

Sex-specific association between Chinese visceral adiposity index and hyperuricemia among adults: a population-based cross-sectional study in Chongqing, China

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Abstract

Research on the association between the Chinese visceral adiposity index (CVAI) and hyperuricemia (HUA) is scarce, and whether the association differs by sex is unclear. This research aimed to explore sex-specific associations between CVAI and HUA and to compare CVAI's predictive performance with other adiposity indices using data from 22,171 adults (30–79 years) in the China Multi-Ethnic Cohort (CMEC) study (Chongqing region). The prevalence of HUA was 20.9% in men and 9.7% in women. Multivariable logistic regression analyses were utilized to assess the adjusted odds ratios (ORs) and 95% confidence intervals (CIs). After multivariable adjustment, CVAI was associated with HUA in men (OR Q4 vs. Q1 = 3.31, 95% CI 2.73, 4.03) and women (OR Q4 vs. Q1 = 7.20, 95% CI 5.12, 10.12). Moreover, Significant interactions were observed between BMI and CVAI on HUA in both sexes (all $P_{\text{interaction}} < 0.001$), with the strongest associations in those with BMI < 24.0 kg/m². The ORs (95% CI) across different BMI groups (< 24.0 , 24.0–27.9, ≥ 28.0 kg/m²) were 1.87 (1.63, 2.13), 1.65 (1.48, 1.85), and 1.30 (1.14, 1.49) for men, and 2.76 (2.18, 3.51), 2.46 (1.98, 3.07), and 1.87 (1.47, 2.39) for women, respectively. Additionally, CVAI showed satisfactory predictive performance for HUA in women, with the largest area under the receiver operating characteristic curve (AUROC) of 0.735, but not in men (0.660). These findings suggest a close association between CVAI and HUA, particularly pronounced in those with BMI < 24.0 kg/m², and a stronger association in women than in men.

Keywords: Chinese visceral adiposity index; Hyperuricemia; Adiposity indices; Adults; Cross-sectional study

Abbreviations:

AUROC, area under the receiver operating characteristic curve; BMI, body mass index; CMI, cardiometabolic index; CMEC, China Multi-Ethnic Cohort; CVAI, Chinese visceral adiposity index; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; HUA, hyperuricemia; HDL-C, high-density lipoprotein cholesterol; LAP, lipid accumulation product index; LDL-C, low-density lipoprotein cholesterol; METs, metabolic equivalent tasks; NC, neck circumference; OR, odds ratios; SAT, subcutaneous adipose tissue; SBP, systolic blood pressure; SUA, serum uric acid; TC, total cholesterol; TG, triglyceride; UA, uric acid; VAI, visceral adiposity index; VAT visceral adipose tissue; WC, waist circumference; WHtR, waist-to-height ratio; XOR, xanthine oxidoreductase.

Introduction

Serum uric acid (SUA) is the end product of purine metabolism⁽¹⁾. Hyperuricemia (HUA) may develop when there is a disturbance in purine metabolism. HUA, as an emerging public health issue, has attracted increasing attention because its prevalence has been steadily rising globally in recent decades^(2, 3). It has been closely linked to gout, hypertension, and cardiovascular disease mortality, as well as all-cause mortality⁽⁴⁻⁶⁾. The prevalence of HUA in China was high, estimated at approximately 20% according to a National Health Survey conducted in China between 2012 and 2017⁽⁷⁾. Thus, identifying modifiable HUA risk factors is vital to implement effective prevention strategies.

Obesity is recognized as a major risk factor for HUA⁽⁸⁻¹⁰⁾. More than 650 million people in the world have obesity⁽¹¹⁾. With approximately 89.6 million individuals classified as obese⁽¹²⁾, China has the largest population with obesity globally. Growing evidence suggests that body fat distribution is correlated with different risks of HUA. Research has shown a stronger association between visceral adipose tissue (VAT) accumulation and the risk of HUA than abdominal subcutaneous fat across diverse populations⁽¹³⁻¹⁵⁾. Magnetic resonance imaging and computed tomography can precisely quantify the visceral fat area, but their application in large-scale epidemiological studies is constrained by their high cost and the potential risk of radiation exposure⁽¹⁶⁾. Waist circumference (WC) and waist-to-height ratio (WHtR), as traditional abdominal adiposity indices, lack the ability to distinguish between subcutaneous and visceral fats⁽¹⁷⁾. Consequently, novel abdominal adiposity indices, such as visceral adiposity index (VAI), lipid accumulation product (LAP) index, cardiometabolic index (CMI), and Chinese visceral adiposity index (CVAI) have been established to differentiate between visceral and subcutaneous adiposity. Notably, Asians have a lower body mass index (BMI) than Caucasians⁽¹⁸⁾, but they seem to be more prone to central fat deposition⁽¹⁹⁾. This means that VAI, which is used to predict visceral adiposity in Caucasians, may not adequately predict visceral adiposity in Asians. The CVAI is a recently established abdominal adiposity index in Chinese adults⁽²⁰⁾. It combines WC, BMI, triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) while considering the influence of gender and age. It is recognized as a dependable indicator for assessing dysfunction in VAT⁽²⁰⁾. In the Chinese population, CVAI is more correlated with hypertension and prehypertension⁽²¹⁾,

arterial atherosclerosis⁽²²⁾, and diabetes complications⁽²³⁾ than other obesity-related indices.

However, research investigating the associations between CVAI and HUA is scarce^(24, 25), and the predictive performance of CVAI for HUA still needs to be explored. Moreover, recent research has identified sex differences in the associations between obesity-related indices and HUA⁽²⁶⁾. However, whether the association between CVAI and HUA differs by sex is unclear. Hence, this study aimed to explore sex-specific association between CVAI and HUA and assess the discriminative ability of CVAI for HUA in comparison with VAI, LAP, CMI, WC, and WHtR by utilizing data from the China Multi-Ethnic Cohort (CMEC) study (Chongqing region). Stratified analysis was conducted with age, smoking, drinking, spicy food intake, BMI, diabetes, and hypertension to explore the effect modifications of sociodemographic characteristics, lifestyle factors, anthropometric measurements, and health status in the relationship between CVAI and HUA.

