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Original Article

Gender-Specific Differences in Prevalence and Association of Cardio-Metabolic Parameters and Hyperuricemia: A Population-Based Cross-Sectional Study, Nakhon Nayok, Thailand

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Abstract

Background: Although the prevalence of HUA is increasing, epidemiologic studies on HUA in the middle-aged and elderly population are limited. The present study aimed to calculate the prevalence and evaluate the sex-related associations between metabolic parameters and hyperuricemia (HUA) among middle-aged and elderly adults.

Methods: This was a population-based cross-sectional study from 2018 to 2019 in rural areas of Nakhon Nayok Province, Thailand. We enrolled 780 subjects aged 40 yr and over for health check-ups and examination surveys. The age-standardized prevalence of HUA was estimated by the direct method. A multiple logistic regression was performed to identify the potential risk factors associated with HUA.

Results: The prevalence of HUA were 30.9% (42% in males vs. 20% in females). Elderly adults were associated with a 35% increase in the risk of HUA. Obesity was found to be strongly associated with an increased prevalence of HUA in both sexes. Hypertriglyceridemia (51% increase in males vs. 23% increase in females), and high fasting glucose (90% increase in males vs. 49% increase in females) were also associated risk factors for HUA in both sexes. However, low high-density lipoprotein was only associated with a 67% increase in the risk of HUA in females.

Conclusion: The age-standardized prevalence of HUA among females is relatively lower than in males. This study also revealed that obesity is strongly associated with HUA in both sexes.

Keywords: Hyperuricemia; Metabolic parameters; Elderly adults; Population-based study; Sex difference

Introduction

Hyperuricemia (HUA) is a risk factor for gout, cardiovascular disease, chronic kidney disease, and diabetes mellitus (1-5). The prevalence rates of HUA are increasing rapidly worldwide. In general, HUA is highly prevalent not only in high-income countries (6-9) however also in-

creasing in low-middle-income countries (10-14). To date, various epidemiological studies have revealed that the prevalence of HUA was 1.83%-6.40% in middle-aged and older (15-17). HUA was more common in males than females (18,19). Moreover, the prevalence rates of HUA in urban areas were higher than in rural areas (13-15, 20-23). The meta-analysis suggested that gender, middle-aged, residents who dwell in urban or rural areas, and economic level may be associated with HUA (24). Several epidemiological studies confirmed that gender, diabetes mellitus, hypertension, dyslipidemia, obesity, metabolic syndrome, smoking, and alcohol intake had a positive association with risk factors of HUA in general adults (8, 9, 18, 19, 23). Moreover, increasing diastolic blood pressure, triglycerides, blood urea nitrogen, creatinine, and decreasing high-density lipoprotein cholesterol were independently associated with risk factors of HUA (25). Consistent with the results in a previous large population-based study (19), HUA is associated with current drinking, including obesity and dyslipidemia in males, whereas singles males were with lower odds of having HUA. Meanwhile, being single, high economic levels, smoking, and metabolic syndrome parameters (obesity, diabetes mellitus, hypertension, and dyslipidemia) were all additionally identified as high-risk factors for the development of HUA in females.

Several previous studies have been performed to show the prevalence rates of HUA in Bangkok (13, 22, 26) and Khon Kaen (20), Thailand. However, the prevalence rates were dependent upon different characteristics of individual studies such as the age-stratified, areas, and the economic level in only the general adults but not in the middle-aged and elderly adults. The relationships between lifestyle factors, metabolic parameters, and HUA in middle-aged and elderly adults remain uncertain. Especially, sex-related associations between metabolic parameters and HUA are not well known.

Therefore, we aimed to calculate the prevalence of HUA and to determine the sex-related associations between metabolic parameters and HUA among middle-aged and elderly adults in Thailand.

