BMJ Open Prevalence and related factors of hyperuricaemia in Shanghai adult women of different ages: a multicentre and cross-sectional study

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ABSTRACT

Objective Women in different age phases have different metabolism and hormone levels that influence the production and excretion of uric acid. We aimed to investigate the prevalence and related factors of hyperuricaemia among women in various age phases.

Study design Observational, cross-sectional study.

Setting Data were obtained from women at three health check-up centres in Shanghai.

Participants Adult women from three health check-up centres were recruited. Exclusion criteria were individuals with pregnancy, cancer, incomplete information. Finally, 11 601 participants were enrolled.

Results The prevalence rates of hyperuricaemia of total subjects were 11.15% (95% CIs 10.57% to 11.72%). The prevalence of hyperuricaemia in 18–29, 30–39, 40–49, 50–59, 60–69 and ≥70 years old was 6.41% (95% CI 4.97% to 7.86%), 5.63% (4.71% to 6.55%), 6.02% (5.01% to 7.03%), 11.51% (10.19% to 12.82%), 16.49% (15.03% to 17.95%) and 23.98% (21.56% to 26.40%), respectively. Compared with 18–29 years old, the ORs for hyperuricaemia in other age phases were 0.870 (95% CI 0.647 to 1.170, $p=0.357$), 0.935 (0.693 to 1.261, $p=0.659$), 1.898 (1.444 to 2.493, $p<0.001$), 2.882 (2.216 to 3.748, $p<0.001$) and 4.602 (3.497 to 6.056, $p<0.001$), respectively. During the 18–29 years old, the related factors for hyperuricaemia were obesity and dyslipidaemia. During the 30–59 years old, the related factors were obesity, dyslipidaemia, hypertension and chronic kidney disease (CKD). Over the 60 years old, the occurrence of hyperuricaemia was mainly affected by obesity, dyslipidaemia and CKD, while hypertension cannot be an impact factor for hyperuricaemia independently of obesity and dyslipidaemia.

Conclusion After 50 years old, the prevalence of hyperuricaemia in Shanghai women has increased significantly and reaches the peak after 70. Obesity and dyslipidaemia are two main related factors for hyperuricaemia during all ages, while diabetes mellitus and nephrolithiasis have no relationship with hyperuricaemia throughout. CKD is an independent impact factor for hyperuricaemia after 30 years old.

INTRODUCTION

Uric acid is the end product of purine metabolism in human body, which is produced

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ We conducted a multicentre study with large sample size, which ensured sufficient power in obtaining the accurate prevalent rate and related factors of hyperuricaemia.
- ⇒ The prevalence of hyperuricaemia, obesity, hypertension, diabetes mellitus, dyslipidaemia, chronic kidney disease, nephrolithiasis as well as related factors of hyperuricaemia was analysed in various age phases.
- ⇒ It was a cross-sectional study and the results could not identify the causative relationship between hyperuricaemia and other metabolic and renal disorders.
- ⇒ The data were from three databases of check-up centres that lacked details in pharmacotherapy, menopausal status, economic, lifestyles and diet, which might affect the deviations of some clinical outcomes.

mainly in the liver and intestines while excreted mostly in the kidney.¹ Xanthine oxidoreductase catalyses two enzymatic reactions, hypoxanthine to xanthine and xanthine to uric acid.² Several conditions can increase the concentration of serum uric acid (SUA) and occurrence of hyperuricaemia (HUA), including increased uric acid production, for example purine-rich food intake and cytotoxic drugs, and decreased uric acid excretion, for example chronic kidney disease (CKD).^{1–3}

In patients with HUA, deposition of urate in joints and kidney promotes the development of gouty arthritis and uric acid nephrolithiasis.^{4 5} Uric acid also causes oxidative stress, inflammation and endothelial dysfunction in a crystal-independent way.¹ Besides that, there is a growing body of evidence to show that HUA or elevated SUA level is associated with obesity, hypertension and cardiovascular disease in the group of adult and elderly

people.^{6–9} Some observational studies also confirmed that increased SUA levels promote the development of CKD, especially in children and adolescents.^{10 11} Although a quite of epidemiological studies have investigated the risk factors of HUA or increased SUA in general people or elderly even children, few studies focus on these relationship among women under different years old. Affected by menstrual cycle, menopause or taking oestrogen, hormones are fluctuant in women of different ages, while this fluctuating hormone level may influence the body fat distribution and metabolic system.^{12 13} Thus, it is necessary to know the relationship between SUA and metabolic disorders such as obesity, hypertension, diabetes mellitus and dyslipidaemia, in woman under the different ages.

This study was aimed to investigate the prevalence of HUA in the women of different ages. The data were from subjects in multiple centres of Shanghai. We also focused on the potential effect of ages on the association between SUA and metabolic and renal disorders in women during all age phages.

METHODS

Study population

A total of 13 001 women aged between 18 and 98 years from three health check-up centres (Shanghai East Hospital Affiliated to Tongji University School of Medicine, Pudong New District Gongli Hospital and Baoshan Branch of Shanghai First People's Hospital) were recruited from June 2015 and December 2018. Studies on human subjects were conducted in accordance with the Declaration of Helsinki. They waived the need for participant consent. We excluded subjects with pregnancy, cancer, incomplete information. Finally, 11 601 participants were enrolled in our study. We divided the woman participants into six groups according to ages (group I: 18–29 years old, group II: 30–39 years old, group III: 40–49 years old, group IV: 50–59 years old, group V: 60–69 years old, group VI: ≥70 years old).

