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Gender-specific association between serum uric acid levels and hypertension in East China: a cross-sectional study

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Abstract

Background This cross-sectional study aimed to investigate the correlation between serum uric acid (SUA) levels and the incidence of sex-specific high blood pressure in East China.

Methods A total of 27,075 patients (14,399 males and 12,676 females) were enrolled in this study. The participants were grouped based on their SUA levels. Thereafter, the quartile (Q1-Q4) nodes of male SUA and female SUA were calculated based on the differences in the mean values of male and female SUA levels. The odds ratio (OR) and 95% confidence interval (CI) were calculated to evaluate the correlation between SUA and high blood pressure incidence.

Results SUA expression levels were higher in males than in females. High SUA levels in males were positively correlated with hypertension. In females, high SUA levels were positively correlated with both hypertension and diabetes. After adjusting for confounding risk factors, SUA was confirmed as an independent risk factor for high blood pressure among males. Additionally, significant differences were observed between SUA and high blood pressure in body mass index (BMI) as well as diabetes subgroup analysis among males. There was a sex-specific correlation between SUA, high diastolic blood pressure (DBP), and high systolic blood pressure (SBP). Finally, there was a linear dose-response relationship between SUA and high blood pressure in males.

Conclusion SUA is an independent risk factor for the incidence of high blood pressure after adjustment for other potential confounding risk factors in males. Sex-specific differences were also observed between SUA levels and high DBP or SBP.

Keywords Cardiovascular disease, Serum uric acid, Diastolic blood pressure, Systolic blood pressure

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Introduction

High blood pressure is the leading cause of cardiovascular disease and mortality [1]. According to Chinese epidemiological data, the incidence rates of high blood pressure in four national sample surveys were 5.1%, 7.7%, 13.6%, and 18.8% [2]. Data released by the Chinese National Center for Cardiovascular Disease in 2018 showed that the incidence of high blood pressure increased to 23.2% [2]. The fundamental purpose of treating hypertension is to reduce the overall risk of cardiobrain, renal, and vascular complications, and ultimately, death [3]. Improving lifestyle is the primary hypertension therapy and should be considered throughout the treatment process [4]. However, the standard treatment rate for hypertension in China is relatively low, which may be because of low awareness rates in the country [5]. Regular blood pressure assessments and timely measurement of high blood pressure are the initial steps toward its prevention and treatment.

Serum uric acid (SUA) is the end product of purine metabolism, and disturbances in purine metabolism, excessive uric acid production, or decreased excretion can increase SUA expression [6]. Excessive uric acid accumulation can lead to the formation of uric acid crystals, thereby causing gout. Additionally, high SUA levels have been shown to be a risk factor for diseases, such as renal dysfunction and cardiovascular diseases [7]. A previous large longitudinal prospective cohort study suggested that elevated SUA levels consistently predicted the development of hypertension and correlated with an increased risk of developing cardiovascular diseases [8]. Furthermore, high SUA levels have been reported to increase the risk of hypertension among young adults [9, 10]. However, there is controversy regarding whether SUA levels are a risk factor for high blood pressure. Several studies have reported that an increase in uric acid levels is accompanied by the occurrence of hypertension; however, the majority of published findings are based on animal studies and epidemiological investigations, with limited clinical evidence to support this correlation.

In this cross-sectional study, we investigated the correlation between SUA levels and the incidence of high blood pressure among the East Chinese population to provide guidance for the prevention and treatment of hypertension.

Methods

Study population

Between September 2020 and May 2022, 55,548 patients underwent physical examinations at the First Affiliated Hospital of Soochow University. Of these, 32,496 participants with complete basic biochemical test data were randomly selected. Of the 35,539 participants, only those aged ≥ 18 years ($n = 27,873$) were included in the analysis. Additionally, 455 patients with a special medical history, 4,758 people with a history of hypertension, 18 people who were pregnant or breastfeeding, and 22 people whose body mass index (BMI) was < 15 kg/m^2 or > 50 kg/m^2 were excluded. Additionally, 108 people with a systolic blood pressure (SBP) < 80 mmHg or diastolic blood pressure (DBP) < 50 mmHg and 53 people with a heart rate < 40 beats/min or > 130 beats/min were excluded (Fig. 1). Therefore, a total of 27,075 people (14,399 males

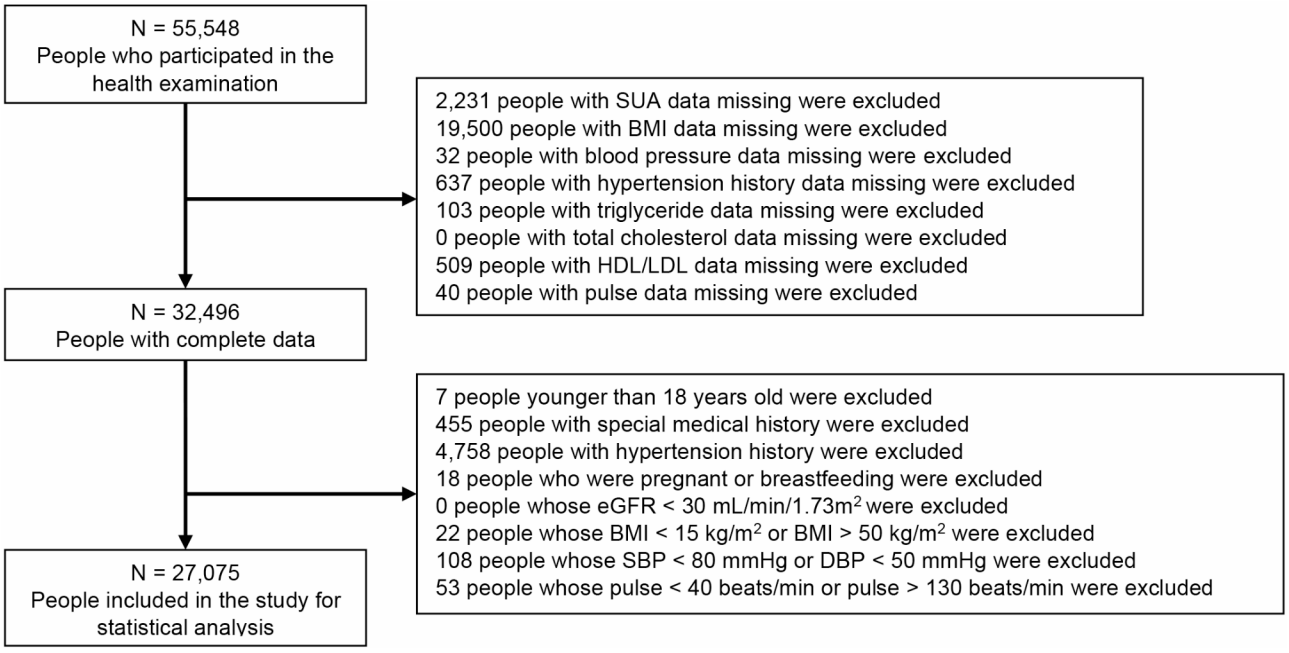

Fig. 1 Flow chart for screening subjects

and 12,676 females) were included in the study. Note: The special medical history includes cardiovascular diseases (coronary heart disease, heart failure, etc.), diabetes, chronic kidney disease, liver diseases (hepatitis, cirrhosis, etc.), malignant tumors, blood system diseases (leukemia, lymphoma, etc.), autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus, etc.) and thyroid diseases (hyperthyroidism, hypothyroidism, etc.).