Materials and Methods

Study design and study population

This was a population-based, cross-sectional design performed from 2018 to 2019 in rural areas of Nakhon Nayok Province, Thailand. All adults aged 40 yr and older were invited to participate in this study. However, individuals with any arthritis disease, kidney disease, cancer, stress/antidepression medication, and those on lower serum uric acid therapy were excluded. Methods for recruiting participants for a research study encompass various approaches, such as establishing communication with the village chief and village health volunteers, or displaying notices soliciting participants at a community sanitarium. The determination of the sample size in this study is based on the logistic regression guideline (27). The study involves approximately 12 independent variables. Therefore, a minimum sample size of 700 subjects is required. By accounting for a potential dropout rate of 10%, this study will require a minimum sample size of 875 subjects. This is calculated by dividing 700 by 0.80. A representative sample for this study was obtained using a stratified multistage cluster sampling method. The initial phase involved selecting one sub-district at random from each stratum, with four sub-districts per stratum. Within each chosen village, a fixed number of 12 villages were then selected using simple random sampling. From each village, approximately 73 elderly individuals were randomly chosen, considering gender and age stratification. This resulted in a theoretical total of 219 participants in each stratum, and a total of 875 participants across Nakhon Nayok Province. Out of these, 780 participants (89%) participated in the physical examination and provided complete questionnaire data, making them eligible for inclusion in the analysis.

The study received approval from the Ethics Committee of Srinakharinwirot University, Thai-

land (MEDSWUEC-148/60E), and each participant provided written informed consent.

Data collection and laboratory measurement

Demographic and socioeconomic variables (e.g., age, marital status, education levels, type of occupation, household income, and health payment systems) were collected through face-to-face interviews by well-trained nursing staff. Data on health behavior variables such as smoking, alcohol intake, menopause, and comorbidity diseases was collected using a self-questionnaire. The anthropometric variables were measured to obtain information on body weight (kg) and height (cm). Blood pressure (BP) measurements were evaluated using an electronic sphygmomanometer. Serum lipid profiles [Triglycerides (TG), Cholesterol, High-density lipoprotein (HDL-C), and Low-density lipoprotein (LDL-C)] were analyzed by the automatic biochemical analyzer (Abbott CI 8200, United States). Fasting plasma glucose (FPG) was measured from each subject after overnight fasting.

Definitions

Body mass index (BMI) was calculated and was defined into five groups (Underweight as BMI <18.5 kg/m^2, Normal as BMI 18.50-22.99, Overweight as BMI 23-24.99 kg/m^2, Obesity as BMI 25.00-29.99 kg/m^2, and Severe obesity as BMI over 30 kg/m^2) (12, 28). HUA was measured as a serum uric acid levels (SUA) over 7.0 mg/dL in males and over 6.0 mg/dL in females (29,30). High BP was measured by BP as over 130/85 mmHg or the use of hypertension medication (29,30). Hypertriglyceridemia was measured as a TG value over 150 mg/dl. Low HDL-C was measured as HDL-C value < 40 mg/d in males and < 50 mg/d in females (29,30). High FPG was measured as glucose over 100 mg/dl or taking diabetic medication (29,30).

Statistical analyses

Descriptive statistics were utilized to present the baseline characteristics of the study participants. Continuous data were summarized using means and standard deviations (SD), while categorical data were reported as frequencies and numbers. The Mann-Whitney U test was employed to examine the differences in SUA levels between males and females. The Kruskal Wallis test was used to compare the variations in SUA levels among different age groups and obesity groups. Furthermore, the age-standardized prevalence rates of HUA were calculated using the direct method (31). The relationship between high-risk factors and HUA was assessed using a multiple logistic regression model, adjusted for age, smoking, alcohol consumption, antihypertensive medication, antidiabetic medication, and lipid-lowering medication. The covariate variables that had a *P*-value less than 0.20 in the univariable analysis found significant in the previous study were included in the initial multivariable analysis. The goodness of model fit was assessed using the area under the receiver operating characteristic (ROC) curve and the Hosmer-Lemeshow test. A *P*-value of less than 5% was considered statistically significant. All statistical analyses were performed using STATA version 14 software.

Results

Overall, 780 subjects aged more than 40 yr were included in this present study. About 70% of the subjects were females, and more than 70% received an elementary education and below. The majority (72%) of the subjects were married, and more than half (57%) were agriculturists. The subjects have an income of 8000 baht a month and above. In addition, a larger proportion (71%) of the subjects had universal health coverage. The demographic characteristics of subjects were similar between male and female subjects (Table 1). In this population, health behavior factors, anthropometric data, and metabolic parameters by gender are shown in Table 2.

