Association Between Serum Uric Acid to High-Density Lipoprotein Cholesterol Ratio and Metabolic Syndrome in Middle-Aged and Elderly Chinese Population: Postprint

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Date: 2023-08-17T00:00:00+00:00

Abstract

Background: The prevalence of metabolic syndrome (MS) among middle-aged and elderly populations in China is increasing year by year. The serum uric acid (SUA) to high-density lipoprotein cholesterol (HDL-C) ratio (UHR) is closely associated with various metabolic diseases, but research on the association between UHR and MS in middle-aged and elderly populations is limited.

Objective: To investigate the correlation between UHR and MS in Chinese middle-aged and elderly populations, and to evaluate the predictive value of UHR for MS.

Methods: This study utilized publicly available data from the 2015 China Health and Retirement Longitudinal Study (CHARLS), enrolling 9,233 participants. General information, physical examination indicators, and blood biochemical test indicators were collected. UHR was calculated for each participant. Participants were divided into non-MS group (n=7,006) and MS group (n=2,227) based on MS status, and simultaneously divided into Q1 group (UHR$ $7.32%, n=2,308), Q2 group (7.32%12.20%, n=2,308) according to UHR quartile levels. Pearson correlation analysis was used to explore the correlation between UHR and metabolic indicators; multivariate logistic regression analysis was used to investigate the relationship between UHR and MS. Receiver operating characteristic (ROC) curves were plotted for UHR predicting MS risk in the overall population and different gender groups, and the area under the ROC curve (AUC) was calculated.

Results: The MS group had higher female proportion, older age, higher urban residence proportion, higher rates of hypertension history, diabetes history, dyslipidemia history, lipid-lowering medication use, glycated hemoglobin, C-reactive protein, triglycerides (TG), total cholesterol (TC), fasting plasma glucose (FPG), SUA, systolic blood pressure (SBP), diastolic blood pressure (DBP), BMI, waist circumference (WC), and UHR than the non-MS group, while HDL-C, low-density lipoprotein cholesterol (LDL-C), and estimated glomerular filtration rate (eGFR) were lower than in the non-MS group. Comparisons of education level, smoking, and drinking status between the two groups showed statistically significant differences ($P<0.05$). With increasing UHR levels, the detection rates of MS, central obesity, hyperglycemia, hypertension, hypertriglyceridemia, and low HDL-C showed an upward trend in Q1-Q4 groups (P trend <0.01). Comparisons of BMI, WC, SBP, DBP, TG, HDL-C, LDL-C, TC, FPG, eGFR, and C-reactive protein levels among Q1-Q4 groups showed statistically significant differences ($P<0.01$). Pearson correlation analysis showed that UHR was positively correlated with TG, FPG, DBP, SBP, BMI, and WC ($P<0.01$), and negatively correlated with HDL-C ($P<0.01$). After stratification by sex, UHR was positively correlated with TG, FPG, DBP, SBP, BMI, and WC in both males and females ($P<0.01$), and negatively correlated with HDL-C ($P<0.01$). Multivariate logistic regression analysis showed that compared with the Q1 group, the risk of MS increased in males in the Q4 group [OR=3.385, 95%CI=(1.778~6.444), $P<0.01$] and in females in the Q4 group [OR=2.886, 95%CI=(1.991~4.184), $P<0.01$]. ROC curve analysis showed that the AUC of UHR for predicting MS was 0.735 [95%CI=(0.723~0.746)] in all participants, 0.773 [95%CI=(0.757~0.790)] in the male population, and 0.750 [95%CI=(0.735~0.766)] in the female population.

Conclusion: UHR level is positively associated with MS in Chinese middle-aged and elderly populations. UHR is closely related to MS and its components. UHR may be a risk factor for MS and has good predictive value for the risk of MS in middle-aged and elderly populations.