Evaluation of SUA

All participants were grouped according to their SUA levels. Due to the differences in the normal mean value between male and female SUA, the quartile nodes of male SUA and female SUA in this study population were calculated independently (Q1–Q4), which were measured as follows: males = Q1: ≤ 346.70; Q2: 346.70–395.30; Q3: 395.30–448.70; and Q4: ≥ 448.70 μ mol/L and female = Q1: ≤ 244.50; Q2: 244.50–281.10; Q3: 281.10–320.80; and Q4: ≥ 320.80 μ mol/L.

Laboratory measurement indicators

The participants' Age were verified by ID cards, height and weight were measured by electronic height weighing scale (DHM-900 C), pulse, SBP and DBP were measured by electronic sphygmomanometer (OMRON, HEM7137), uric acid (UA), fasting blood glucose (FBG), creatinine, estimated glomerular filtration rate (eGFR), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were measured by biochemical analyzer (Beckman Coulter, AU480). The health care workers who participated in the project received professional training to ensure the consistency and accuracy of their operations, thus reducing the impact of human error on the research results.

Statistical analysis

SPSS 20. 0 software was used for the data analysis. Kolmogorov-Smirnov test was used to test the normality of the data. Data with a normal distribution are presented as mean ± standard deviation (x ± s), whereas data with a non-normal distribution are presented as median (interquartile range [IQR]). Odds ratios (OR) and 95% confidence intervals (CIs) were used to assess the associations between SUA levels and the incidence of hypertension. The non-parametric rank-sum test (Mann–Whitney U test) was used for comparisons between the two groups. All participants were classified according to the quartiles of SUA. The baseline characteristics were compared across the SUA quartiles of men and women. Baseline characteristics of the participants were reported as medians (quartile intervals) for continuous variables (the continuous variables were not normally distributed) and numbers (percentages) for categorical variables. Kruskal–Wallis tests were used to compare continuous variables, whereas categorical variables were compared by $\chi 2$ trend tests. Univariate and multivariate logistic regression analysis were used to estimated odds ratios (ORs) and 95% confidence intervals (CIs) of high blood pressure incidence for changes in SUA in men and women. SUA as a categorized variable in quartiles are used as independent variables(Q1 as reference), with high blood pressure as the dependent variable, to build the model. Covariate adjustments are made stepwise: (1) unadjusted.; (2) further adjustments for age, gender, BMI, FBG, diabetes, TG, TC, LDL, and HDL; (3) further adjustments for age, gender, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse and eGFR. Additionally, a trend test for OR values across the SUA quartile groups is conducted by reassigning the median SUA values of each group and entering these as continuous variables into the model to calculate p-values. The significance of the pooled OR values was determined using the Z-test. To detect any possible linear or nonlinear dependency in regression models and to allow for flexible interpretation of the relationship between continuous covariates and high blood pressure incidence, continuous changes in SUA were assessed through shape-restricted cubic spline regression models with knots at the 5th, 35th, 65th, and 95th percentiles, and with the 12.5th percentile as the reference category. $P < 0.05$ was considered as statistically significant.

Results

Baseline characteristics of participants

Increased SUA levels were higher in males compared than in females. Male participants with high SUA levels were younger and had higher levels of BMI, pulse, SBP, DBP, creatinine, TG, TC, and LDL, and a higher prevalence of hypertension. Female participants with relatively higher SUA levels had higher BMI, SBP, DBP, FBG, creatinine, LDL, TG, and TC levels, and a higher prevalence of hypertension and diabetes (Table 1).

Changes in SUA for high blood pressure incidence

In Table 2, the results suggested that in males, the quartiles of SUA could function as independent risk factors for high blood pressure incidence in model 1 (Unadjusted), model 2 (Adjusted for age, sex, BMI, FBG, diabetes, TG, TC, LDL, and HDL), and model 3 (Adjusted for age, sex, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse, and eGFR). The OR with 95% CI for Q4 in model 1 was 1.36 (1.22, 1.52) with $P < 0.0001$, in model 2 was 1.15 (1.01, 1.30) with $P = 0.0310$, in model 3 was 1.17 (1.03, 1.33) with $P = 0.0182$, respectively. For females, a significant difference was only observed in model 1 ($P < 0.0001$). For the total population (males + females), increased SUA levels were correlated with a higher risk of developing high blood pressure.

Table 1 Characteristics of the study participants according to serum uric acid quartiles by gender