Table 1: Demographic and clinical characteristics of participants

Variables	*Overall (n = 780)*	*Women (n = 548)*	*Men (n = 232)*
Age (yr), mean (SD)	52.60(7.84)	52.48(7.44)	52.87(8.72)
Marital Status, n (%)			
Single	113(14.49)	84(15.33)	29(12.50)
Married	560(71.79)	372(67.88)	188(81.03)
Widowed	58(7.44)	56(10.22)	2(0.86)
Separated	49(6.28)	36(6.57)	13(5.60)
Education levels, n (%)			
Elementary education and below	542(69.49)	402(73.36)	140(60.34)
Middle/high school	161(20.64)	98(17.88)	63(27.16)
College and higher	77(9.87)	48(8.76)	29(12.50)
Type of occupation, n (%)			
Unemployed	63(8.08)	38(6.93)	25(10.78)
Professional & technical	112(14.36)	70(12.77)	42(18.10)
Sale & service	164(21.03)	93(16.97)	71(30.60)
Agriculture	441(56.54)	347(63.32)	94(40.52)
Income (Baht/month), median (IQR)	8,000 (5,000-12,000)	8,000 (5,000-10,000)	10,000 (6,000-15,000)
Health payment systems, n (%)			
No Health Insurance	9(1.15)	5(0.91)	4(1.72)
Universal health coverage	553(70.90)	389(70.99)	164(70.69)
Social security scheme	186(23.85)	130(23.72)	56(24.14)
Civil servant medical benefit scheme	32(4.10)	24(4.38)	8(3.45)
Comorbidities, n (%)			
HT+DLP	76(9.74)	56(10.22)	20(8.62)
Dyslipidemia (DLP)	71(9.10)	50(9.12)	21(9.05)
Hypertension (HT)	45(5.77)	33(6.02)	12(5.17)
DM+HT+DLP	35(4.49)	29(5.29)	6(2.59)
DM+DLP	14(1.79)	7(1.28)	7(3.02)
Diabetes mellitus(DM)	11(1.41)	9(1.64)	2(0.86)
DM+HT	7(0.90)	6(1.09)	1(0.43)

Table 2: Health behavior factors and anthropometric data of participants

Variables	*Overall (n = 780)*	*Women (n = 548)*	*Men (n = 232)*
Current smokers, n (%)	40(5.13)	4(0.73)	36(15.52)
Former smokers, n (%)	69(8.85)	7(1.28)	62(26.72)
Current alcohol intake, n (%)	55(7.05)	28(5.11)	27(11.64)
Former alcohol intake, n (%)	85(10.90)	23(4.20)	62(26.72)
Weight (kg), mean(SD)	63.94(13.21)	62.33(12.74)	68.37(13.50)
BMI (kg/m^2), mean(SD)	25.55(5.88)	25.96(6.36)	24.43(4.10)
SBP (mmHg), mean(SD)	133.53(17.20)	133.36(17.56)	134.04(16.21)
DBP (mmHg), mean(SD)	78.11(14.54)	77.39(14.51)	80.06(14.49)
Cholesterol (mg/dL), mean(SD)	212.86(41.06)	214.41(41.27)	209.18(40.40)
Triglycerides (mg/dL), mean(SD)	137.21(80.76)	129.89(71.14)	154.51(97.90)
HDL (mg/dL), mean(SD)	53.68(13.36)	55.40(13.20)	49.64(12.89)
LDL (mg/dL), mean(SD)	132.81(37.71)	134.32(38.07)	129.24(36.68)
FPG (mg/dL), mean(SD)	104.81(31.56)	103.23(29.24)	108.54(36.25)

BMI body mass index, DBP diastolic blood pressure, FPG fasting plasma glucose, HDL high density lipoprotein, LDL low density lipoprotein, SD standard deviation, SBP systolic blood pressure

The present results revealed that SUA was higher in males than in females. Comparing SUA levels by gender and age groups, there is no significant difference in serum uric acid in overall and gender-stratified subjects (Table 3). In contrast, a significant difference in SUA levels was found in obesity and severe obesity subjects when compared to underweight and normal-weight subjects (Fig. 1A). Furthermore, the obese subjects had higher SUA levels than the underweight and normal-weight subjects of both sexes (Fig. 1B-C).