Method

Study Population

Data for this study were obtained from the CMEC study in Chongqing region. Detailed information about the CMEC study has been introduced previously⁽²⁷⁾. A total of 23,308 Han adults aged 30–79 years were enrolled using multistage, stratified cluster sampling methods in Chongqing Municipality, located in Southwest China, between September 2018 and February 2019. In brief, the cluster sampling method was used to select 13 districts and counties (districts and counties of the same administrative level) in Chongqing. Subsequently, based on the age and gender structure of Chongqing in 2018, stratified random sampling was employed to allocate the number of people in each district and county. Participants with missing data for SUA levels ($n = 859$), anthropometric parameters ($n = 39$), biochemical measurement indices ($n = 290$), and covariates ($n = 39$) were excluded. The remaining 22,171 participants (men: 10,355; women: 11,816) were finally included in the current analysis (**Fig. S1**). This study protocol was conducted in accordance with the guidelines laid down in the Declaration of Helsinki and all procedures involving human participants were approved by the Sichuan University Medical Ethical Review Board (K2016038) and the Research Ethics Committee of the Chongqing Centre for Disease Control and Prevention [2017(001)]. Written informed consent was obtained from all participants prior to participation.

Anthropometric and Biochemical Measurements

Anthropometric measurements, including weight (kg), height (cm), and WC (cm), were conducted by trained staff in accordance with standard protocols. Participants were checked for weight and height while standing barefoot and wearing light clothing. WC was measured using the lower edge of the tape 1 cm above the navel. BMI was calculated by dividing weight (kg) by the square of height (m). WHtR was calculated by dividing WC (cm) by height (cm).

After sitting at rest for at least 5 minutes, the participants' blood pressure was measured three times at 45-second intervals by a trained interviewer using an electronic oscillometric blood pressure measurement device (Omron HEM-7600T). The systolic blood pressure (SBP) or diastolic blood pressure (DBP) in this study was determined as the average of three measurements for SBP or DBP. Blood samples of participants were collected following an overnight fast (minimum of 8 hours) and tested at the Di'an Medical Laboratory Center. Fasting blood glucose (FBG), total cholesterol (TC), TG, low-density lipoprotein cholesterol (LDL-C), HDL-C, SUA, and creatinine were measured on an automated biochemical analyzer (HITACHI 7600 Series, Chongqing, China). The estimated glomerular filtration rate (eGFR) was computed by utilizing the newly formulated equation provided by the Chronic Kidney Disease Epidemiology Collaboration⁽²⁸⁾.

Definitions

HUA was defined as having a SUA level of $\geq 360 \mu\text{mol/L}$ in women and $\geq 420 \mu\text{mol/L}$ in men⁽²⁹⁾. The formulas for VAI⁽³⁰⁾, CMI⁽³¹⁾, LAP⁽³²⁾, CVAI⁽²⁰⁾ were as follows:

$$\text{VAI}(\text{men}) = \left(\frac{\text{WC}(\text{cm})}{39.68 + 1.88 \times \text{BMI}(\text{kg}/\text{m}^2)} \right) \times \left(\frac{\text{TG}(\text{mmol}/\text{L})}{1.03} \right) \times \left(\frac{1.31}{\text{HDL}(\text{mmol}/\text{L})} \right)$$

$$\text{VAI}(\text{women}) = \left(\frac{\text{WC}(\text{cm})}{36.58 + 1.89 \times \text{BMI}(\text{kg}/\text{m}^2)} \right) \times \left(\frac{\text{TG}(\text{mmol}/\text{L})}{0.81} \right) \times \left(\frac{1.52}{\text{HDL}(\text{mmol}/\text{L})} \right)$$

$$\text{LAP}(\text{men}) = (\text{WC}(\text{cm}) - 65) \times \text{TG}(\text{mmol}/\text{L})$$

$$\text{LAP}(\text{women}) = (\text{WC}(\text{cm}) - 58) \times \text{TG}(\text{mmol}/\text{L})$$

$$\begin{aligned} \text{CVAI}(\text{men}) = & -267.93 + 0.68 \times \text{age}(\text{years}) + 0.03 \times \text{BMI}(\text{kg}/\text{m}^2) + 4.00 \times \text{WC}(\text{cm}) \\ & + 22.00 \times \text{Lg TG}(\text{mmol}/\text{L}) - 16.32 \times \text{HDL}(\text{mmol}/\text{L}) \end{aligned}$$

$$\begin{aligned} \text{CVAI}(\text{women}) = & -187.32 + 1.71 \times \text{age}(\text{years}) + 4.32 \times \text{BMI}(\text{kg}/\text{m}^2) + 1.12 \times \text{WC}(\text{cm}) \\ & + 39.76 \times \text{Lg TG}(\text{mmol}/\text{L}) - 11.66 \times \text{HDL}(\text{mmol}/\text{L}) \end{aligned}$$

$$\text{CMI} = \left(\frac{\text{TG (mmol/L)}}{\text{HDL (mmol/L)}} \right) \times \text{WhtR}$$