Characteristics	Males					Females				
	Q1	Q2	Q3	Q4	*P* Value	Q1	Q2	Q3	Q4	*P* Value
N (participants, %)	3599 (25.0)	3599 (25.0)	3602 (25.0)	3599 (25.0)		3170 (25.0)	3164 (25.0)	3173 (25.0)	3169 (25.0)	
Age, y	44 (35, 54)	42 (34, 51)	40 (33, 49)	38 (32, 47)	< 0.0001	39 (33, 46)	38 (32, 47)	39 (32, 48)	39 (32, 50)	0.0197
Uric acid, μ mol/L	314.4 (287.7, 332.7)	372.4 (360.1, 384,0)	420.2 (407.6, 434.0)	489.1 (465.9, 524.2)	< 0.0001	221.2 (202.5, 234.0)	263.7 (254.5, 272.5)	299.4 (290.0, 309.7)	353.5 (335.0, 382.5)	< 0.0001
BMI, kg/m^2	23.7 (21.8, 25.5)	24.4 (22.7, 26.2)	25.1 (23.4, 27.0)	26.1 (24.2, 28.3)	< 0.0001	21.1 (19.7, 22.8)	21.5 (20.0, 23.3)	21.9 (20.4, 23.9)	23.1 (21.1, 25.4)	< 0.0001
Pulse, beats/min	78 (70, 86)	78 (71, 86)	78 (71, 87)	79 (72, 87)	< 0.0001	83 (76, 91)	83 (75, 91)	83 (75, 92)	83 (75, 91)	0.6124
SBP, mm Hg	124 (115, 135)	124 (116, 135)	125 (116, 135)	127 (118, 137)	< 0.0001	115 (107, 125)	115 (107, 125)	116 (107, 126)	119 (109, 130)	< 0.0001
DBP, mm Hg	76 (70, 84)	77 (71, 84)	78 (71, 86)	79 (73, 87)	< 0.0001	70 (65, 77)	71 (65, 77)	71 (65, 78)	73 (66, 80)	< 0.0001
FBG, mmol/L	5.2 (4.9, 5.6)	5.1 (4.8, 5.5)	5.2 (4.9, 5.5)	5.2 (4.9, 5.5)	< 0.0001	4.9 (4.7, 5.2)	4.9 (4.7, 5.2)	5.0 (4.7, 5.3)	5.0 (4.7, 5.4)	< 0.0001
Creatinine, μ mol/L	70.2 (64.5, 76.2)	72.7 (67.1, 78.6)	73.7 (67.9, 79.9)	75.6 (69.3, 82.3)	< 0.0001	49.9 (45.9, 54.1)	51.9 (47.7, 56.4)	52.6 (48.3, 57.3)	54.5 (49.4, 59.8)	< 0.0001
eGFR, mL/min/1.73m^2	137.0 (123.7, 152.3)	132.9 (120.4, 146.4)	131.7 (118.5, 145.6)	128.7 (115.7, 143.1)	< 0.0001	154.4 (139.2, 171.0)	147.8 (133.3, 164.2)	144.6 (130.1, 161.2)	138.8 (123.2, 156.7)	< 0.0001
TG, mmol/L	1.2 (0.9, 1.7)	1.4 (1.0, 1.9)	1.6 (1.1, 2.2)	1.9 (1.3, 2.7)	< 0.0001	0.8 (06, 1.1)	0.9 (0.7, 1.2)	1.0 (0.7, 1.3)	1.2 (0.8, 1.7)	< 0.0001
TC, mmol/L	4.8 (4.3, 5.4)	4.9 (4.4, 5.5)	5.0 (4.4, 5.5)	5.1 (4.6, 5.7)	< 0.0001	4.7 (4.2, 5.2)	4.7 (4.2, 5.3)	4.8 (4.3, 5.4)	5.0 (4.4, 5.6)	< 0.0001
HDL, mmol/L	1.2 (1.1, 1.4)	1.2 (1.0, 1.3)	1.11(1.0, 1.3)	1.1 (1.0, 1.2)	< 0.0001	1.5 (1.3, 1.8)	1.5 (1.3, 1.7)	1.4 (1.2, 1.7)	1.4 (1.2, 1.6)	< 0.0001
LDL, mmol/L	2.9 (2.4, 3.4)	3.0 (2.5, 3.5)	3.1 (2.6, 3.6)	3.2 (2.6, 3.7)	< 0.0001	2.6 (2.1, 3.1)	2.7 (2.2, 3.2)	2.8 (2.3, 3.3)	2.9 (2.4, 3.5)	< 0.0001
Diabetes, *N* (%)					< 0.0001					0.0320
Yes	203 (5.6)	103 (2.9)	83 (2.3)	53 (1.5)		22 (0.7)	23 (0.7)	14 (0.4)	34 (1.1)	
No	3396 (94.4)	3496 (97.1)	3519 (97.7)	3546 (98.5)		3148 (99.3)	3141 (99.3)	3159 (99.6)	3135 (98.9)	
Hypertension, *N* (%)					< 0.0001					< 0.0001
Yes	742 (20.6)	761 (21.1)	791 (22.0)	939 (26.1)		248 (7.8)	291 (9.2)	307 (9.7)	456 (14.4)	
No	2857 (79.4)	2838 (78.9)	2811 (78.0)	2660 (73.9)		2922 (92.2)	2873 (90.8)	2866 (90.3)	2713 (85.6)	
High SBP, *N* (%)					< 0.0001					< 0.0001
Yes	554 (15.4)	552 (15.3)	569 (15.8)	682 (19.0)		196 (6.2)	226 (7.1)	247 (7.8)	371 (11.7)	
No	3045 (84.6)	3047 (84.7)	3033 (84.2)	2917 (81.1)		2974 (93.8)	2938 (92.9)	2926 (92.2)	2798 (88.3)	
High DBP, *N* (%)					< 0.0001					< 0.0001
Yes	379 (10.5)	413 (11.5)	493 (13.7)	575 (16.0)		111 (3.5)	112 (3.5)	123 (3.9)	187 (5.9)	
No	3220 (89.5)	3186 (88.5)	3109 (86.3)	3024 (84.0)		3059 (96.5)	3052 (96.5)	3050 (96.1)	2982 (94.1)	

Cut-points: Serum uric acid quartiles (Q1–Q4) in men (Q1: ≤ 346.70; Q2: 346.70–395.30; Q3: 395.30–448.70; and Q4: ≥ 448.70 μ mol/L). In women (Q1: ≤ 244.50; Q2: 244.50–281.10; Q3: 281.10–320.80; and Q4: ≥ 320.80 μ mol/L). BMI„ body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; TG, triglycerides; TC, total cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein. *Continuous variables are expressed as median (interquartile range). Categorical variables are expressed as frequency (percent)

Table 2 OR and 95% CI for changes in SUA for high blood pressure incidence

	Model 1		Model 2		Model 3	
Variable	**OR, 95% CI**	***P* Value**	**OR, 95% CI**	***P* Value**	**OR, 95% CI**	***P* Value**
Males						
Q1	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
Q2	1.03 (0.92, 1.16)	0.5817	1.05 (0.93, 1.19)	0.4222	1.08 (0.96, 1.22)	0.2142
Q3	1.08 (0.97, 1.21)	0.1639	1.03 (0.91, 1.16)	0.6251	1.06 (0.93, 1.20)	0.4003
Q4	1.36 (1.22, 1.52)	< 0.0001**	1.15 (1.01, 1.30)	0.0310*	1.17 (1.03, 1.33)	0.0182*
p for trend	< 0.0001**		0.0494*		0.0343*	
Female						
Q1	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
Q2	1.20 (1.00, 1.43)	0.0503	1.03 (0.86, 1.25)	0.7276	1.10 (0.90, 1.33)	0.3612
Q3	1.26 (1.06, 1.50)	0.0092*	0.90 (0.74, 1.08)	0.2537	0.94 (0.77. 1.15)	0.5523
Q4	1.98 (1.68, 2.33)	< 0.0001**	0.96 (0.79, 1.16)	0.65	1.03 (0.84, 1.26)	0.7677
p for trend	< 0.0001**		0.3863		0.8472	
Total						
Q1	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
Q2	1.43 (1.28, 1.58)	< 0.0001**	0.98 (0.87, 1.10)	0.6756	0.99 (0.88, 1.12)	0.8699
Q3	2.19 (1.98, 2.42)	< 0.0001**	1.08 (0.96, 1.22)	0.2158	1.12 (0.99, 1.27)	0.0846
Q4	2.88 (2.61, 3.18)	< 0.0001**	1.13 (0.99, 1.29)	0.0774	1.17 (1.02, 1.34)	0.0272*
p for trend	< 0.0001**		0.0221*		0.0065*	

Notes: Serum uric acid quartiles (Q1–Q4) in men (Q1: ≤ 346.70; Q2: 346.70–395.30; Q3: 395.30–448.70; and Q4: > 448.70 μ mol/L). In women (Q1: ≤ 244.50; Q2: 244.50–281.10; Q3: 281.10–320.80; and Q4: > 320.80 μ mol/L). In total population (Q1: ≤ 278.30; Q2: 278.30–338.60; Q3: 338.60–407.20; and Q4: > 407.20 μ mol/L). BMI, body mass index; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; TG, triglycerides; TC, total cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein

Model 1: Unadjusted

Model 2: Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, and HDL

Model 3: Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse and eGFR

*P Value < 0.05

**P Value < 0.0001

There was a dose-response correlation between the level of SUA and the incidence of hypertension (Fig. 2). Multivariable regression models werehave been established tofor investigateing the association between SUA levels the level of SUA and high blood pressure, and the results demonstrated a linear dose-response relationship in males ($P = 0.0131$), but not in females ($P = 0.8902$ or $P = 0.5032$).