Table 3: Mean serum uric acid level according to gender and age

Factors	***Serum uric acid levels (mg/dl), mean (SD)***					
	Overall	*P*-value	Women	*P*-value	Men	*P*-value
Total	5.65(1.44)		5.19(1.15)		6.74(1.47)	<0.0001
Age group		0.4403		0.0802		0.3108
40-44	5.69(1.56)		5.01(1.18)		6.96(1.40)	
45-49	5.51(1.52)		5.03(1.14)		6.88(1.66)	
50-54	5.70(1.40)		5.25(1.11)		6.78(1.44)	
55-59	5.69(1.49)		5.25(1.20)		6.80(1.59)	
60-64	5.62(1.13)		5.39(1.09)		6.34(0.97)	
65+	5.72(1.24)		5.39(1.14)		6.16(1.25)	

SD standard deviation

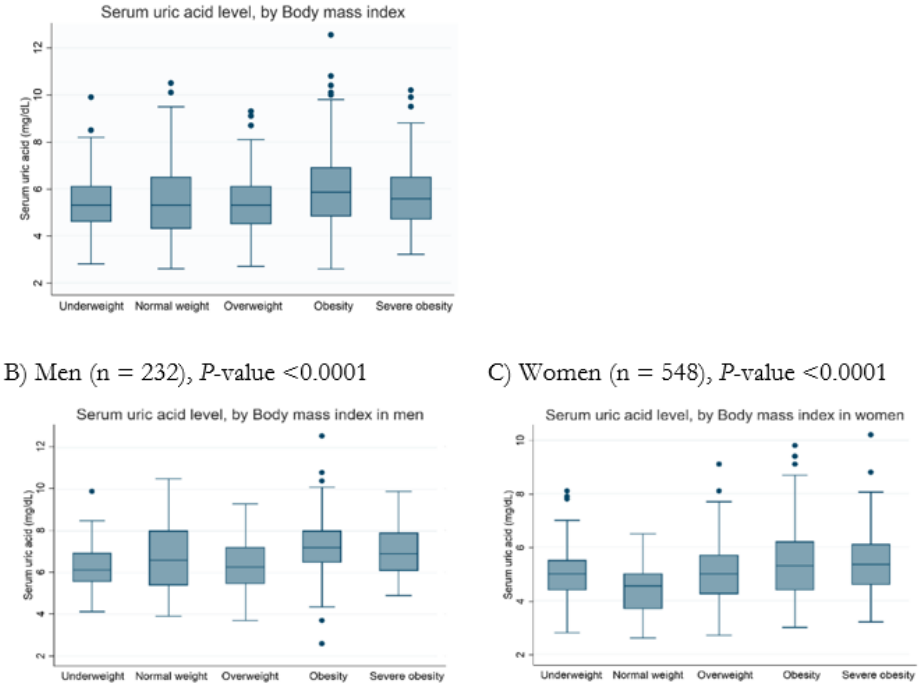

Fig. 1: Level of serum uric acid in different BMI (kg/m²) categories

The overall prevalence rate of HUA was 31% (95% CI 29.5-32.3). The prevalence rate adjusted for age of the standard population in males was higher than that of females (42 % (95% CI 36.4-47.1) vs. 20% (95% CI 20.0-20.1)) (Fig. 2). Obesity and male subjects were strongly associated with HUA among middle-aged and elderly adults (Table 4). The logistic regression analysis revealed that only elderly people older than 60 yr were associated with a 35% increased risk of HUA. In addition, high fasting glucose, hypertriglyceridemia, and low HDL also increased the prevalence of HUA. In a subgroup analysis, older subjects of age over 60 yr were with higher odds of having HUA in females, whereas older age was positively associated with HUA in males. However, being underweight was associated with HUA only in males, whereas low HDL-C was significantly associated with HUA only in females. In both sexes, the results revealed that subjects who were obese were at higher risk of HUA than those with normal body weight. The association remained consistent among high FPG, and hypertriglyceridemia subjects.