Assessment of Covariates

Face-to-face interviews were conducted utilizing structured questionnaires to collect detailed information on sociodemographic status (e.g., gender, age, area, marital status, and educational level), lifestyle factors (such as smoking status, drinking status, physical activity, and dietary intake), and health status. Area was divided into two categories: urban areas and rural areas, based on participants' residential addresses. Smoking was defined as having smoked ≥ 100 cigarettes in their lifetime, and drinking was defined as alcohol intake ≥ 12 times during the last year⁽²⁷⁾. The participants' physical activity levels were assessed by aggregating the respective metabolic equivalent tasks (METs) across four domains: housework, transportation, work, and leisure^(33, 34). Dietary intake information was obtained through a food frequency questionnaire. The Dietary Approaches to Stop Hypertension (DASH) score was calculated based on the scoring method developed by Fung et al⁽³⁵⁾. Scores of 1–5 were assigned to seven food categories (whole grains, fresh fruits, fresh vegetables, legumes, red meat products, dairy products, and sodium) in accordance with the quintile of average food intake in this study. For whole grains, fresh fruits, fresh vegetables, legumes, and dairy products, the highest quintile scored 5, and the lowest quintile scored 1. Conversely, for red meat products and sodium, this study aimed for lower intake, so the scoring pattern was reversed. Subsequently, the scores for these seven components were aggregated to yield an overall DASH score within the range of 7–35. The participants were divided into two groups (≤ 21 and > 21) on the basis of median DASH score. Non-spicy eaters were defined as those who have not consumed any spicy foods in the past month. BMI was grouped into < 24.0 , 24.0 – 27.9 , and ≥ 28.0 kg/m^2 ⁽³⁶⁾. Hypertension was diagnosed as the average measurements of SBP/DBP $\geq 140/90$ mmHg or having a self-reported history of physician-diagnosed hypertension⁽³⁷⁾. Diabetes was defined as fasting blood glucose ≥ 7.0 mmol/L, glycosylated hemoglobin percentage of $\geq 6.5\%$, or having a self-reported history of physician-diagnosed diabetes⁽³⁸⁾.

Statistical Analyses

Continuous variables, including age, physical activity, SBP, DBP, FBG, TC, TG, HDL-C, LDL-C, SUA, eGFR, BMI, WC, WHtR, VAI, CMI, and CVAI, were presented as medians and interquartile ranges (IQR) because of skewed distribution and examined using Wilcoxon two sample test, whereas categorical variables, including area, marital status, educational level, smoking status, drinking status, spicy food intake, DASH score, diabetes, and hypertension, were expressed as numbers (percentages) and were analyzed using chi-square tests. All analyses were performed separately by sex.

Logistic regression analyses were used to explore the association between CVAI and HUA and assess the odds ratios (ORs) with corresponding 95% confidence intervals (CIs) for HUA, considering CVAI as either a continuous variable (per 1-SD increment) or a categorical variable (quartiles). A series of models was employed to adjust for potential confounding factors. Model 1 included no adjustments; model 2 adjusted for age, area, educational level, marital status, smoking, drinking, spicy food intake, DASH score, and physical activity; model 3 extended these adjustments by including diabetes, hypertension, BMI, eGFR, TC, and LDL-C. The covariates included in the models were selected based on previous studies investigating the relationship between obesity and metabolic diseases^(14, 21, 23, 39, 40). Collinearity among all adjusted variables was examined, revealing no definitive evidence of multicollinearity (the variance inflation factor for all included variables was < 5 ; **Fig. S2**). The interaction between sex and CVAI on HUA in logistic regression analysis was as follows: Model outcome (y) = $x_1 + x_2 + x_1 \times x_2 + \text{covariates}$, where y represents HUA, x_1 represents sex, x_2 represents CVAI (per 1-SD), $x_1 \times x_2$ was the interaction term, and covariates referred to the adjusted variables in model 3. Restricted cubic spline (RCS) analysis was conducted with four knots positioned at the 5th, 35th, 65th, and 95th percentiles of CVAI to examine potential nonlinear associations and depict the dose–response relationship of between CVAI and HUA. The predictive powers of CVAI, VAI, LAP, CMI, WC, and WHtR for HUA were evaluated using receiver operating characteristic curve. A nonparametric approach described by De Long et al.⁽⁴¹⁾ was employed to compare the area under the receiver operating characteristic curve (AUROC) of CVAI in predicting HUA with those of other adiposity indices (VAI, LAP, CMI, WC, and WHtR). Stratified analyses were conducted across diverse

subgroups, including age, smoking status, drinking status, BMI, diabetes, and hypertension, to evaluate the effect modifications of CVAI on the risk of HUA and explore potential interaction effects using a multiplicative interaction term [CVAI \times (subgroups)]. Sensitivity analyses were performed by excluding participants with self-reported coronary artery disease, stroke, or cancer to validate the robustness of the results.

RCS was calculated using R (version 4.3.3, R Foundation, Boston, MA) with the “rms” package, and other analyses were conducted using SPSS (version 26.0, SPSS, Inc). A two-sided $P < 0.05$ was deemed statistically significant.

Results

Baseline characteristics of participants

Overall, 22,171 participants (10,355 men: 46.7%; 11,816 women: 53.3%) were included for analysis. Among them, 3320 participants (2173 men: 20.9%; 1147 women: 9.7%) were defined as having HUA. The baseline characteristics of the participants are presented in **Table 1**. The participants with HUA, regardless of sex, exhibited a higher proportion of hypertension at baseline; higher BMI, WC, WHtR, VAI, LAP, CMI, CVAI, SBP, DBP, FBG, TC, TG, LDL-C, and SUA levels; lower HDL-C and eGFR levels; and less physical activity compared to those without HUA (all $P < 0.05$). However, women with HUA tended to live in rural areas, showed a lower proportion of being married/cohabiting, and had a higher proportion of diabetes at baseline than those without HUA (all $P < 0.05$). Meanwhile, these significant differences were not observed in men with and without HUA. Moreover, women with HUA tended to be older, less educated, and non-drinkers, whereas men with HUA exhibited the opposite trend. The general characteristics of included and excluded participants were compared in Table S1. There were no significant differences in sex (Men: 47.85% vs. 46.71%; Women: 52.15% vs. 53.29%; $P=0.452$) and age (49.66 (IQR: 43.36–60.83) vs. 50.61 (IQR: 44.63–61.03); $P=0.154$) between included and excluded participants.