Subgroup analysis of the incidence of high blood pressure based on the levels of SUA

To explore the consistency of the observed association between SUA and high blood pressure incidence, we performed subgroup analyses of participants according to age (≤ 50 and > 50 years), BMI (≤ 25 and > 25 kg/m2), and diabetes (yes or no) in different populations. The results demonstrated in Table 3 show that the correlation between SUA level and high blood pressure was significantly different among males in the subgroup analysis stratified by BMI and diabetes status. However, there were no significant differences in each subgroup analysis for females.

The sex-stratified analysis showed that in males, when BMI ≤ 25 kg/m^2, after adjusting for age, FBG, diabetes, TG, TC, LDL, HDL, pulse, and eGFR, the risk of high blood pressure incidence significantly increased for Q4 of SUA, with an OR (95% CI) of 1.29 (1.05, 1.58) with $P = 0.0150$. When BMI was > 25 kg/m^2, no significant difference between SUA levels and high blood pressure incidence was observed. These differences were not observed in females.

In the diabetes subgroup analysis, after adjusting for age, BMI, FBG, TG, TC, LDL, HDL, pulse, and eGFR, Q4 of SUA was an independent risk factor for high blood pressure incidence. In males with diabetes, the OR with 95% CI for Q4 was 2.68 (1.27, 5.68) with $P = 0.0099$, P trend = 0.0304. In males without diabetes, the OR with 95% CI for Q4 was 1.15 (1.00, 1.31) with $P = 0.0462$. No significant associations were observed between SUA levels and high blood pressure among females in the subgroup analysis of diabetes. Additionally, there was no evidence of statistical significance between the interaction of various subgroup variables with SUA and the incidence of high blood pressure (all P interaction > 0.05).

Furthermore, significant linear dose-response relationships were observed in males. In the age subgroup analysis, there was no dose-response relationship between SUA and high blood pressure incidence in males or females (Fig. 3). In the BMI subgroup analysis, a positive dose-response relationship between SUA and high blood

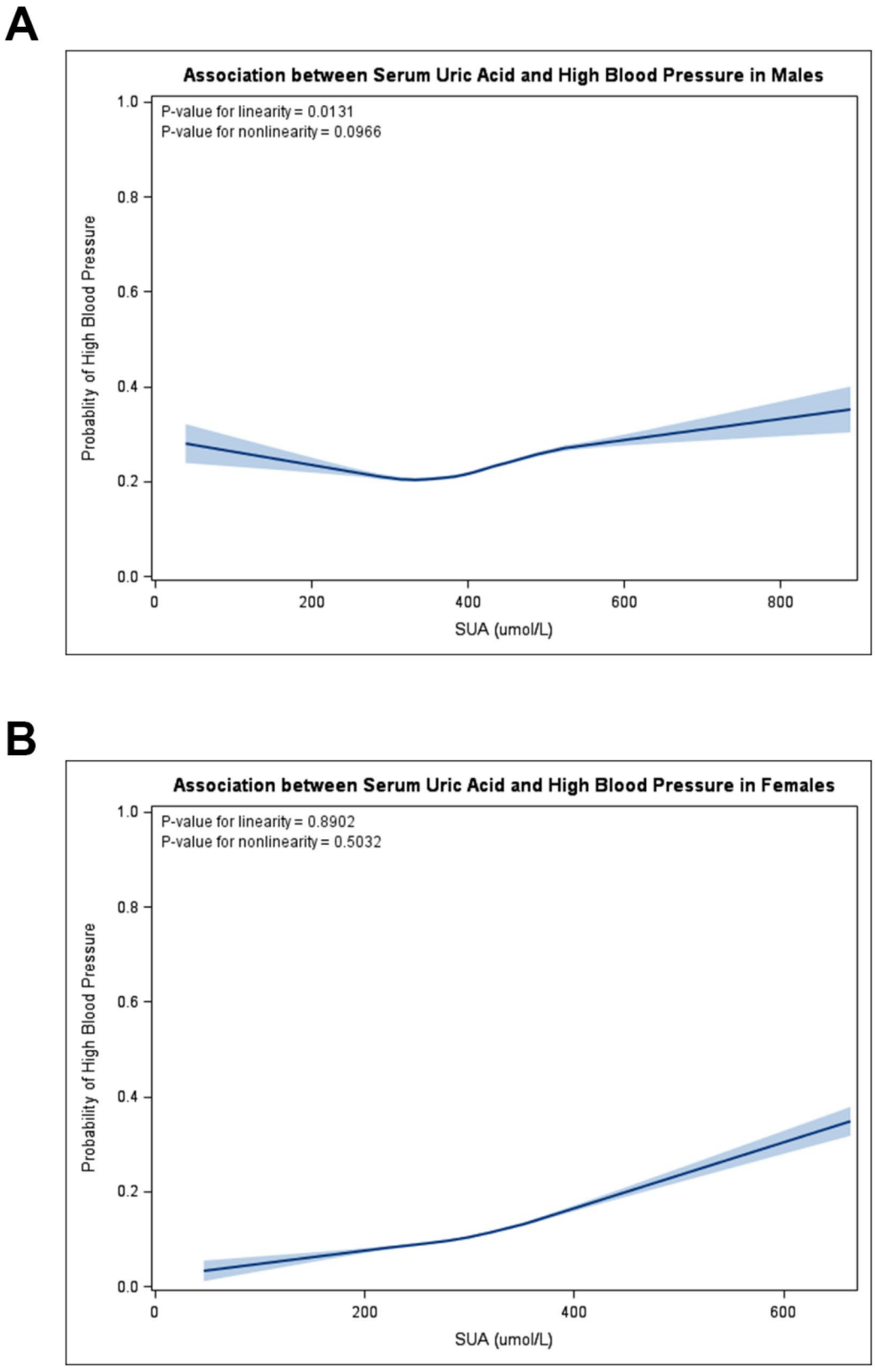

Fig. 2 Association between SUA and incidence of high blood pressure in males and females after adjusting age, BMI, pulse, SBP, DBP, FBG, eGFR, TG, TC, HDL, and LDL, respectively

Table 3 Subgroup analysis of adjusted ORs with 95% CIs of high blood pressure incidence according to serum uric acid levels