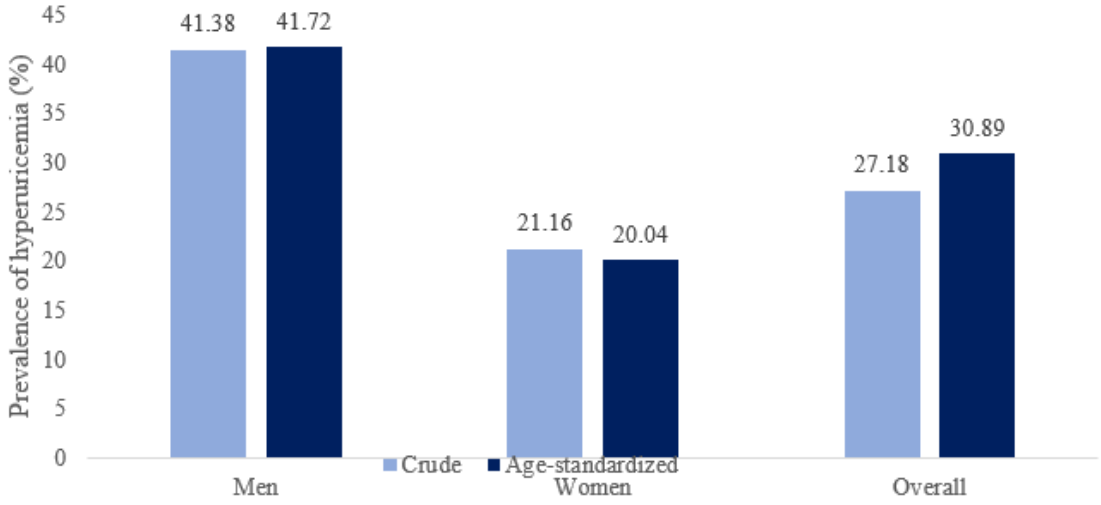

Fig. 2: The age-standardized prevalence of hyperuricemia in the middle-aged and elderly population

Table 4: The odds ratios for the presence of hyperuricemia according to gender

Factors	*Overall*		*Men (n = 232)*		*Women (n = 548)*	
	COR (95%CI)	AOR (95%CI)	COR (95%CI)	AOR (95%CI)	COR (95%CI)	AOR (95%CI)
Men	2.36(1.70-3.28)*	2.93(2.03-4.21)*	-	-	-	-
Age (Year)						
50-59	1.16(0.82-1.64)	1.25(0.85-1.85)	0.73(0.41-1.29)	0.97(0.50-1.89)	1.59(1.01-2.51)	1.46(0.88-2.42)
60+	1.27(1.10-2.01)*	1.35(1.08-2.28)*	1.58(1.27-1.26)*	1.74(1.29-1.83)*	2.00(1.11-3.61)*	2.00(1.04-3.84)*
Education						
Secondary education	0.96(0.53-1.75)	0.83(0.44-1.60)	0.70(0.29-1.69)	0.64(0.25-1.66)	1.28(0.52-3.17)	1.02(0.39-2.66)
Primary	0.91(0.54	0.80(0.44	0.58(0.26	0.74(0.29	1.61(0.73-	0.83(0.35

Table 4: Continued…

education	-1.54)	-1.46)	-1.31)	-1.86)	3.56)	-1.98)
Body mass index (kg/m²)						
Under-weight	1.47(0.81 -2.66)	1.41(0.72 -2.76)	2.37(1.04 -5.42)*	2.96(1.08 -8.12)*	0.48(0.15-1.51)	0.53(0.16 -1.73)
Overweight	1.08(0.63 -1.85)	1.19(0.68 -2.08)	1.19(0.48 -3.03)	1.43(0.53 -3.85)	1.12(0.57-2.19)	1.08(0.54 -2.16)
Obesity	2.54(1.67 -3.86)*	2.75(1.75 -4.33)*	3.92(1.94 -7.92)*	4.36(2.00 -9.56)*	2.31(1.35-3.96)*	2.16(1.22 -3.80)*
High fasting glucose	1.39(1.02 -1.90)*	1.21(1.16 -1.71)*	1.99(1.52 -3.88)*	1.90(1.05 -2.64)*	1.63(1.09-2.40)*	1.49(1.04 -2.31)*
Hypertriglyc-eridemia	1.66(1.21 -2.27)*	1.32(1.29 -1.89)*	2.06(1.07 -3.93)*	1.51(1.08 -2.81)*	1.61(1.08-2.46)*	1.23(1.07 -1.93)*
Low HDL	1.48(1.05 -2.09)*	1.58(1.08 -2.31)*	1.55(0.80 -3.01)	1.40(0.74 -2.67)	1.66(1.05-2.62)*	1.67(1.02 -2.76)*
High Blood Pressure	1.08(0.76 -1.51)	0.72(0.49 -1.05)	1.48(1.24 -1.96)	0.37(0.18 -0.79)	1.14(0.54-1.75)	0.88(0.55 -1.40)

AOR adjusted for age, smoking, alcohol consumption, antihypertensive medication, antidiabetic medication, and lipid-lowering medication, COR crude odds ratio, HDL high density lipoprotein, 95%CI 95% confidence intervals.
*P-value <0.001, Hosmer-Lemeshow test = 0.5383, receiver operating characteristic (ROC) curve = 0.72765 (72.77%)