Sex-specific association between CVAI and HUA

The sex-specific association between CVAI and HUA are presented in **Table 2**. After adjusting for confounding factors, compared to the first quartile (Q_1) of CVAI, the ORs with corresponding 95% CIs for HUA in the second, third, and fourth quartiles (Q_2 , Q_3 , and Q_4) of CVAI were 1.67 (1.40, 1.99), 2.38 (1.98, 2.85), and 3.31 (2.73, 4.03), respectively, for men

and 2.03 (1.51, 2.73), 3.78 (2.81, 5.09), and 7.20 (5.12, 10.12), respectively, for women in model 3. Furthermore, the association between each 1-SD increase in CVAI and HUA was significantly stronger in women (OR = 2.38, 95% CI 2.09, 2.72) than in men (OR = 1.60, 95% CI 1.48, 1.71) in model 3. This sex-specific difference was statistically supported by a significant interaction between sex and CVAI on HUA ($P_{\text{interaction}} < 0.001$). After participants who self-reported coronary artery disease, stroke, or cancer were excluded, the positive association between CVAI and HUA persisted (**Table S2**).

RCSs revealed a nonlinear dose–response relationship between CVAI and HUA in both sexes (all $p_{\text{overall}} < 0.001$, $p_{\text{non-linear}} < 0.05$; **Fig. 1**). In men, With the knot at 50th percentile of CVAI as the reference, the ORs with corresponding 95% CIs for the four knots of CVAI (22.10, 78.43, 109.86, and 161.22) were 0.41 (0.33, 0.50), 0.74 (0.70, 0.79), 1.30 (1.24, 1.38), and 2.12 (1.82, 2.47), respectively. The risk of HUA decreased when CVAI was < 95.82 , and increased when CVAI was ≥ 95.82 (**Fig. 1a**). In women, With the knot at 50th percentile of CVAI as the reference, the ORs with corresponding 95% CIs for the four knots of CVAI (12.23, 58.93, 91.75, and 143.58) were 0.31 (0.22, 0.44), 0.61 (0.57, 0.66), 1.72 (1.57, 1.89), and 4.37 (3.47, 5.50), respectively. The risk of HUA decreased when CVAI was < 75.81 , and increased when CVAI was ≥ 75.81 (**Fig. 1b**).

Comparison of the predictive power of CVAI, VAI, LAP, CMI, WHtR, and WC for HUA

The receiver operating characteristic curve analysis showed the predictive ability of CVAI, VAI, LAP, CMI, WHtR, and WC for HUA in both sexes (**Fig. S3**). The AUROC with 95% CIs of CVAI, VAI, LAP, CMI, WHtR, and WC in men were 0.660 (0.648, 0.673), 0.695 (0.682, 0.707), 0.709 (0.697, 0.721), 0.698 (0.686, 0.711), 0.621 (0.608, 0.634), and 0.648 (0.635, 0.661), respectively, and 0.735 (0.720, 0.749), 0.713 (0.697, 0.728), 0.728 (0.713, 0.743), 0.724 (0.709, 0.739), 0.672 (0.656, 0.689), and 0.670 (0.653, 0.686), respectively, in women. Among them, LAP had the largest AUROC for HUA in men, with a cutoff of 34.03 (sensitivity: 68.3%, specificity: 64.1%), and CVAI had the largest AUROC for HUA in women, with a cutoff of 84.52 (sensitivity: 73.4%, specificity: 62.3%; **Table 3**). Additionally, the AUROC of CVAI was further compared with those of other adiposity indices among different sexes. Among men, the AUROC of CVAI statistically weaker than those of LAP, CMI, and VAI and greater than those of WC and WHtR (all $P < 0.001$). Among women, the

AUROC of CVAI were statistically greater than those of WC, WHtR, and VAI (all $P < 0.05$). Meanwhile, no significant differences were observed in the AUROC between CVAI and CMI and between CVAI and LAP (**Table 3**). Similar results were observed in the sensitivity analysis (**Table S3**).

Stratified analysis

The participants were grouped based on age (< 60 and ≥ 60 years), smoking status (no and yes), drinking status (no and yes), spicy food (no and yes), BMI (< 24.0 , $24.0-27.9$, and ≥ 28.0 kg/m²), diabetes (no and yes), and hypertension (no and yes) to evaluate the effect modification of these factors on the association between CVAI and HUA. The positive association between CVAI and HUA persisted across various subgroups for both sexes. In both sexes, significant interactions were observed between BMI and CVAI on HUA (all $P_{\text{interaction}} < 0.001$). When analyses were stratified by BMI, the association between CVAI and HUA was strongest in individuals with BMI < 24.0 kg/m². Specifically, for men, the percentage increase in OR of HUA (calculated as $[\text{OR}-1] \times 100\%$) was 87% in the BMI < 24.0 kg/m² group (OR=1.87, 95%CI 1.63, 2.13), 65% in the BMI $24.0-27.9$ kg/m² group (OR=1.65, 95%CI 1.48, 1.85), and 30% in the BMI ≥ 28.0 kg/m² group (OR=1.30, 95%CI 1.14, 1.49). Similarly, among women, the corresponding percentage increases were 176% (OR=2.76, 95%CI 2.18, 3.51), 146% (OR=2.46, 95%CI 1.98, 3.07), and 87% (OR=1.87, 95%CI 1.47, 2.39) across different BMI groups (**Fig. 2**). Moreover, a significant interaction was found between age and CVAI on HUA in women ($P_{\text{interaction}} < 0.05$). However, the magnitude of the association changed minimally across different age groups, with an OR of 2.39 (95% CI 2.02, 2.80) per 1-SD increase in CVAI for women aged < 60 years and 2.34 (95% CI 1.86, 3.01) for those aged ≥ 60 years (**Fig. 2**). Similar positive associations were observed in the sensitivity analysis (**Fig. S4**).