Primary and secondary outcome measures

HUA was defined as $\text{SUA} \geq 6 \text{ mg/dL}$ for women.¹⁴ The prevalence of HUA as well as its relationships with metabolic, renal disorders were assessed according to different age status (18–29, 30–39, 40–49, 50–59, 60–69, ≥70 years old).

Measurements and definition

Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). According to WHO guidelines for the Asian Pacific population, normal weight was defined as $18.5 \leq \text{BMI} < 24.0 \text{ kg/m}^2$, underweight was defined as $\text{BMI} < 18.5 \text{ kg/m}^2$, overweight and obesity were defined as $24.0 \leq \text{BMI} < 28.0 \text{ kg/m}^2$ and $\text{BMI} \geq 28.0 \text{ kg/m}^2$, respectively.¹⁵ Blood pressure (BP) measurements were taken according to the Joint National Committee VII criteria.¹⁶ Normal BP was defined as an systolic blood pressure (SBP) $< 120 \text{ mm Hg}$ and diastolic blood pressure

(DBP) $< 80 \text{ mm Hg}$. Prehypertension was defined as an SBP of 120–139 mm Hg and/or DBP of 80–89 mm Hg. Grade 1 hypertension was defined as an SBP of 140–159 mm Hg and/or DBP of 90–99 mm Hg. Grade 2 or grade 3 hypertension was defined as an SBP $\geq 160 \text{ mmHg}$ and/or DBP $\geq 100 \text{ mm Hg}$.¹⁶ According to the Chinese adult dyslipidaemia prevention guide (2007 edition), individuals with a fasting total cholesterol (TC) $\geq 6.22 \text{ mmol/L}$, triglyceride (TG) $\geq 2.26 \text{ mmol/L}$, high-density lipoprotein cholesterol (HDL-C) $< 1.04 \text{ mmol/L}$ and/or low-density lipoprotein cholesterol (LDL-C) $> 4.14 \text{ mmol/L}$ or currently undergoing pharmacologic treatment were defined as the dyslipidaemia.¹⁷ Type 2 diabetes was defined based on WHO 1999 diagnostic criteria as fasting plasma glucose (FPG) $\geq 7.0 \text{ mmol/L}$ or 2-hour plasma glucose $\geq 11.1 \text{ mmol/L}$, impaired fasting glucose (IFG) was defined as $6.1 \text{ mmol/L} \leq \text{FPG} < 7.0 \text{ mmol/L}$, and normal condition was defined as $\text{FPG} < 6.1 \text{ mmol/L}$.¹⁸ The estimated glomerular filtration rate (eGFR) was calculated using Modification of Diet in Renal Disease formula¹⁹: $186 \times (\text{serum creatinine (mg/dL)})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ (if woman)})$. According to the Kidney Disease Outcomes Quality Initiative clinical practice guideline, $\text{eGFR} < 60 \text{ mL/min/1.73 m}^2$, proteinuria and haematuria were defined as CKD.²⁰ Urine proteinuria were recorded as negative (–), trace, 1+, 2+ and 3+. Albuminuria was defined as $\geq 1+$.

Data collection

The participants attended to the medical centre in the morning after overnight fasting for at least 8 hours. After 5 min resting, sitting blood pressure was measured in right arm by an electronic blood pressure monitor. Mean value of the three records was used in the analysis. Midstream urine specimen was collected for urinary analysis by the dipstick method. Urine pH and proteinuria were recorded as categorical data. Laboratory reagents were purchased from Nanjing Jiancheng Bioengineering Institute (Nanjing, China). Venous Blood samples were drawn from all subjects and quickly centrifuged at room temperature. SUA was determined using the uricase-peroxidase method. Other biochemical indexes were analysed as described previously.²¹ Basic characteristics were collected by medical staffs. Anthropometric data including height and weight were measured according to a standardised protocol. Renal ultrasonography scanning was performed by an experienced radiologist using GE LOGIQ P5 scanner (GE Healthcare, Milwaukee, USA).

Patient and public involvement

Patients and the public were not involved in any aspects of the study, including the development of study question, study design, conduct of the study and dissemination of results.

Statistical analysis

All the statistical analyses were carried out using IBM SPSS statistics V.22.0. The continuous variables with a normal