	Q1	Q2		Q3		Q4			
Variable	**OR**	**OR, 95% CI**	***p* Value**	**OR, 95% CI**	***p* Value**	**OR, 95% CI**	***p* Value**	***p* Trend**	***p* Interaction**
Males									
Age, y									0.4244
≤ 50	1	1.02 (0.87, 1.20)	0.8526	0.99 (0.84, 1.16)	0.8644	1.11 (0.94, 1.30)	0.2165	0.2431	
> 50	1	1.19 (0.97, 1.45)	0.0902	1.18 (0.95, 1.46)	0.1367	1.17 (0.92, 1.48)	0.1934	0.1703	
BMI, kg/m^2									0.8677
≤ 25	1	1.18 (1.00, 1.40)	0.0504	1.04 (0.86, 1.25)	0.6981	1.29 (1.05, 1.58)	0.0150*	0.0671	
> 25	1	1 (0.83, 1.20)	0.9802	1.04 (0.87, 1.25)	0.6382	1.08 (0.90, 1.28)	0.4212	0.3206	
Diabetes									0.0872
Yes	1	0.88 (0.49, 1.60)	0.6832	1.18 (0.64, 2.20)	0.5961	2.68 (1.27, 5.68)	0.0099*	0.0304*	
No	1	1.1 (0.97, 1.24)	0.1591	1.05 (0.92, 1.19)	0.4674	1.15 (1.00, 1.31)	0.0462*	0.0944	
Female									
Age, y									0.321
≤ 50	1	0.94 (0.73, 1.21)	0.6188	0.91 (0.71, 1.17)	0.4563	0.96 (0.74, 1.26)	0.7874	0.742	
> 50	1	1.3 (0.95, 1.79)	0.1039	0.94 (0.68, 1.29)	0.6776	0.94 (0.68, 1.29)	0.7977	0.5519	
BMI, kg/m^2									0.1689
≤ 25	1	1.15 (0.92, 1.43)	0.2154	0.94 (0.75, 1.18)	0.6094	1.12 (0.89, 1.42)	0.3344	0.7409	
> 25	1	0.86 (0.55, 1.36)	0.5187	0.82 (0.54, 1.27)	0.377	0.8 (0.54, 1.21)	0.2946	0.3372	
Diabetes									0.8582
Yes	1	1.68 (0.39, 7.23)	0.486	0.47 (0.08, 2.70)	0.3954	1.77 (0.46, 6.74)	0.4042	0.6686	
No	1	1.08 (0.89, 1.32)	0.4336	0.94 (0.77, 1.15)	0.5468	1.02 (0.83, 1.25)	0.8618	0.7867	

Notes: Serum uric acid quartiles (Q1–Q4) in men (Q1: ≤ 346.70; Q2: 346.70–395.30; Q3: 395.30–448.70; and Q4: > 448.70 μ mol/L). In women (Q1: ≤ 244.50; Q2: 244.50–281.10; Q3: 281.10–320.80; and Q4: > 320.80 μ mol/L). In total population (Q1: ≤ 278.30; Q2: 278.30–338.60; Q3: 338.60–407.20; and Q4: > 407.20 μ mol/L). BMI, body mass index; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; TG, triglycerides; TC, total cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein

Model: Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse and eGFR. Corresponding factors were not adjusted for each subgroup

*P-Value < 0.05

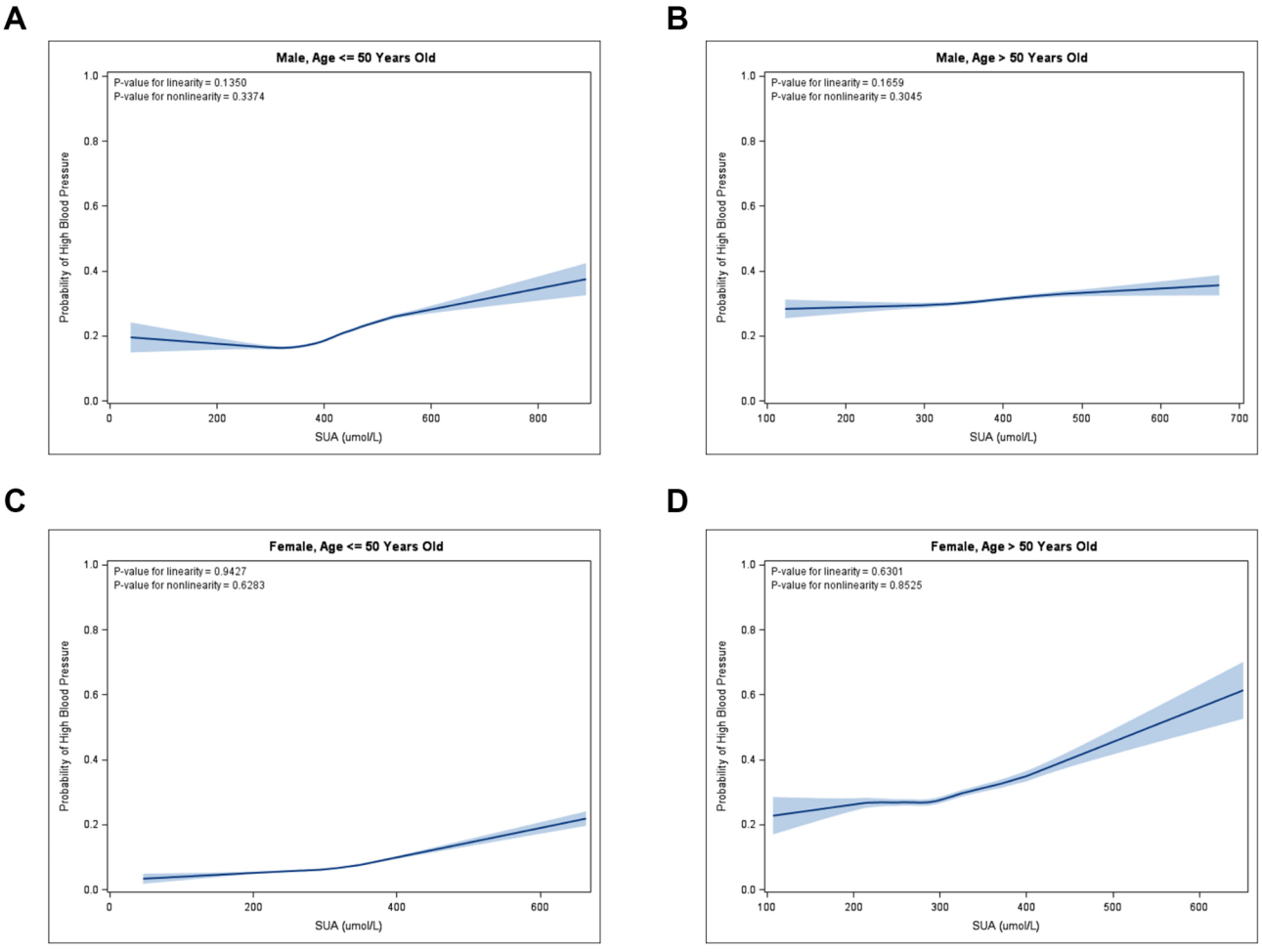

Fig. 3 Age subgroup analysis for association between SUA and incidence of high blood pressure in males and females

pressure incidence was observed in males when BMI was ≤ 25 kg/m^2 (Fig. 4, $P = 0.0103$). In the diabetes subgroup analysis, a linear dose-response relationship between SUA and high blood pressure incidence in males was also observed (Fig. 5, $P = 0.0307$).

