumption of wine and liquor in some subjects. Surprisingly, all hyperuricemic subjects showed normal renal function; further investigation would be necessary to address this issue.

Table 5. Comparison of the prevalence of diabetes mellitus between the hyperuricemic subjects and the control subjects.

Group	Male Subjects			Female Subjects		
	n	Patients	Incidence	n	Patients	Incidence
Controls	2395	200	8.3%	2608	219	8.4%
HUA	435	34	7.8%	225	37	16.4%*

* $p < 0.001$ vs control subjects. HUA: hyperuricemia.

Obesity and metabolic syndrome have been suggested to contribute to the increasing prevalence of gout[4,6,7,9,22]. China was once considered to have one of the leanest populations, but it is fast catching up to the West in terms of the prevalence of overweight and obesity[23]. We found that 58.6% of the hyperuricemic subjects were overweight or obese. Particularly, the average BMI (25.8 ± 3.5 kg/m^2) and WHR (0.9 ± 0.07) for all hyperuricemic subjects were within the overweight range. In addition to those diagnosed with overweight or obesity, a large proportion of the hyperuricemic subjects were close to borderline overweight. We also found that hypertension and TG are associated with increased serum urate concentration. Forty-five percent of the hyperuricemic subjects were hypertensive, versus only 26% of the control subjects. Similarly, the average levels for TG in the hyperuricemic and gouty subjects were out of normal range as compared to that of control subjects (Table 2).

Hyperuricemia is one of the symptoms of hyperinsulinism, and the level of uricemia correlates with the degree of insulin resistance[5,24]. To our surprise, we only observed a significant higher prevalence for diabetes in the women with hyperuricemia (Table 5). The factors that contribute to this discrepancy are currently unknown. The differences of lifestyle, physical activities, environmental exposures, overweight or obesity, and especially the age of onset of hyperuricemia between the male and female subjects are possible causative factors.

We have demonstrated the prevalence of hyperuricemia and gout in the coastal cities of Shandong province in Eastern China. A significant steady increase for the prevalence of hyperuricemia and gout was observed, which is strongly associated with economic development characterized by dietary and lifestyle changes and increased consumption of alcoholic beverages such as beer.

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REFERENCES

1. Nriagu JO. Saturnine gout among Roman aristocrats. Did lead poisoning contribute to the fall of the Empire? N Engl J Med 1983;308:660-3.
2. Kamienski M. Gout: not just for the rich and famous! Everyman's disease. Orthop Nurs 2003;22:16-20.
3. Choi HK, Atkinson K, Karlson EW, Willett W, Curhan G. Purine-rich foods, dairy and protein intake, and the risk of gout in men. N Engl J Med 2004;350:1093-103.
4. Roddy E, Zhang W, Doherty M. The changing epidemiology of gout. Nat Clin Pract Rheumatol 2007;3:443-9.
5. Novak S, Melkonian AK, Patel PA, Kleinman NL, Joseph-Ridge N, Brook RA. Metabolic syndrome-related conditions among people with and without gout: prevalence and resource use. Curr Med Res Opin 2007;23:623-30.
6. Korochina IE, Bagirova GG. Metabolic syndrome and rheumatic diseases [in Russian]. Ter Arkh 2006;78:39-47.
7. Rho YH, Choi SJ, Lee YH, et al. The prevalence of metabolic syndrome in patients with gout: a multicenter study. J Korean Med Sci 2005;20:1029-33.
8. Fam AG. Gout, diet, and the insulin resistance syndrome. J Rheumatol 2002;29:1350-5.
9. Vuorinen-Markkola H, Yki-Jarvinen H. Hyperuricemia and insulin resistance. J Clin Endocrinol Metab 1994;78:25-9.
10. Mikuls TR, Farrar JT, Bilker WB, Fernandes S, Schumacher HR Jr, Saag KG. Gout epidemiology: results from the UK General Practice Research Database, 1990-1999. Ann Rheum Dis 2005;64:267-72.
11. Fang W, Zeng X, Li M, Chen LX, Schumacher HR Jr, Zhang F. The management of gout at an academic healthcare center in Beijing: a physician survey. J Rheumatol 2006;33:2041-9.
12. Li Y, Stamler J, Xiao Z, Folsom A, Tao S, Zhang H. Serum uric acid and its correlates in Chinese adult populations, urban and rural, of Beijing. The PRC-USA Collaborative Study in Cardiovascular and Cardiopulmonary Epidemiology. Int J Epidemiol 1997;26:288-96.
13. Shi F, Gu K, Lu W, et al. Study on the prevalence of arthritis and relevant factors in Shanghai [in Chinese]. Zhonghua Liu Xing Bing Xue Za Zhi 2003;24:1136-40.
14. Zeng Q, Wang Q, Chen R, Xiao Z, Huang S, Xu J. Primary gout in Shantou: a clinical and epidemiological study. Chin Med J Engl 2003;116:66-9.
15. Nan H, Qiao Q, Dong Y, et al. The prevalence of hyperuricemia in a population of the coastal city of Qingdao, China. J Rheumatol 2006;33:1346-50.
16. Wallace SL, Robinson H, Masi AT, Decker JL, McCarty DJ, Yu TF. Preliminary criteria for the classification of the acute arthritis of primary gout. Arthritis Rheum 1977;20:895-900.
17. Whitworth JA. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. J Hypertens 2003;21:1983-92.
18. Fang Q, Chen HZ, Yu Z. Survey of uric acid among healthy Chinese and its relation to blood lipids [in Chinese]. Zhonghua Nei Ke Za Zhi 1983;22:434-8.
19. Chen S, Du H, Wang Y, Xu L. The epidemiology study of hyperuricemia and gout in a community population of Huangpu District in Shanghai. Chin Med J Engl 1998;111:228-30.
20. Jiang BF, Zhang YC, Xu XF. Epidemiological survey of gout and hyperuricemia in littoral of Shandong province. Zhong Guo Gong Gong Wei Sheng 1999;15:502-10.
21. Choi HK, Atkinson K, Karlson EW, Willett W, Curhan G. Alcohol intake and risk of incident gout in men: a prospective study. Lancet 2004;363:1277-81.
22. Rathmann W, Funkhouser E, Dyer AR, Roseman JM. Relations of hyperuricemia with the various components of the insulin resistance syndrome in young black and white adults: the CARDIA study. Coronary Artery Risk Development in Young Adults. Ann Epidemiol 1998;8:250-61.
23. Wu Y. Overweight and obesity in China. BMJ 2006 Aug 19;333:362-3.
24. Choi HK, Ford ES, Li C, Curhan G. Prevalence of the metabolic syndrome in patients with gout: the Third National Health and Nutrition Examination Survey. Arthritis Rheum 2007;57:109-15.