Discussion

The sex-specific association between CVAI and HUA was thoroughly explored for the first time by using a large population-based sample from Chongqing, China. A significant positive association was found between CVAI and HUA, even after adjusting for a wide range of biochemical and lifestyle factors. Sex differences were observed, with a stronger association in women than in men. Moreover, a nonlinear dose-response relationship

between CVAI and HUA was observed in both sexes. Further stratified analysis revealed that the association between CVAI and HUA was strong in both sexes with BMI <24.0 kg/m². A significant interaction was found between age and CVAI on HUA in women. However, the magnitude of association showed minimal variation across different age groups.

This research also showed that CVAI performed well in predicting HUA in women (with the largest AUROC value), but relatively poorly in men. A Chinese study of 329 patients with type 2 diabetes revealed that except for visceral fat area, CVAI had the best diagnostic ability for HUA among other obesity indicators (BMI, neck circumference (NC), WC, and hip circumference), regardless of sex⁽²⁴⁾. However, new adiposity indices, such as VAI, LAP, and CMI, were not considered in their study⁽²⁴⁾. Another study including 7848 participants explored the predictive ability of different obesity indices (including new adiposity indices) for HUA, indicating that CMI had the largest AUROC in both sexes, with no significant differences in the AUROC among CVAI, CMI, and LAP for women⁽²⁵⁾. Differences in results across studies may be attributed to variations in study populations, sample sizes, statistical analyses, and adjustment factors.

Moreover, our study found that LAP demonstrated the best predictive capability for HUA among men, with the largest AUROC. LAP's calculation formula incorporates WC and TG, which are closely related to abdominal obesity and lipid metabolism⁽⁴²⁾. Men and women typically exhibit significant differences in lipid metabolism and visceral fat distribution⁽⁴³⁾, potentially making LAP a more sensitive predictor of HUA in men. Previous studies have indicated that LAP has been more strongly correlated with HUA than other adiposity indices and has exhibited satisfactory predictive capability for HUA^(26, 44). However, these studies did not include CVAI. Our findings suggest that CVAI had satisfactory predictive capability for HUA in women, while LAP was effective in men. Therefore, considering sex-specific factors, combining different obesity indices may be necessary for comprehensive HUA assessment.

Furthermore, CVAI was more strongly associated with HUA in women than in men, similar to findings from a recent Taiwan study that showed a stronger correlation between obesity-related indices and HUA in women⁽²⁶⁾. They hypothesized that this discrepancy may be attributed to higher xanthine oxidoreductase (XOR) activity in men⁽²⁶⁾, which catalyzes the synthesis of uric acid (UA) through the oxidation of hypoxanthine and xanthine⁽⁴⁵⁾.

Tsushima et al. suggested that adipose tissue is rich in XOR, which plays a key role in UA production utilizing a mouse model⁽⁴⁶⁾. A previous study has indicated higher levels of xanthine, hypoxanthine, and plasma XOR in men than in women, with hypoxanthine concentration independently associated with obesity⁽⁴⁷⁾. Thus, higher XOR activity in men may explain the weaker correlation between obesity indicators and HUA. Additionally, previous studies have found a stronger association between visceral fat and adverse metabolic outcomes in women than in men, possibly due to sex differences in adipocyte size, basal lipolysis, and fatty acid oxidation rates^(48, 49). Women tended to have lower levels of basal fatty acid oxidation than men, making them more susceptible to metabolic disturbances⁽⁵⁰⁾. Further studies are needed to explore the sex physiology associated with HUA and obesity.

Additionally, the stratified analysis suggested that BMI could potentially modulate the association between CVAI and HUA, a more pronounced interaction effect of CVAI on HUA was observed in individuals with BMI < 24.0 kg/m². BMI, serving as a general obesity metric, is incapable of evaluating specific regional adipose tissue content. For instance, a computed tomography study demonstrated that individuals with normal BMI (18.5–25.0 kg/m²) exhibited a high proportion of visceral obesity—a condition strongly linked to metabolic disorders⁽⁵¹⁾. In Asians, visceral obesity has emerged as a more reliable indicator of obesity than BMI⁽⁵²⁾. Research has shown stronger correlations between abdominal obesity indices (WC, VAI, LAP, and CVAI) and incident cardiovascular events in the subgroup with BMI < 25 kg/m² compared to the overweight/obese group⁽¹⁷⁾. Another study had similar findings⁽²³⁾. These findings collectively indicate that BMI inadequately captures visceral fat accumulation—a key factor of obesity-related diseases like HUA and cardiovascular disease. To the best of the authors' knowledge, this study was the first stratified analysis conducted to explore the relationship between CVAI and HUA.

SUA is produced as a result of purine metabolism, with its levels primarily governed by the balance between UA production and excretion⁽⁵³⁾. Our study found an association between CVAI and HUA. The mechanisms may include: (1) The buildup of obese adipose tissue in individuals with obesity can increase free fatty acid levels, which are closely associated with de-novo purine synthesis, thereby promoting SUA production^(15, 46). (2) Adiposity is associated with hyperinsulinemia and insulin resistance, which may affect the

reabsorption of sodium and UA on renal tubules, leading to reduced UA excretion and increased UA levels, ultimately fostering the development of HUA⁽⁵⁴⁻⁵⁶⁾. (3) VAT exhibits a higher level of lipolysis than subcutaneous adipose tissue. The higher the lipolytic activity of VAT, the greater the flow of free fatty acids to the liver, affecting purine metabolism and accelerating UA production⁽⁵⁷⁾.

The key strengths of this study include that it is the first to explore the sex-specific association between CVAI and HUA in a large population-based sample from Chongqing, as well as the first to examine their dose-response relationship, which was not considered in previous research. However, several limitations should be noted. First, as a cross-sectional study, causality cannot be determined. Second, self-reported data on variables, such as physical activity, smoking, drinking, dietary habits, may introduce reporting and recall biases. Third, participants with HUA may have altered their lifestyles to reduce visceral fat accumulation, potentially underestimating the association. Therefore, longitudinal studies are warranted to validate these findings. Finally, since the study was conducted exclusively in Chongqing, China, the results may not be generalizable to broader Chinese populations.