Changes in the levels of SUA for the incidence of high DBP

As shown in Table 4, Q3 and Q4 of SUA in models 1 and 2 among males were significantly related to high DBP incidence. OR with 95% CI for Q3 to Q4 was 1.35 (1.17, 1.55) and 1.62 (1.41, 1.86) in model 1, respectively ($P < 0.0001$). OR with 95% CI for Q3 was 1.16 (1.00, 1.35) in model 2 ($P = 0.0493$). In females, only Q4 of SUA in model 1 was significant, the OR with 95% CI was 1.73 (1.36, 2.20) with $P < 0.0001$. In the total population, SUA levels were strongly correlated with high DBP incidence. OR with 95% CI for Q2 to Q4 was 1.55 (1.33, 1.80), 2.51 (2.17, 2.89) with, and 3.89 (3.39, 4.45), respectively ($P < 0.0001$).

Changes in the levels of SUA for the incidence of high SBP

As Table 5 shows, the correlation between Q4 of SUA and high SBP incidence was statistically significant in model 1 (OR = 1.29, 95%CI: 1.14–1.45, $P < 0.0001$) and model 3 (OR = 1.17, 95%CI: 1.01–1.36, $P = 0.0321$) among males. The OR with 95% CI in model 4 (SUA [μmol/L] as a continuous variable. Adjusted for age, sex, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse, and eGFR.) and model 5 (SUA [mg/dL] as a continuous variable. Adjusted for age, sex, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse, and eGFR.) was 1.001 (1.000, 1.001) with $P = 0.0344$, and 1.07 (1.01, 1.13) with $P = 0.0344$, respectively. In females, a significant difference in the correlation was found in model 1, the OR with 95% CI for Q3 to Q4 was 1.28 (1.06, 1.56) with $P = 0.0125$, 2.01 (1.68, 2.41) with $P < 0.0001$, respectively. For total population, levels SUA were correlated to increased risk of high SBP incidence in model 1 (Q2 [OR = 1.42, 95% CI: 1.26–1.60, $P < 0.0001$], Q3 [OR = 2.03,

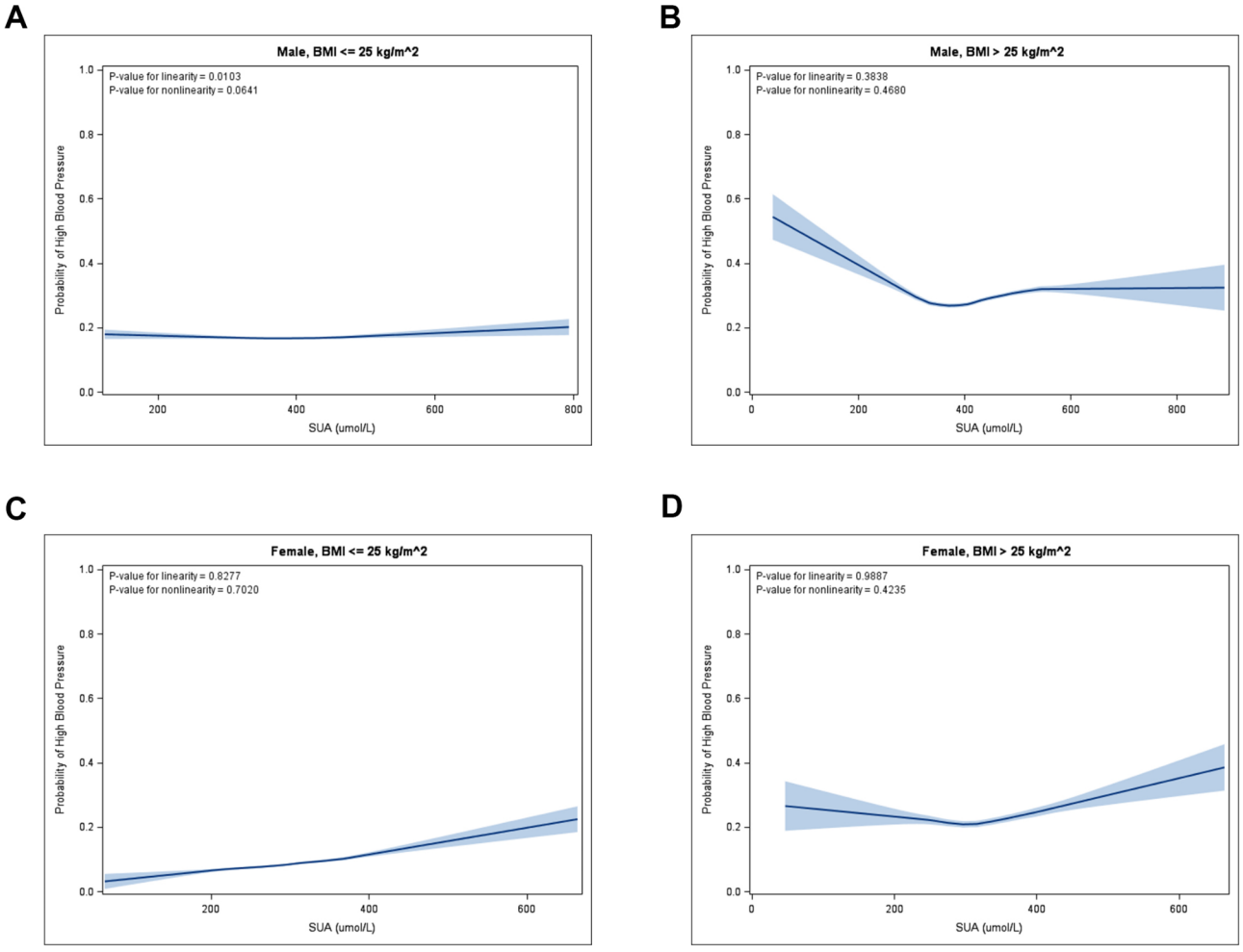

Fig. 4 BMI subgroup analysis for association between SUA and incidence of high blood pressure in males and females

95% CI: 1.81–2.27, $P < 0.0001$], Q4 [OR = 2.54, 95% CI: 2.28–2.84, $P < 0.0001$]), model 3 (Q4 [OR = 1.18, 95% CI: 1.01–1.37, $P = 0.0388$]), model 4 (OR = 1.001, 95% CI: 1.000–1.001, $P = 0.0022$) and model 5 (OR = 1.08, 95% CI: 1.03–1.14, $P = 0.0022$).