Discussion

This present study indicated that the age-standardized prevalence rates of HUA were high estimated at 30.9% and were found in males more frequently than females (41.7% in males and 20% in females). The rates of HUA among elderly individuals in Thailand were found to be lower compared to the rates observed among elderly individuals in Taiwan (36% overall, 46% in males, and 26% in females) (32), as well as in China (15.6-32.3% overall, 23.2-39.6% in males, and 7.8-10.7% in females) (33-35). However, the present results found that the prevalence of HUA was higher than that of the elderly agricultural and fishing adults in Taiwan (30.4% overall, 30.2% in males, and 30.6% in females) (29). The results of this study consistent with previous study that found a higher prevalence of hyperuricemia (HUA) in males (14.9%) compared to females (8.9%) among rural residents in Khon Kaen, Thailand (20). Furthermore, the prevalence rates tend to be significantly higher in individuals aged 50 yr and above (34-37). Furthermore, the present results revealed that the prevalence rates of HUA in middle-aged and elderly adults (30.9%) were higher than that shown in general adults in Japan (26.8% in males and 0.9% in females) (9), India (25.8%) (11), Thailand (urban areas; 24.4%) (13), America (21.4%) (6), Italy (11.9%) (38), and China (11.3-15.1%) (18, 39,40). The differences in ethnicities such as genetic factors, geographical variables, and demographic and lifestyle factors (13-15, 20-23) were probably the main contributors to the differences in prevalence rates of HUA. However, the meta-analysis suggested that gender, middle-aged, residents who dwell in urban or rural areas, and economic level may be associated with HUA (24). In Western countries, the prevalence rate of HUA increased with age (6, 38, 41). However, the prevalence rates decreased in adults at the age of 60 yr and then increased between them the age of 70 to 80 yr (8, 42). Furthermore, the inconsistent threshold for HUA could have also caused these differences in previous studies.

The present study indicated a significant association between hypertriglyceridemia, high FPG, and HUA in both sexes, whereas low HDL-C level was correlated with HUA only in females. Consistent with other studies, the authors found a correlation between HUA and metabolic pa-

rameters (hypertriglyceridemia, high FPG, and low HDL-C level) in previous study populations (19, 29). The metabolic syndrome parameters increased the prevalence rates and also significantly increased uric acid activity (30,43,44). Although serum uric acid is associated with metabolic syndrome (45), which leads to the two disorders, the mechanisms of this syndrome remain unknown.

In addition, the present study revealed that elderly obese subjects were at higher risk of HUA than those with normal body weights in both sexes. SUA concentration is correlated with serum leptin concentration (46,47). Serum leptin could be a pathogenic determinant responsible for HUA in obese subjects. Furthermore, this could be a result of the increase in Xanthine oxidoreductase (XOR) in obese subjects (48). The present results also indicated that older females had a higher risk of HUA than older males. The increase in the risk of HUA among elderly females may be described by postmenopausal changes in the endocrine system and the loss of the uricosuric action of estrogen levels (43). However, HUA was still a men-dominated disease as demonstrated in the present results. The present results are consistent with the findings of the previous hospital- and community-based studies for general and occupational adults (29, 43, 49).

The present study has some limitations, considered. First, the screened middle-aged and elderly adults were enrolled from only a single area. This selection bias may have affected the evaluated prevalence rates of HUA and its related high-risk factors. Second, the subjects in this present study might have individualities differing from those of Thai adults. These populations are more susceptible to HUA than other populations in Thailand. Third, some not eligible participants and/or non-respondents who did not return for biochemical tests may have had more prevalent HUA; thus, the prevalence rates of HUA may have been underestimated. Fourth, measurements in this present study were measured at a single time point. Thus, the authors cannot be used to reflect the effects of long-term exposure to the various high-risk factors of critically affect HUA. Longitudinal studies are required, the findings of which may complement the results of this current study. Finally, only a limited number of possible associated high-risk factors were included for multiple logistic regression analysis. Because of the availability of information, the effects of some well-proven related HUA such as food consumption, alcohol consumption, diuretic use, and smoking could not be assessed.

Conclusion

This study indicated a high prevalence of HUA in middle-aged and elderly males. Obesity is increased with HUA in males, whereas obesity and old age are increased with HUA in females. Additionally, metabolic syndrome components such as hypertriglyceridemia and high fasting glucose are associated with HUA in this study, but only low high-density lipoprotein is associated with HUA in females. However, longitudinal cohort studies are warranted to confirm causality.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interests

The authors have no conflict of interest to declare.

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