Table 1 Clinical characteristics of women in different age groups

	Total women	Group I 18–29 years old	Group II 30–39 years old	Group III 40–49 years old	Group IV 50–59 years old	Group V 60–69 years old	Group VI over 70 years old	P value
N (%)	11 601 (100.0%)	1107 (9.5%)	2417 (20.8%)	2126 (18.3%)	2268 (19.6%)	2486 (21.4%)	1197 (10.3%)	–
Biochemical variables								
Age (years)	50.08±15.29	26.56±2.07	34.34±2.75***	44.55±2.85***	54.69±2.85***	63.95±2.73***	75.92±5.19***	<0.001
BMI (kg/m ²)	23.41±3.54	21.18±2.99	22.11±3.22***	23.27±3.14***	24.15±3.34***	24.51±3.49***	24.66±3.90***	<0.001
SBP (mm Hg)	125.01±20.09	111.12±11.12	112.40±12.18**	118.14±15.44***	128.43±18.04***	136.31±18.75***	145.59±20.89***	<0.001
DBP (mm Hg)	75.36±11.19	69.49±8.72	71.16±9.57***	74.09±11.08***	78.31±11.16***	79.27±10.89***	77.84±11.62***	<0.001
FPG (mmol/L)	5.19±1.21	4.70±0.53	4.78±0.74***	4.93±0.77***	5.36±1.38***	5.61±1.45***	5.79±1.53***	<0.001
TC (mmol/L)	4.85±0.95	4.33±0.77	4.39±0.79*	4.65±0.82***	5.14±0.92***	5.27±0.96***	5.16±0.98***	<0.001
TG (mmol/L)	1.27±0.95	0.88±0.60	0.95±0.57**	1.14±0.85***	1.47±1.17***	1.58±1.06***	1.53±0.92***	<0.001
HDL-C (mmol/L)	1.49±0.35	1.55±0.34	1.53±0.35*	1.49±0.34***	1.47±0.35***	1.46±0.35***	1.45±0.36***	<0.001
LDL-C (mmol/L)	2.91±0.81	2.53±0.69	2.59±0.70**	2.80±0.72***	3.14±0.81***	3.19±0.83***	3.08±0.87***	<0.001
eGFR (ml/(min*1.73m ²))	96.19±24.28	112.84±25.98	103.31±22.68***	98.39±22.82***	94.95±22.86***	89.24±21.46***	79.28±20.64***	<0.001
Cr (umol/L)	64.36±15.04	61.70±11.77	63.37±11.35***	63.68±20.93***	63.34±12.99***	65.01±13.55***	70.61±16.62***	<0.001
BUN (mmol/L)	4.91±1.35	4.28±1.05	4.42±1.03***	4.53±1.24***	5.15±1.24***	5.36±1.32***	5.82±1.66***	<0.001
SUA (mmol/L)	280.15±66.38	270.72±56.07	264.44±58.42**	261.87±58.41***	285.43±63.69***	295.05±69.47***	312.09±80.24***	<0.001
Comorbidities								
Hyperuricaemia (n, %)	1293 (11.1%)	71 (6.4%)	136 (5.6%)	128 (6.0%)	261 (11.5%)***	410 (16.5%)***	287 (24.0%)***	<0.001
Obesity (n, %)	1179 (10.2%)	40 (3.6%)	128 (5.3%)	163 (7.7%)***	268 (11.8%)***	365 (14.7%)***	215 (18.0%)***	<0.001
Hypertension (n, %)	2869 (24.7%)	29 (2.6%)	111 (4.6%)**	266 (12.5%)***	670 (29.5%)***	1088 (43.8%)***	705 (58.9%)***	<0.001
Diabetes mellitus (n, %)	572 (4.9%)	2 (0.2%)	17 (0.7%)*	31 (1.5%)***	141 (6.2%)***	228 (9.2%)***	153 (12.8%)***	<0.001
Dyslipidaemia (n, %)	2582 (22.3%)	85 (7.7%)	260 (10.8%)**	331 (15.6%)***	651 (28.7%)***	869 (35.0%)***	386 (32.2%)***	<0.001
CKD (n, %)	354 (3.1%)	1 (0.1%)	7 (0.3%)	14 (0.7%)*	45 (2.0%)***	96 (3.9%)***	191 (16.0%)***	<0.001
Nephrolithiasis (n, %)	1433 (12.4%)	63 (5.7%)	202 (8.4%)**	239 (11.2%)***	314 (13.8%)***	412 (16.6%)***	203 (17.0%)***	<0.001

The continuous variables are reported in means±SD and categorical variables are presented in percentages. In case of non-parametric data distribution, medians with IQR are presented. *p<0.05, **p<0.01, ***p<0.001 versus the Group I. As for the post-hoc test of normally distributed data, we used least significance difference test if the variance was homogeneous, and we used Tamhane's T2 test if not. Non-normally distributed data were compared using Kruskal-Wallis test. As for the post-hoc test of categorical variables, we used χ^2 tests. BMI, body mass index; BUN, blood urea nitrogen; CKD, chronic kidney disease; Cr, creatinine; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

Figure 1 The prevalence of metabolic disorders and kidney diseases.

distribution were described by means $\pm$ SD and categorical variables were presented in frequency and percentage. In case of non-parametric data distribution, medians with IQR were presented. The univariate analysis of variance was performed to measure the data among the groups or a Kruskal-Wallis test in case of non-parametric data distribution. χ^2 test was used to calculate the differences between categorical variables. If the results showed differences between the groups, the post-hoc tests would be done. As for the post-hoc test, we used least significance difference test, if the variance was homogeneous, and we used Tamhane's T2 test if not. Considering that SUA, age, BMI, SBP, DBP, FPG, TC, TG, HDL-C, LDL-C, eGFR were normally distributed in this study, Pearson's correlation test was used to assess the correlation between two variables. Multivariable logistic regression analysis was used

to calculate the OR for HUA according to different age status. Two-tailed probability values <0.05 were considered statistically significant.