Conclusions

The research findings indicated a close association between CVAI and HUA in adults aged 30–79 years in Chongqing, China, particularly pronounced in those with BMI <24.0 kg/m², and with sex differences. A stronger association was found in women than in men. For women, CVAI served as a satisfactory predictor of HUA, while for men, LAP proved to be a more effective predictor. Considering the sex factor, different obesity-related indices should be combined to provide a comprehensive evaluation for HUA.

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Supplementary Materials

Supplementary materials are available from the file entitled "Supplementary data".

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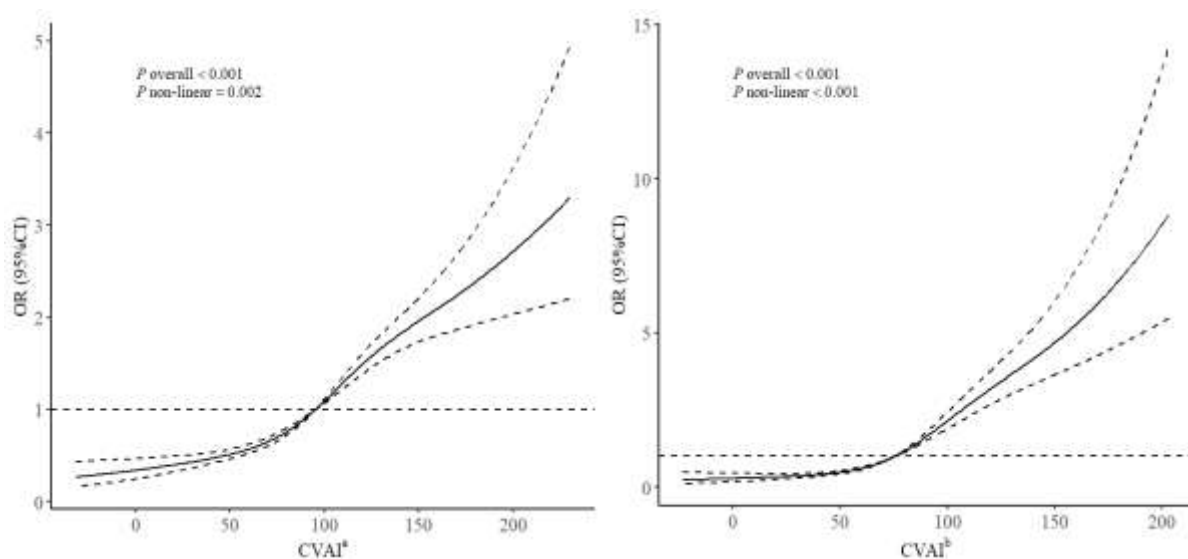


Fig. 1. Dose-response relationship between Chinese visceral adiposity index (CVAI) and hyperuricemia (HUA) among adults enrolled in the Chinese Multi-Ethnic Cohort study, using restricted cubic splines based on a logistic regression model. The plot shows a non-linear relationship between CVAI and HUA. Data are odds ratio (OR) and 95% confidence interval (CI), Solid lines indicate OR, shadow shape indicates 95% CI. ^aThere was a nonlinear dose-response relationship between CVAI and the risk of HUA in men ($p_{\text{overall}} < 0.001$, $p_{\text{non-linear}} = 0.002$). ^bThere was a nonlinear dose-response relationship between CVAI and the risk of HUA in women ($p_{\text{overall}} < 0.001$, $p_{\text{non-linear}} < 0.001$).

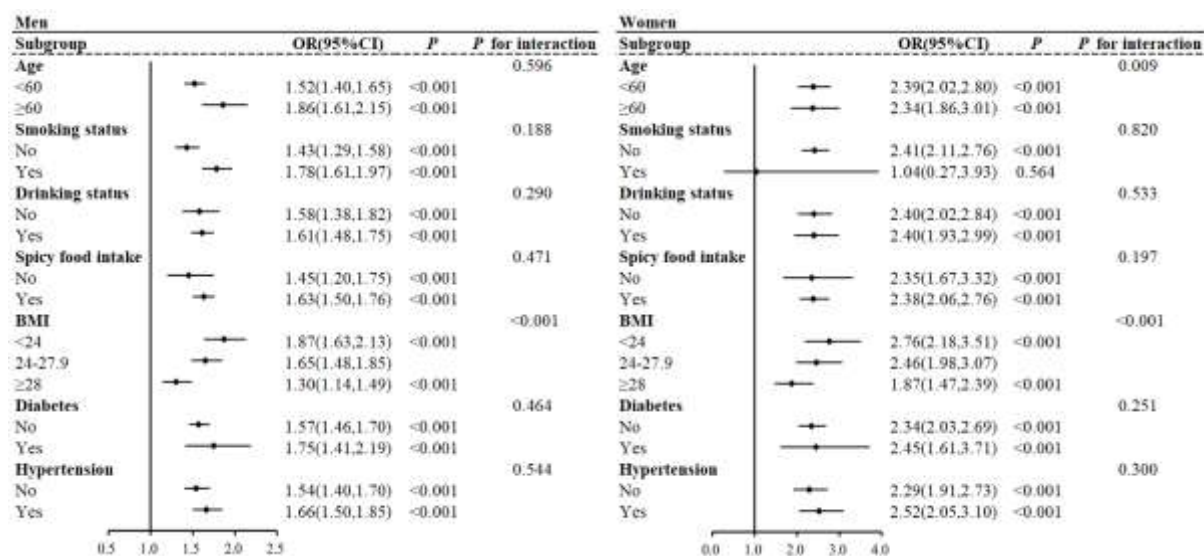


Fig. 2. Association between Chinese visceral adiposity index (CVAI) (per-SD increase) and hyperuricemia (HUA) among adults enrolled in the Chinese Multi-Ethnic Cohort study, stratified by age, smoking, drinking, spicy food, body mass index (BMI), diabetes, and hypertension, using logistic regression model. The model was adjusted for age, area, education level, marital status, smoking, drinking, spicy food intake, DASH score, physical activity, diabetes, hypertension, BMI, eGFR, TC and LDL-C, except for stratify. Data are odds ratio (OR) and 95% confidence interval (CI). BMI, body mass index; CVAI, Chinese visceral adiposity index; DASH, Dietary Approaches to Stop Hypertension; eGFR, estimated glomerular filtration rate; HUA, hyperuricemia; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol.