Discussion

Several studies have reported a correlation between SUA and hypertension; however, most of these studies were epidemiological studies, animal studies, or drug clinical experiments [11–13]. The current study used hospital-based data acquired from the physical examination results of patients in East China to assess the correlation between SUA levels and high blood pressure through stratification analysis. These findings suggest that increased SUA may function as an independent risk factor for high blood pressure in males. Furthermore, sex-specific differences between SUA levels and high DBP or SBP were observed. A linear dose-response relationship was found between SUA levels and high blood pressure incidence in males.

A cross-sectional study in China including 78,596 participants (47,781 males and 30,815 females) in physical examination [14] showed that during 2011–2015, the prevalence of hypertension and hyperuricemia in both males and females showed an increasing trend; meanwhile, the overall prevalence of hypertension and hyperuricemia was significantly higher in males than in females. A previous study also reported that high UA levels in males may serve as an independent risk factor for increased systolic and DBP, which is consistent with the findings of the present study. Recently, a study focused on the potential risk of coronary artery disease among 5,115 young adults in the USA aged 18–30 years for 20 years.

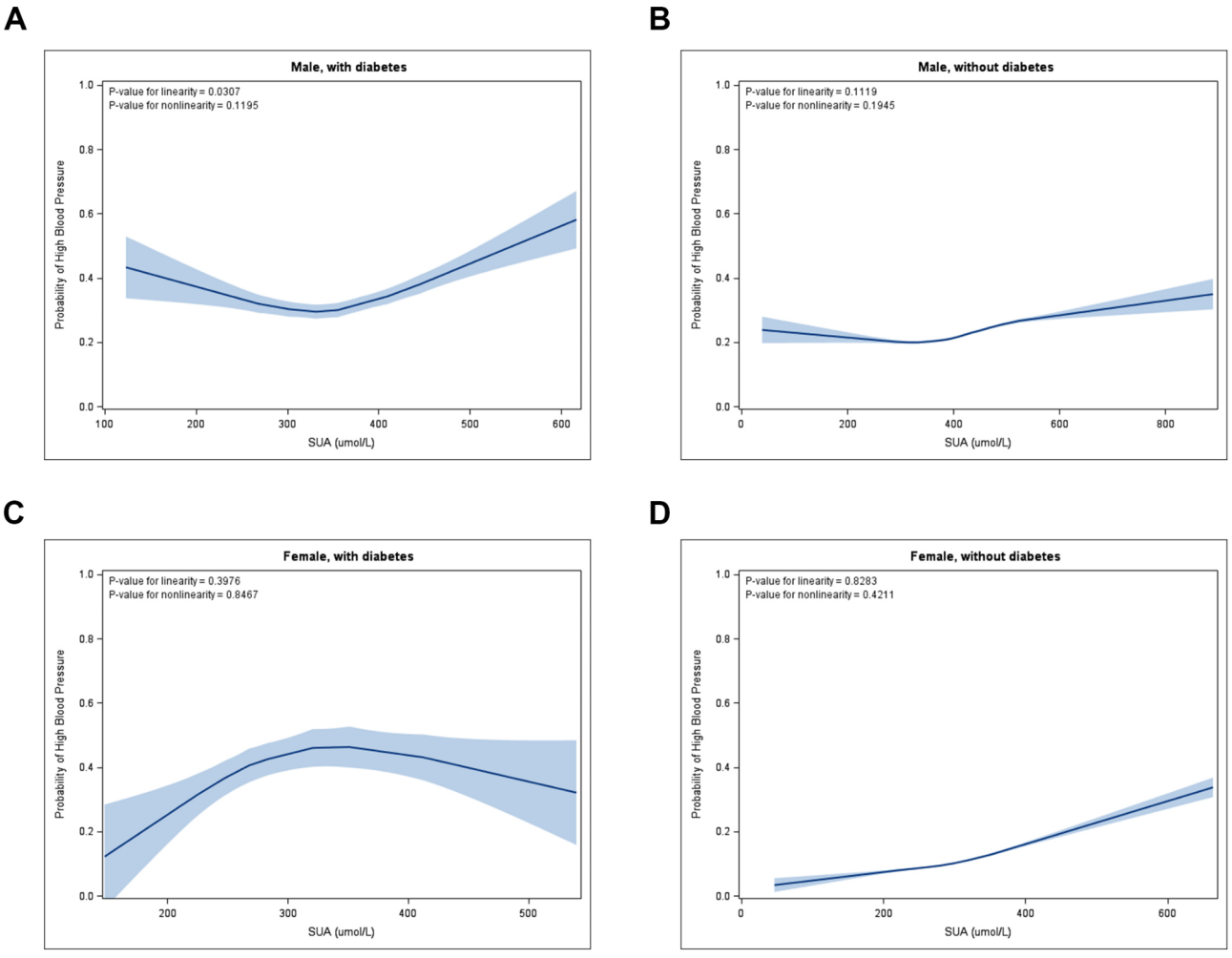

Fig. 5 Diabetes subgroup analysis for association between SUA and incidence of high blood pressure in males and females

The study found that even within the normal range, increased SUA levels were correlated with an increased risk of hypertension, and the above correlation was linear in the male population but non-linear in the female population [15]. These results correlated with those of the present study and showed that the association between SUA levels and high blood pressure in men is more significant. In addition, this study showed significant associations between SUA levels and high blood pressure among males in the diabetes subgroup analysis.

As a purine metabolite, UA is an important indicator of metabolic diseases. Hypertensive diseases are common metabolic diseases, and the two are closely related [16]. Epidemiological studies suggest that SUA is positively correlated with peripheral vascular endothelial dysfunction, inflammatory factors, and peripheral arteriosclerosis, which leads to increased blood pressure [17, 18]. Animal studies have shown that SUA increases blood pressure by stimulating the proliferation of vascular smooth muscle cells, resulting in vascular inflammation,

Table 4 OR and 95% CI for changes in SUA for high diastolic blood pressure incidence

	Model 1		Model 2		Model 3		Model 4		Model 5	
Variable	**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**
Males										
Q1	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-	1.001	0.05	1.07	0.05
Q2	1.10 (0.95, 1.28)	0.201	1.06 (0.91, 1.23)	0.4801	1.08 (0.92, 1.26)	0.3332	(1.000, 1.001)		(1.00, 1.13)	
Q3	1.35 (1.17, 1.55)	< 0.0001**	1.16 (1.00, 1.35)	0.0493*	1.18 (1.01, 1.38)	0.0354				
Q4	1.62 (1.41, 1.86)	< 0.0001**	1.14 (0.98, 1.34)	0.0931	1.15 (0.98, 1.34)	0.0982				
p for trend	< 0.0001**		0.054		0.0659					
Female										
Q1	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-	1	0.6123	0.97	0.6123
Q2	1.01 (0.77, 1.32)	0.9342	0.87 (0.66, 1.14)	0.3212	0.91 (0.69, 1.20)	0.4978	(0.998, 1.001)		(0.84, 1.11)	
Q3	1.11 (0.86, 1.44)	0.4286	0.79 (0.60, 1.03)	0.0853	0.83 (0.63, 1.09)	0.1761				
Q4	1.73 (1.36, 2.20)	< 0.0001**	0.83 (0.64, 1.08)	0.1733	0.89 (0.68, 1.18)	0.421				
p for trend	< 0.0001**		0.1653		0.3843					
Total										
Q1	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-	1.001	0.0569	1.057	0.0569
Q2	1.55 (1.33, 1.80)	< 0.0001**	0.98 (0.83, 1.15)	0.7999	0.99 (0.84, 1.17)	0.9199	(1.000, 1.001)		(0.998, 1.119)	
Q3	2.51 (2.17, 2.89)	< 0.0001**	1.01 (0.86, 1.20)	0.8913	1.04 (0.88, 1.24)	0.6496				
Q4	3.89 (3.39, 4.45)	< 0.0001**	1.10 (0.93, 1.32)	0.2704	1.13 (0.95, 1.36)	0.1751				
p for trend	< 0.0001**		0.1198		0.0753					