RESULTS

Clinical characteristics of female participants in different age groups

There were a total of 11 601 female participants with a mean age of 50.08 ± 15.29 years old. The prevalence rates of HUA of total subjects were 11.15% (95% CIs 10.57% to 11.72%). The prevalence of HUA in group I (18–29 years old), group II (30–39 years old), group III (40–49 years old), group IV (50–59 years old), group V (60–69 years old) and group VI (≥ 70 years old) were 6.41% (95% CI 4.97% to 7.86%), 5.63% (4.71% to 6.55%), 6.02%

Table 2 Correlation coefficients between SUA and various clinical parameters in different age groups of women

Variable	Group I (18–29 years old)		Group II (30–39 years old)		Group III (40–49 years old)		Group IV (50–59 years old)		Group V (60–69 years old)		Group VI (over 70 years old)	
	r	P value	r	P value	r	P value	r	P value	r	P value	r	P value
BMI (kg/m ²)	0.345	<0.001	0.332	<0.001	0.277	<0.001	0.248	<0.001	0.282	<0.001	0.273	<0.001
SBP (mm Hg)	0.098	0.001	0.184	<0.001	0.165	<0.001	0.141	<0.001	0.087	<0.001	0.072	0.012
DBP (mm Hg)	0.054	0.074	0.170	<0.001	0.193	<0.001	0.141	<0.001	0.060	0.003	0.018	0.527
FPG (mmol/L)	0.048	0.113	0.087	<0.001	0.153	<0.001	0.027	0.192	0.033	0.099	0.039	0.182
TC (mmol/L)	0.126	<0.001	0.190	<0.001	0.175	<0.001	0.135	<0.001	0.050	0.012	0.041	0.156
TG (mmol/L)	0.267	<0.001	0.348	<0.001	0.305	<0.001	0.275	<0.001	0.290	<0.001	0.252	<0.001
HDL-C (mmol/L)	–0.201	<0.001	–0.200	<0.001	–0.283	<0.001	–0.247	<0.001	–0.263	<0.001	–0.302	<0.001
LDL-C (mmol/L)	0.188	<0.001	0.241	<0.001	0.190	<0.001	0.123	<0.001	0.033	0.097	0.062	0.031
eGFR (mL/(min*1.73m ²))	–0.049	0.100	–0.081	<0.001	–0.084	<0.001	–0.140	<0.001	–0.131	<0.001	–0.330	<0.001

BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

Table 3 The OR for hyperuricaemia according to different status of parameters of women in different age groups (Group I–III)

	Group I (18–29 years old)		Group II (30–39 years old)		Group III (40–49 years old)	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
BMI (kg/m ²)						
18.5≤BMI<24.0 (Ref.)						
BMI <18.5	0.415 (0.122 to 1.411)	0.159	0.920 (0.375 to 2.260)	0.856	1.093 (0.251 to 4.765)	0.905
24.0≤BMI<28.0	4.061 (2.101 to 7.849)	<0.001	3.237 (2.074 to 5.054)	<0.001	2.241 (1.448 to 3.469)	<0.001
BMI≥28.0	9.477 (4.180 to 21.486)	<0.001	4.891 (2.673 to 8.951)	<0.001	3.037 (1.638 to 5.632)	<0.001
Blood pressure (mm Hg)						
Normotensive (Ref.)						
Pre-HT	1.487 (0.823 to 2.684)	0.188	1.189 (0.774 to 1.827)	0.430	0.974 (0.623 to 1.521)	0.907
Grade1 HT	1.701 (0.498 to 5.811)	0.397	1.694 (0.782 to 3.668)	0.181	1.582 (0.882 to 2.837)	0.124
Grade 2/3 HT	13.906 (0.761 to 254.245)	0.076	5.733 (1.736 to 18.938)	0.004	2.062 (0.881 to 4.823)	0.095
FPG (mmol/L)						
FPG <6.1 (Ref.)						
6.1≤FPG<7.0	5.191 (0.141 to 191.013)	0.371	5.827 (2.052 to 16.549)	0.001	1.062 (0.379 to 2.970)	0.909
FPG≥7.0	–	–	1.598 (0.426 to 5.991)	0.487	0.637 (0.172 to 2.364)	0.500
Cholesterol (mmol/L)						
TC ≤6.22 (Ref.)						
TC >6.22	5.220 (0.311 to 87.682)	0.251	0.434 (0.101 to 1.869)	0.263	1.388 (0.504 to 3.824)	0.526
Triglyceride (mmol/L)						
TG ≤2.26 (Ref.)						
TG >2.26	6.720 (2.131 to 21.191)	0.001	3.534 (1.904 to 6.562)	<0.001	1.381 (0.765 to 2.495)	0.284
HDL-C (mmol/L)						
HDL-C ≥1.04 (Ref.)						
HDL-C <1.04	1.841 (0.709 to 4.780)	0.210	2.172 (1.230 to 3.834)	0.007	3.937 (2.348 to 6.601)	<0.001
LDL-C (mmol/L)						
LDL-C ≤4.14 (Ref.)						
LDL-C >4.14	–	–	2.265 (0.762 to 6.735)	0.142	1.608 (0.599 to 4.317)	0.346
eGFR (mL/(min*1.73 m ²))						
eGFR ≥90 (Ref.)						
60≤eGFR≤89	1.698 (0.883 to 3.265)	0.112	2.097 (1.392 to 3.158)	<0.001	2.057 (1.374 to 3.079)	<0.001
eGFR ≤59	–	–	25.866 (3.719 to 179.914)	0.001	18.045 (5.201 to 62.602)	<0.001
Albuminuria						
± (Ref.)						
+	–	–	–	–	2.020 (0.254 to 16.078)	0.506
++	–	–	4.558 (0.463 to 44.879)	0.194	1.118 (0.169 to 7.400)	0.908
+++	–	–	0.679 (0.029 to 15.939)	0.810	6.224 (0.654 to 59.223)	0.112
Urinary pH						
6≤pH≤7 (Ref.)						
pH <6	1.392 (0.777 to 2.495)	0.266	2.099 (1.352 to 3.258)	0.001	2.308 (1.530 to 3.482)	<0.001
pH >7	0.235 (0.030 to 1.858)	0.170	1.191 (0.492 to 2.882)	0.698	0.374 (0.089 to 1.566)	0.178
Nephrolithiasis						
No (Ref.)						
Yes	1.115 (0.419 to 2.962)	0.828	1.001 (0.533 to 1.880)	0.998	1.206 (0.690 to 2.108)	0.510