Full Text

Title and Authors

Correlation between Serum Uric Acid to High-Density Lipoprotein Cholesterol Ratio and Metabolic Syndrome in Middle-Aged and Elderly Population in China

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Abstract

Background The prevalence of metabolic syndrome (MS) among middle-aged and elderly populations in China continues to rise annually. While the serum uric acid to high-density lipoprotein cholesterol ratio (UHR) is closely associated with various metabolic diseases, few studies have examined the relationship between UHR and MS specifically in middle-aged and elderly individuals.

Objective To investigate the correlation between UHR and MS in Chinese middle-aged and elderly populations and to evaluate the predictive value of UHR for MS.

Methods This study utilized publicly available data from the 2015 China Health and Retirement Longitudinal Survey (CHARLS), enrolling 9,233 participants. General demographic information, physical examination indices, and blood biochemical parameters were collected, and UHR values were calculated for all subjects. Participants were divided into a non-MS group (n=7,006) and an MS group (n=2,227) based on MS diagnosis. Additionally, subjects were stratified by UHR quartiles: Q1 (UHR $\leq$ 7.32%, n=2,308), Q2 (7.32% $<$ UHR $\leq$ 9.45%, n=2,307), Q3 (9.45% $<$ UHR $\leq$ 12.20%, n=2,310), and Q4 (UHR $>$ 12.20%, n=2,308). Pearson correlation analysis was used to examine associations between UHR and metabolic indicators, while multivariate logistic regression analysis explored the relationship between UHR and MS. Receiver operating characteristic (ROC) curves were constructed for the overall population and by gender to assess UHR' s predictive value for MS risk, with area under the curve (AUC) calculated.

Results The MS group exhibited significantly higher proportions of females, older age, urban residence, hypertension history, diabetes history, dyslipidemia history, lipid-lowering medication use, glycated hemoglobin, C-reactive protein, triglycerides (TG), total cholesterol (TC), fasting plasma glucose (FPG), serum uric acid (SUA), systolic blood pressure (SBP), diastolic blood pressure (DBP), BMI, waist circumference (WC), and UHR compared to the non-MS group. HDL-C, LDL-C, and estimated glomerular filtration rate (eGFR) were significantly lower in the MS group, with statistically significant differences in education level, smoking, and alcohol consumption ($P<0.05$). As UHR levels increased from Q1 to Q4, detection rates of MS, central obesity, hyperglycemia, hypertension, hypertriglyceridemia, and low HDL-C showed upward trends (P-trend <0.01). Significant differences were observed across Q1-Q4 groups for BMI, WC, SBP, DBP, TG, HDL-C, LDL-C, TC, FPG, eGFR, and C-reactive protein ($P<0.01$). Pearson correlation analysis revealed positive correlations between UHR and TG, FPG, DBP, SBP, BMI, and WC ($P<0.01$), and a negative correlation with HDL-C ($P<0.01$). After stratification by gender, both males and females showed the same correlation patterns ($P<0.01$). Multivariate logistic regression demonstrated that compared with Q1, the Q4 group had significantly increased MS risk in males [OR=3.385, 95%CI (1.778-6.444), P<0.01] and females [OR=2.886, 95%CI (1.991-4.184), P<0.01]. ROC analysis yielded an AUC of 0.735 [95%CI (0.723-0.746)] for UHR predicting MS in the overall population, 0.773 [95%CI (0.757-0.790)] in males, and 0.750 [95%CI (0.735-0.766)] in females.

Conclusion In Chinese middle-aged and elderly populations, elevated UHR levels are positively associated with MS risk. UHR is closely correlated with MS and its components and may serve as a risk factor for MS, demonstrating good predictive value for MS occurrence in this population.

Keywords: Metabolic syndrome; Uric acid; High-density lipoprotein cholesterol; China Health and Retirement Longitudinal Study; Aged; Forecasting

Introduction

Metabolic syndrome (MS) is a clinical syndrome characterized by clustering of multiple cardiovascular risk factors including insulin resistance, hypertension, central obesity, impaired glucose metabolism, and dyslipidemia, which is closely associated with chronic diseases such as type 2 diabetes and atherosclerosis [1]. Recent studies indicate that MS prevalence increases with age, particularly among middle-aged and elderly populations [2]. Epidemiological research shows that the prevalence of MS among Chinese adults over 60 years old reaches as high as 36.4% [3].