Fig. S1. Flow chart of the selection of study participants.

Fig. S2. The variance inflation factors for all included variables in model 3.

model 3: included age, area, education level, marital status, smoking, drinking, spicy food intake, DASH score, physical activity, diabetes, hypertension, BMI, eGFR, TC, and LDL-C.

Fig. S3. Receiver operating characteristic curve of waist circumference (WC), waist-to-height ratio (WHtR), visceral adiposity index (VAI), lipid accumulation product index (LAP), cardiometabolic index (CMI), and Chinese visceral adiposity index (CVAI) for predicting hyperuricemia (HUA) among men and women enrolled in the Chinese Multi-Ethnic Cohort study.

Fig. S4. Sensitivity analyses for association between Chinese visceral adiposity index (CVAI) (per-SD increase) and hyperuricemia (HUA) among adults enrolled in the Chinese Multi-Ethnic Cohort study, stratified by age, smoking, drinking, spicy food, body mass index (BMI), diabetes, and hypertension, using logistic regression model.

Table 1. Baseline characteristics of 22,171 participants with and without hyperuricemia (HUA), stratified by sex, recruited from the Chinese Multi-Ethnic Cohort study in Chongqing, China

(Median and interquartile ranges (IQR); numbers and percentages)

Variables	Men (n=10,355)					Women (n=11,816)				
	non-HUA (n=8182)		HUA (n=2173)		<i>P</i>	non-HUA (n=10,669)		HUA (n=1147)		<i>P</i>
	Media n	IQR	Media n	IQR		Media n	IQR	Media n	IQR	
Age(years)	51.00	44.00–62.00	48.00	41.00–58.00	< 0.001	49.00	43.00–58.00	55.00	47.00–65.00	< 0.001
Area(n,%)					0.168					0.040
Urban	2354	28.77	658	30.28		3051	28.60	295	25.72	
Rural	5828	71.23	1515	69.72		7618	71.40	852	74.28	
Marital status(n,%)					0.625					< 0.001
Married/cohabiting	7412	90.59	1961	90.24		9200	86.23	921	80.30	
Others	770	9.41	212	9.76		1469	13.77	226	19.70	
Education(n,%)					<					<

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					0.001				0.001
Primary school or below	2454	29.99	468	21.54		3860	36.18	474	41.33
Junior high school	2742	33.51	701	32.26		3328	31.19	360	31.39
High school or above	2986	36.49	1004	46.20		3481	32.63	313	27.29
Smoking(n,%)					0.313				0.391
No	3606	44.07	984	45.28		10517	98.58	1127	98.26
Yes	4576	55.93	1189	54.72		152	1.42	20	1.74
Drinking(%)					<				0.006
					0.001				
No	2499	30.54	527	24.25		6388	59.87	735	64.08
Yes	5683	69.46	1646	75.75		4281	40.13	412	35.92
Spicy food intake (n,%)					<				0.182
					0.001				
No	1188	14.52	230	10.58		1528	14.32	181	15.78
Yes	6994	85.48	1943	89.42		9141	85.68	966	84.22
DASH score(n,%)					0.397				0.700
≤21	5029	61.46	1314	60.47		5003	46.89	531	46.29
>21	3153	38.54	859	39.53		5666	53.11	616	53.71

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Physical activity (METs/h/day)	26.00	17.10–40.01	24.17	16.97–36.02	< 0.001	24.22	16.60–36.22	21.9	15.05–32.76	< 0.001
Diabetes(n,%)					0.137					< 0.001
No	7250	88.61	1950	89.74		9868	92.49	969	84.48	
Yes	932	11.39	223	10.26		801	7.51	178	15.52	
Hypertension(n,%)					< 0.001					< 0.001
No	5108	62.43	1122	51.63		7590	71.14	564	49.17	
Yes	3074	37.57	1051	48.37		3079	28.86	583	50.83	
SBP(mmHg)	129.6 7	119.67–142. 33	133.00	123.33–145. 67	< 0.001	124.00 3	113.00–139.3	135.0 0	122.00–149. 33	< 0.001
DBP(mmHg)	80.33	73.33–87.67	83.67	76.67–91.33	< 0.001	74.67	68–82.33	79.33	72.33–86.67	< 0.001
FBG(mmol/L)	5.30	4.95–5.78	5.38	5.02–5.90	< 0.001	5.20	4.91–5.60	5.53	5.13–6.14	< 0.001

TC(mmol/L)	4.91	4.35–5.51	5.10	4.49–5.72	< 0.001	4.89	4.32–5.53	5.19	4.56–5.9	< 0.001
TG(mmol/L)	1.28	0.90–1.88	1.95	1.34–2.90	< 0.001	1.12	0.84–1.57	1.66	1.17–2.31	< 0.001
HDL-C(mmol/L)	1.40	1.17–1.70	1.23	1.04–1.48	< 0.001	1.67	1.41–1.95	1.44	1.19–1.69	< 0.001
LDL-C(mmol/L)	2.74	2.23–3.28	2.81	2.28–3.36	0.016	2.60	2.11–3.15	2.86	2.33–3.48	< 0.001
SUA(umol/L)	330.0 0	293.00–369. 00	462.00	437.00–503. 00	< 0.001	260.00	226.00–297.0 0	390.0 0	371.00–419. 00	< 0.001
eGFR(ml/min/1.73m ²)	97.43	88.43–105.0 4	92.98	80.62–102.5 4	< 0.001	103.01	93.10–110.36	90.86	78.67–102.1 7	< 0.001
BMI(kg/m ²)	24.58	22.65–26.58	26.29	24.12–28.27	< 0.001	23.82	21.90–26.02	26.14	23.83–28.57	< 0.001
WC(cm)	85.00	80.00–90.73	90.00	84.00–95.00	< 0.001	80.00	74.00–85.50	85.00	79.00–91.00	< 0.001