Blood pressure (mm Hg): normotensive: SBP <120 and DBP<80; pre-HT: SBP of 120–139 and/or DBP of 80–89; Grade 1 HT: SBP of 140–159 and/or DBP of 90–99; Grade 2/3 HT: SBP ≥160 and/or DBP≥100.
 BMI, body mass index; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

(5.01% to 7.03%), 11.51% (10.19% to 12.82%), 16.49% (15.03% to 17.95%) and 23.98% (21.56% to 26.40%), respectively (table 1 and figure 1A). Women over 50 years old had a higher prevalence of HUA than those under 50. With increasing age, female individuals had more metabolic disease (obesity, hypertension, diabetes and dyslipidaemia) and renal diseases (CKD, nephrolithiasis) (figure 1B–G, all p values for trend <0.001) as well as elevated levels of BMI, SBP, DBP, TC, TG, LDL-C, creatinine, blood urea nitrogen (BUN) and decreased levels of HDL-C and eGFR (table 1, all p values for trend <0.001).

The correlation between SUA and various clinical parameters in different age groups of women

In this study, SUA, BMI, SBP, DBP, FPG, TC, TG, HDL-C, LDL-C, eGFR were normally distributed. Thus, Pearson's correlation test was adopted to investigate the relationships between SUA and various parameters in different age groups and the results are shown in table 2. In all age groups of women, the level of SUA was positively correlated with BMI, SBP and TG and negatively correlated with HDL-C (all p values <0.001, except SBP in group I, p=0.001 and in group VI, p=0.012). Among the women over 30, SUA was significantly negatively correlated with eGFR (all p values <0.001).

Association between HUA and different status of clinical parameters in various age groups of women

Multivariable logistic regression models (full-adjusted) were analysed, and the results are shown in tables 3 and 4, with the OR for HUA according to different status of clinical parameters. We found that after adjustment for confounders, increased levels of BMI and TG and decreased levels of HDL-C and eGFR were positively related to increased OR of HUA. However, there was no significant relationship between HUA and increased FPG, TC, LDL-C and nephrolithiasis. These results suggested that women with overweight/obesity were more susceptible to HUA in all age phases. Moreover, in the population of HUA, women with increased TG and HDL-C were more likely to suffer the HUA than those with increased TC and LDL-C. Renal insufficiency was closely related to the occurrence of HUA among the women over 30.

Relationship between HUA and metabolic, renal disorders in women during all age phases

Univariate logistic regression analysis showed that compared with 18–29 years old, the ORs for HUA in other age phases were 0.870 (95% CI 0.647 to 1.170, p=0.357), 0.935 (95% CI 0.693 to 1.261, p=0.659), 1.898 (95% CI 1.444 to 2.493, p<0.001), 2.882 (95% CI 2.216 to 3.748, p<0.001) and 4.602 (95% CI 3.497 to 6.056, p<0.001), respectively (figure 2). Multivariable logistic regression analysis for various group was studied, and the results are shown in table 5 and figure 3. The ORs for HUA in obesity for women during all age phases were 6.939 (95% CI 3.281 to 14.673, p<0.001), 3.746 (95% CI 2.239 to 6.268, p<0.001), 2.018 (95% CI 1.190 to 3.423,