Notes: Serum uric acid quartiles (Q1–Q4) in men (Q1: ≤ 346.70; Q2: 346.70–395.30; Q3: 395.30–448.70; and Q4: > 448.70 μ mol/L). In women (Q1: ≤ 244.50; Q2: 244.50–281.10; Q3: 281.10–320.80; and Q4: > 320.80 μ mol/L). In total population (Q1: ≤ 278.30; Q2: 278.30–338.60; Q3: 338.60–407.20; and Q4: > 407.20 μ mol/L). BMI, body mass index; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; TG, triglycerides; TC, total cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein

Model 1: Unadjusted

Model 2: Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, and HDL

Model 3: Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse and eGFR

Model 4: Serum uric acid (μ mol/L) as continuous variable. Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse and eGFR

Model 5: Serum uric acid (mg/dL) as continuous variable. Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse and eGFR

No adjustment for gender in men and women

*P Value < 0.05

**P Value < 0.0001

damaging endothelial cells, insulin resistance, and activation of the renin-angiotensin system [12, 19]. Several clinical experiments have suggested that pharmacologically increasing SUA levels can increase blood pressure by activating the renin-angiotensin system, resulting in reduced vascular nitric oxide production and increased peripheral vascular resistance, with blood pressure returning to normal once UA levels are normalized [20, 21].

Therefore, this study assessed the effects of the association between SUA levels and the incidence of high blood pressure in a large population-based sample of adults. The participants included in the present study were from a standard hospital with a large sample size, and separate analysis of males and females guaranteed sufficient parameters and accurate results to help reach reliable conclusions. This study has a few limitations. First, given the cross-sectional design of this study, we could not establish a causal relationship between SUA elevation and hypertension. Second, findings from retrospective observational analyses and UA measurements may be inaccurate. Future prospective studies are needed to determine whether SUA levels are independent predictors of long-term hypertension outcomes and whether lowering SUA levels reduces the occurrence of adverse blood pressure events.

Table 5 OR and 95% CI for changes in SUA for high systolic blood pressure incidence

	Model 1		Model 2		Model 3		Model 4		Model 5	
Variable	**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**
Males										
Q1	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-	1.001	0.0344*	1.07	0.0344*
Q2	1.00 (0.88, 1.13)	0.9479	1.04 (0.90, 1.19)	0.6172	1.08 (0.94, 1.24)	0.3084	(1.000, 1.001)		(1.01, 1.13)	
Q3	1.03 (0.91, 1.17)	0.6369	1.02 (0.89, 1.16)	0.8275	1.05 (0.91, 1.21)	0.5355				
Q4	1.29 (1.14, 1.45)	< 0.0001**	1.14 (0.99, 1.31)	0.0608	1.17 (1.01, 1.36)	0.0321*				
p for trend	< 0.0001**		0.0862		0.0552					
Female										
Q1	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-	1	0.8125	0.99	0.8125
Q2	1.17 (0.96, 1.42)	0.1259	0.99 (0.80, 1.22)	0.9173	1.04 (0.84, 1.30)	0.7079	(0.999, 1.001)		(0.88, 1.10)	
Q3	1.28 (1.06, 1.56)	0.0125*	0.88 (0.71, 1.09)	0.2289	0.92 (0.74, 1.15)	0.4781				
Q4	2.01 (1.68, 2.41)	< 0.0001**	0.91 (0.73, 1.12)	0.3529	0.97 (0.78, 1.21)	0.7767				
p for trend	< 0.0001**		0.2346		0.5467					
Total										
Q1	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-	1.001	0.0022*	1.08	0.0022*
Q2	1.42 (1.26, 1.60)	< 0.0001**	1.01 (0.89, 1.15)	0.8945	1.03 (0.90, 1.17)	0.6689	(1.000, 1.001)		(1.03, 1.14)	
Q3	2.03 (1.81, 2.27)	< 0.0001**	1.09 (0.95, 1.25)	0.2252	1.13 (0.99, 1.30)	0.081				
Q4	2.54 (2.28, 2.84)	< 0.0001**	1.13 (0.98, 1.31)	0.1048	1.18 (1.01, 1.37)	0.0388*				
p for trend	< 0.0001**		0.0575		0.0196*					

Notes: Serum uric acid quartiles (Q1–Q4) in men (Q1: ≤ 346.70; Q2: 346.70–395.30; Q3: 395.30–448.70; and Q4: > 448.70 μ mol/L). In women (Q1: ≤ 244.50; Q2: 244.50–281.10; Q3: 281.10–320.80; and Q4: > 320.80 μ mol/L). In total population (Q1: ≤ 278.30; Q2: 278.30–338.60; Q3: 338.60–407.20; and Q4: > 407.20 μ mol/L). BMI, body mass index; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; TG, triglycerides; TC, total cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein

Model 1: Unadjusted

Model 2: Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, and HDL

Model 3: Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse and eGFR

Model 4: Serum uric acid (μ mol/L) as continuous variable. Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse and eGFR

Model 5: Serum uric acid (mg/dL) as continuous variable. Adjusted for age, gender, BMI, FBG, diabetes, TG, TC, LDL, HDL, pulse and eGFR

No adjustment for gender in men and women

*P Value < 0.05

**P Value < 0.0001

Conclusion

This study showed that SUA levels were an independent risk factor for high blood pressure after adjustment for other potential confounding risk factors in males. Sex-specific differences in SUA levels and the incidence of high DBP or SBP were also identified.

Abbreviations

BMI Body mass index
CI Confidence interval
DBP Diastolic blood pressure
FBG Fasting blood glucose
HDL High-density lipoprotein
LDL Low-density lipoprotein
OR Odds ratio
SBP Systolic blood pressure
SUA Serum uric acid
TC Total cholesterol
UA Uric acid

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-22064-0.

Supplementary Material 1

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Author contributions

Dan Liu and Xiang Zheng the main manuscript text; Jing Zhu, Jianshu Yang and Yongqin Luo prepared figures; Li Lu, Xiaodong Ji and Jie Hui prepared the tables. All authors reviewed the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study protocol was approved by the Ethics Committee of The First Affiliated Hospital of Soochow University(No.86392357). Written informed consent was provided prior to the study.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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