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WHtR	0.52	0.48–0.55	0.54	0.51–0.57	< 0.001	0.52	0.48–0.56	0.56	0.51–0.60	< 0.001
VAI	1.13	0.69–1.93	2.05	1.19–3.41	< 0.001	1.21	0.81–1.95	2.13	1.34–3.43	< 0.001
LAP	25.57	14.04–43.68	48.50	28.65–77.47	< 0.001	23.92	14.25–39.32	45.36	28.06–70.52	< 0.001
CMI	0.47	0.28–0.81	0.87	0.50–1.47	< 0.001	0.35	0.22–0.57	0.64	0.40–1.06	< 0.001
CVAI	89.89	61.20–116.1 9	112.67	87.27–136.5 0	< 0.001	71.58	44.88–99.38	107.8 8	81.89–132.7 5	< 0.001

DASH, dietary approaches to stop hypertension; METs, metabolic equivalent values; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; SUA, serum uric acid; eGFR, estimated glomerular filtration rate; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio; VAI, visceral adiposity index; CVAI, Chinese visceral adiposity index; LAP, lipid accumulation product index; CMI, cardiometabolic index; HUA, hyperuricemia. others in marital status including separated/divorced/widowed/unmarried.

Table 2. Association between Chinese visceral adiposity index (CVAI) and hyperuricemia (HUA) among adults enrolled in the Chinese Multi-Ethnic Cohort study, stratified by sex, according to CVAI as categorical (quartile) or continuous variables, using logistic regression (Odds ratios (OR) and 95% confidence intervals (CI); numbers)

CVAI	No. of cases/participants	Model 1	Model 2	Model 3
		OR(95%CI)	OR(95%CI)	OR(95%CI)
Men				
CVAI (Quartiles)				
Q1(≤ 65.86)	258/2589	1.00(ref)	1.00(ref)	1.00(ref)
Q2(65.87-95.05)	421/2590	1.75(1.49,2.07)*	1.71(1.45,2.02)*	1.67(1.40,1.99)*
Q3(95.06-121.21)	610/2588	2.79(2.38,3.26)*	2.74(2.33,3.21)*	2.38(1.98,2.85)*
Q4(> 121.21)	884/2588	4.69(4.03,5.46)*	4.75(4.07,5.55)*	3.31(2.73,4.03)*
<i>P</i> for trend		< 0.001	< 0.001	< 0.001
CVAI (per-SD increase)	2173/10,355	1.80(1.71,1.89)*	1.82(1.73,1.92)*	1.60(1.48,1.71)*
Women				
CVAI (Quartiles)				
Q1(≤ 47.19)	74/2956	1.00(ref)	1.00(ref)	1.00(ref)
Q2(47.20-75.30)	151/2952	2.10(1.58,2.79)*	2.29(1.72,3.04)	2.03(1.51,2.73)*
Q3(75.31-104.20)	297/2954	4.35(3.36,5.65)*	5.04(3.86,6.58)	3.78(2.81,5.09)*
Q4(> 104.20)	625/2954	10.45(8.16,13.38)*	13.01(9.92,17.06)*	7.20(5.12,10.12)*
<i>P</i> for trend		< 0.001	< 0.001	< 0.001
CVAI (per-SD increase)	1147/11,816	2.45(2.29,2.63)*	2.83(2.59,3.09)*	2.38(2.09,2.72)*

Model 1: without adjustments. Model 2: adjusted for age, area, education level, marital status, smoking, drinking, spicy food intake, DASH score, and physical activity. Model 3: further adjusted for diabetes, hypertension, BMI, eGFR, TC, and LDL-C. SD, standard deviation. * $P < 0.001$.

Table 3. Area under the receiver operating characteristic curve (AUROC) of adiposity indices for predicting hyperuricemia (HUA) among men (N=10,355) and women (N=11,816) enrolled in the Chinese Multi-Ethnic Cohort study

Adiposity indices	AUROC(95%CI)	Cutoff	Sensitivity (%)	Specificity (%)	Youden index (%)	<i>P</i>
Men						
WC	0.648(0.635-0.661)	89.95	52.5	69.5	22.0	<0.001
WHtR	0.621(0.608-0.634)	0.52	65.5	52.4	17.9	<0.001
VAI	0.695(0.682-0.707)	1.38	69.5	60.0	29.5	<0.001
LAP	0.709(0.697-0.721)	34.03	68.3	64.1	32.4	<0.001
CMI	0.698(0.686-0.711)	0.54	72.1	57.2	29.3	<0.001
CVAI	0.660(0.648-0.673)	101.22	62.8	61.3	24.1	-
Women						
WC	0.670(0.653-0.686)	83.75	58.0	68.3	26.3	<0.001
WHtR	0.672(0.656-0.689)	0.53	67.0	58.4	25.4	<0.001
VAI	0.713(0.697-0.728)	1.55	68.7	64.2	32.9	0.003
LAP	0.728(0.713-0.743)	32.67	68.4	66.7	35.1	0.199
CMI	0.724(0.709-0.739)	0.47	68.3	66.9	35.2	0.106
CVAI	0.735(0.720-0.749)	84.52	73.4	62.3	35.7	-

WC, waist circumference; WHtR, waist-to-height ratio; VAI, visceral adiposity index; LAP, lipid accumulation product; CMI, cardiometabolic index; CVAI, Chinese visceral adiposity index; HUA, hyperuricemia; AUROC, area under the receiver operating characteristic curve; CI, confidence intervals.