p=0.009), 2.420 (95% CI 1.720 to 3.404, p<0.001), 1.907 (95% CI 1.448 to 2.511, p<0.001) and 2.319 (95% CI 1.659 to 3.243, p<0.001), respectively. The OR for HUA in dyslipidaemia for women during all age phases were 2.694 (95% CI 1.374 to 5.284, p=0.004), 3.689 (95% CI 2.432 to 5.597, p<0.001), 3.540 (95% CI 2.393 to 5.236, p<0.001), 2.718 (95% CI 2.073 to 3.563, p<0.001), 2.368 (95% CI 1.901 to 2.951, p<0.001) and 2.064 (95% CI 1.536 to 2.775, p<0.001), respectively. Women over 30 years old, CKD and hypertension became the risk factors for HUA. The OR for HUA in CKD for women who were in over 30 years old groups were 21.932 (95% CI 4.456 to 107.939, p<0.001), 12.116 (95% CI 3.908 to 37.566, p<0.001), 5.699 (95% CI 3.024 to 10.738, p<0.001), 2.920 (95% CI 1.865 to 4.570, p<0.001) and 4.867 (95% CI 3.461 to 6.844, p<0.001), respectively. The OR for HUA in hypertension for females who were in group II (30–39 years old), group III (40–49 years old), group IV (50–59 years old) were 2.133 (95% CI 1.152 to 3.950, p=0.016), 1.940 (95% CI 1.236 to 3.043, p=0.004) and 1.460 (95% CI 1.102 to 1.934, p=0.008). However, hypertension in group V (60–69 years old), group VI (over 70 years old) did not relate to the occurrence of HUA. Moreover, diabetes mellitus and nephrolithiasis also had nothing to do with HUA in all age groups of women.

DISCUSSION

Previous studies concentrated more on the prevalence of HUA in the overall population or children or elderly people, rare study was focused on females under the different age phases, who had a fluctuant metabolism and hormone level that might influence the production and excretion of uric acid. Thus, our current study investigated the prevalence of HUA and its related factors in different age phases of women.

Our research showed that the prevalence rates of HUA in Shanghai women were 11.15% (95% CI 10.57% to 11.72%), which was similar to the nationwide survey of HUA in 31 provinces in mainland China, that 8.3%–12.9% in women and 13.7%–18.8% in total.²² As a regional study, the prevalence of our result was close to other regional investigation in China, that 11.3% of HUA in Eastern Chinese general population²³ and 13.6% in Northern China.²⁴ Similarly, in Central China, a rural cohort study from Henan Province indicated that the prevalence of HUA was 12.6%.²⁵ In Southern China, an epidemiological study from Foshan areas in Guangdong Province showed that the standardised prevalence rate of HUA was 15.27%, in which the prevalence in women was 10.54%.²⁶ However, the prevalence of HUA in our female population was lower than USA 14.6%,²⁷ which might be attributed to economic status and dietary habit. We also found that our data were also higher than Japan 1%–3%,²⁸ which might due to the early antiurate therapy to asymptomatic patients, and their high cut-off of HUA (7.0 mg/dL in both sex).²⁹ Notably, there was a lack of agreement on cut-off value of HUA. Previously, HUA was defined with

Table 4 The OR for hyperuricaemia according to different status of parameters of women in different age groups (Group IV–VI)

	Group IV (50–59 years old)		Group V (60–69 years old)		Group VI (over 70 years old)	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
BMI (kg/m ²)						
18.5≤BMI<24.0 (Ref.)						
BMI <18.5	–	–	0.735 (0.253 to 2.131)	0.570	0.641 (0.247 to 1.661)	0.360
24.0≤BMI<28.0	1.676 (1.224 to 2.295)	0.001	1.963 (1.514 to 2.545)	<0.001	1.328 (0.936 to 1.883)	0.112
BMI≥28.0	3.156 (2.123 to 4.692)	<0.001	2.472 (1.783 to 3.428)	<0.001	2.610 (1.752 to 3.890)	<0.001
Blood pressure (mm Hg)						
Normotensive (Ref.)						
Pre-HT	0.989 (0.688 to 1.421)	0.952	0.977 (0.695 to 1.364)	0.894	1.121 (0.597 to 2.104)	0.723
Grade1 HT	1.091 (0.732 to 1.624)	0.669	1.023 (0.721 to 1.454)	0.897	1.447 (0.776 to 2.700)	0.246
Grade 2/3 HT	2.016 (1.214 to 3.347)	0.007	0.926 (0.601 to 1.428)	0.729	1.372 (0.719 to 2.619)	0.338
FPG (mmol/L)						
FPG <6.1 (Ref.)						
6.1≤FPG<7.0	0.895 (0.521 to 1.539)	0.689	0.869 (0.591 to 1.279)	0.477	1.781 (1.154 to 2.749)	0.009
FPG≥7.0	0.973 (0.591 to 1.603)	0.915	0.812 (0.551 to 1.198)	0.294	0.732 (0.465 to 1.154)	0.179
Cholesterol (mmol/L)						
TC ≤6.22 (Ref.)						
TC >6.22	1.287 (0.780 to 2.124)	0.323	1.110 (0.755 to 1.631)	0.597	0.793 (0.459 to 1.369)	0.405
Triglyceride(mmol/L)						
TG ≤2.26 (Ref.)						
TG >2.26	2.601 (1.836 to 3.687)	<0.001	2.505 (1.907 to 3.291)	<0.001	2.679 (1.787 to 4.018)	<0.001
HDL-C (mmol/L)						
HDL-C ≥1.04 (Ref.)						
HDL-C <1.04	1.683 (1.111 to 2.549)	0.014	1.619 (1.135 to 2.309)	0.008	1.592 (1.002 to 2.527)	0.049
LDL-C (mmol/L)						
LDL-C ≤4.14 (Ref.)						
LDL-C >4.14	1.156 (0.685 to 1.950)	0.587	1.164 (0.761 to 1.780)	0.483	1.625 (0.929 to 2.842)	0.089
eGFR (ml/(min*1.73 m ²))						
eGFR ≥90 (Ref.)						
60≤eGFR≤89	1.592 (1.190 to 2.130)	0.002	1.275 (1.000 to 1.626)	0.050	1.694 (1.146 to 2.506)	0.008
eGFR ≤59	7.388 (3.694 to 14.777)	<0.001	3.120 (1.892 to 5.147)	<0.001	7.644 (4.816 to 12.133)	<0.001
Albuminuria						
± (Ref.)						
+	2.575 (0.854 to 7.765)	0.093	4.828 (1.729 to 13.485)	0.003	2.997 (1.399 to 6.420)	0.005
++	0.353 (0.044 to 2.830)	0.327	3.257 (1.141 to 9.299)	0.027	2.262 (0.686 to 7.460)	0.180
+++	1.738 (0.385 to 7.848)	0.472	10.136 (3.526 to 29.137)	<0.001	3.672 (0.782 to 17.240)	0.099
Urinary pH						
6≤pH≤7 (Ref.)						
pH <6	1.429 (1.069 to 1.911)	0.016	1.748 (1.379 to 2.216)	<0.001	2.357 (1.729 to 3.212)	<0.001
pH >7	0.742 (0.358 to 1.537)	0.422	1.139 (0.639 to 2.029)	0.659	0.295 (0.084 to 1.035)	0.057
Nephrolithiasis						
No (Ref.)						
Yes	1.362 (0.934 to 1.985)	0.108	1.016 (0.753 to 1.370)	0.918	1.234 (0.832 to 1.831)	0.295

Blood pressure (mm Hg): normotensive: SBP <120 and DBP<80; pre-HT: SBP of 120–139 and/or DBP of 80–89; Grade 1 HT: SBP of 140–159 and/or DBP of 90–99; Grade 2/3 HT: SBP ≥160 and/or DBP≥100.
 BMI, body mass index; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

Figure 2 OR of hyperuricaemia to women exposed to different age phases.

the classic cut-off (>7.0 mg/dL in men and >6.0 mg/dL in women), but recent evidences suggested that a lower level should be considered as a more appreciate cut-off when addressing its negative impact on cardiovascular system (5.6 mg/dL for both sex).^{7 11} However, 2020 American College of Rheumatology Guideline for the Management of Gout Guidelines and Japanese Guideline on Management of Hyperuricemia and Gout third edition suggested that the normal upper limit is 6.8 mg/dL, and anything over 7 mg/dL (for both sex) is considered saturated, and symptoms can occur.²⁹ We did the addition analysis for the prevalence and related factors analysis of HUA based on the new cut-off (>7.0 mg/dL) (online supplemental table 1 and online supplemental figure 1). The prevalence rates of HUA (>7.0 mg/dL) of total subjects were 3.65% (95% CI 3.30% to 3.98%). Logistic regression analysis also showed the similar trend of ORs for HUA cut-off 7.0 mg/dL, expect for nephrolithiasis (online supplemental table 2 and online supplemental figure 2). There was no relationship between nephrolithiasis and HUA when HUA was defined as SUA >6.0 mg/dL. Using the higher cut-off (>7.0 mg/dL), HUA tended to be associated with nephrolithiasis in the group V (60–69 years old) with $p=0.019$, group VI (over 70 years old) although $p=0.082$. We speculated that the association between HUA (>6 mg/dL) and nephrolithiasis might be covered by the lower cut-off of HUA. Since 7 mg/dL was the saturation point of uric acid, which would increase the deposition of urate crystals in kidney or joint.

In addition, we also calculated the prevalence of HUA in various age groups and found that after 50 years old, the prevalence of HUA in Shanghai women has increased greatly and reached the peak after 70 years old, 23.98%, which was closed the prevalence in adult men, 22.2%.²¹ Consistently, compared with those under 30 years old, the ORs for HUA in over 50 age phases also increased significantly and reached the highest at the age over 70 (OR=4.602, 95% CI 3.497 to 6.056, $p<0.001$). Therefore, we identified that 50 years old was an important inflection point for HUA in women, which was earlier than some cohort studies that enrolled postmenopausal women with a mean age closed to 60.^{30 31} Our result suggested an earlier attention and intervene for HUA in women.

Furthermore, our study investigated the relationship between HUA and metabolic, renal disorders in women

Table 5 The association between hyperuricaemia and obesity , hypertension , diabetes mellitus , dyslipidaemia , chronic kidney disease and nephrolithiasis

	Group I (18–29 years old)		Group II (30–39 years old)		Group III (40–49 years old)		Group IV (50–59 years old)		Group V (60–69 years old)		Group VI (over 70 years old)	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Obesity (yes vs no)	6.939 (3.281 to 14.673)	<0.001	3.746 (2.239 to 6.268)	<0.001	2.018 (1.190 to 3.423)	0.009	2.420 (1.720 to 3.404)	<0.001	1.907 (1.448 to 2.511)	<0.001	2.319 (1.659 to 3.243)	<0.001
Hypertension (yes vs no)	2.478 (0.830 to 7.393)	0.104	2.133 (1.152 to 3.950)	0.016	1.940 (1.236 to 3.043)	0.004	1.460 (1.102 to 1.934)	0.008	1.085 (0.866 to 1.358)	0.480	1.283 (0.956 to 1.722)	0.097
Diabetes mellitus (yes vs no)	–	–	1.610 (0.449 to 5.771)	0.465	0.764 (0.223 to 2.620)	0.668	1.115 (0.691 to 1.799)	0.657	1.111 (0.780 to 1.581)	0.561	0.882 (0.581 to 1.340)	0.557
Dyslipidaemia (yes vs no)	2.694 (1.374 to 5.284)	0.004	3.689 (2.432 to 5.597)	<0.001	3.540 (2.393 to 5.236)	<0.001	2.718 (2.073 to 3.563)	<0.001	2.368 (1.901 to 2.951)	<0.001	2.064 (1.536 to 2.775)	<0.001
Chronic kidney disease (yes vs no)	–	–	21.932 (4.456 to 107.939)	<0.001	12.116 (3.908 to 37.566)	<0.001	5.699 (3.024 to 10.738)	<0.001	2.920 (1.865 to 4.570)	<0.001	4.867 (3.461 to 6.844)	<0.001
Nephrolithiasis (yes vs no)	1.461 (0.591 to 3.611)	0.411	1.240 (0.705 to 2.181)	0.455	1.144 (0.671 to 1.953)	0.621	1.260 (0.877 to 1.808)	0.211	1.110 (0.835 to 1.476)	0.473	1.238 (0.856 to 1.791)	0.256

Figure 3 The association between hyperuricaemia and obesity, hypertension, diabetes mellitus, dyslipidaemia, chronic kidney disease and nephrolithiasis.

during all age phases. We found that obesity and dyslipidaemia were two main risk factors for HUA during all ages (all $p < 0.05$). It was well recognised that estrogens promoted the accumulation of fat in gluteofemoral rather than in abdominal and visceral depots.^{32 33} While in old women, decreased level of oestrogen tended to form a central distribution of adiposity, making the body shape similar to the men.³³ This could in part explain the phenomenon of increased prevalence of obesity and dyslipidaemia in older women, and this change was accompanied by increased SUA. Other main component of metabolic disorders, hypertension, mainly affected the occurrence of HUA during 30–59 years old. Although the prevalence of hypertension had a sustainable growth after 30 years old, it was not associated with HUA after 60-year old. We used backward elimination method to select variables and analyse the reason, the result showed that hypertension could not be a related factor of HUA independent of obesity and dyslipidaemia in the age older than 60.

Although the prevalence of diabetes mellitus increased with age, this cross-sectional study indicated that FPG or diabetes mellitus almost had no significant relationship with HUA during all age phases of women. This was inconsistent with previous studies. A meta-analysis of 12 cohort studies, including a total of 6340 cases and 62 834 participants, revealed a positive non-linear relationship between SUA levels and diabetes and IFG.³⁴ In the development of hyperglycaemic or diabetes, HUA had been reported to be a risk factor. A retrospective cohort study among 1923 patients

showed that HUA was associated with a significantly higher risk of developing diabetes. Diabetes rates from Kaplan-Meier analysis were 19% for $SUA \leq 7$ mg/dL, 23% for $7 < SUA \leq 9$ mg/dL and 27% for $SUA > 9$ mg/dL at the end of follow-up period (80 months).³⁵ Another prospective cohort study followed up 13 328 women and 41 350 men without diabetes for 4 years, and the results showed that any abnormality in SUA concentrations was associated with an increased risk for the development of IFG in men, while such association was not found in women.³⁶ On the other hand, in the development of HUA, hyperglycaemic might also be an inducer. One hypothesis was that hyperglycaemic exceeded renal glucose threshold and induced hyperfiltration and elevated the rate of renal glomerular filtration increased excretion of uric acid.³⁷ It seemed that hyperglycaemic was more likely relate to hypouricaemia in the early period of diabetes. During the late phase of diabetic nephropathy, fibrotic glomeruli could not compensate the filtration, reduced eGFR and decreased SUA excretion would appear concomitantly.³⁸ However, our cross-section study can not find the relationship between SUA and hyperglycaemic or diabetes. Their uncertain relationship might largely attribute to hyperglycaemia-induced hyperfiltration. And their causal relationship still need more prospective studies to verify.

There were several limitations in our study. First, we lacked the data of pharmacotherapy and menopausal status. Since that oestrogen could promote urate excretion,³⁹ which might affect the results on population who under perimenopause or with hormone replacement therapy. And antihypertension drugs also affected urate metabolism, that diuretic (such as thiazides) increased the urate reabsorption,⁴⁰ while angiotensin receptor inhibitor (such as losartan) decreased it. There might be some biases on hypertension subjects. Additionally, the data about economics, lifestyles and diet were also absent. Second, this was a local survey, not a national study. And the cross-sectional study can not identify the causative relationship between HUA and metabolic and renal disorders. Nonetheless, the strengths of our study included a multicentre sample with a large size, which ensured a much solid statistics result. And the prevalence of HUA in different age phases was analysed and compared.

CONCLUSION

In Shanghai female population, the prevalence of HUA increases significantly since 50 years old and reaches the peak after 70. Obesity and dyslipidaemia are close related to HUA during all ages, while diabetes and nephrolithiasis have no relationship with HUA throughout. CKD is an independent impact factor for HUA after 30 years old.

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