Serum uric acid (SUA) is the end product of hypoxanthine and xanthine metabolism. Both excessive SUA production and/or reduced renal excretion can lead to hyperuricemia (HUA), contributing to the development and progression of various chronic diseases including MS, cardiovascular disease, and chronic kidney disease [4]. Previous studies have demonstrated that SUA exhibits pro-inflammatory and pro-oxidant effects, and elevated SUA levels are closely associated with MS [5]; however, other research has reported no association between SUA and MS in female health examination populations [6], leaving the causal relationship between SUA and MS controversial.

Recent research has identified the serum uric acid to high-density lipoprotein cholesterol (HDL-C) ratio (UHR) as a novel biomarker that reflects inflammatory burden and oxidative stress levels. UHR has been linked to metabolic diseases including coronary heart disease, non-alcoholic fatty liver disease, and type 2 diabetes [7-9]. Studies have shown that the pathogenesis of MS is closely related to inflammatory responses and oxidative stress [10-11]. Therefore, as a new inflammatory and metabolic marker, UHR may be a better predictor of MS than SUA alone [12]. Currently, few studies have examined the association between UHR and MS, and large-scale studies in middle-aged and elderly populations are particularly scarce. This study, based on nationally representative data from the 2015 China Health and Retirement Longitudinal Survey

(CHARLS), investigates the relationship between UHR and MS among Chinese middle-aged and elderly populations and evaluates UHR' s predictive value for MS risk, providing new evidence for MS prevention and control in this demographic.

Methods

Data Source

This study utilized publicly available data from the 2015 CHARLS. The survey employed multistage stratified sampling in 2011 to select 150 counties and 450 communities/villages across 28 provinces (autonomous regions, municipalities) in China, targeting residents aged 45 years and older. The 2015 wave represented the third follow-up survey, collecting high-quality microdata from approximately 11,797 households and 20,284 middle-aged and elderly individuals [13]. This study included subjects aged 45 and older who completed SUA and HDL-C measurements, excluding those with missing key variables including demographic indicators, lifestyle behaviors, physical examination data, blood biochemical tests, chronic disease history, and medication history. The final sample comprised 9,233 participants.

Data Collection

From the CHARLS database, we collected general demographic indicators (sex, age, residence type, education level, marital status), lifestyle behaviors (smoking status, alcohol consumption, physical activity), chronic disease history (hypertension, diabetes, dyslipidemia), medication history (lipid-lowering drug use), physical examination measurements [height, weight, waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP)], and blood biochemical indicators [fasting plasma glucose (FPG), HDL-C, SUA, triglycerides (TG), LDL-C, total cholesterol (TC), serum creatinine (Cr), C-reactive protein, glycated hemoglobin]. UHR was calculated for each participant.

Definitions and Diagnostic Criteria

MS diagnosis followed the criteria in the "Chinese Guidelines for the Prevention and Treatment of Type 2 Diabetes (2017 Edition)" [14], defined as having three or more of the following components: (1) Central obesity: WC $\geq$ 90 cm in men and $\geq$ 85 cm in women; (2) Hyperglycemia: FPG $\geq$ 6.10 mmol/L and/or previously diagnosed diabetes under treatment; (3) Hypertension: SBP $\geq$ 130 mmHg and/or DBP $\geq$ 85 mmHg and/or previously diagnosed hypertension under treatment; (4) Hypertriglyceridemia: TG $\geq$ 1.70 mmol/L; (5) Low HDL-C: HDL-C $<$ 1.04 mmol/L.

Smoking status was defined as: (1) Current smoker: having smoked for $ $1 month at the time of survey; (2) Former smoker: previously smoked but had quit for at least 1 year; (3) Never smoker. Alcohol consumption was defined as: (1) Current drinker: having consumed alcohol for $ $1 month at survey; (2) Former drinker: previously drank but had abstained for $ $1 year; (3) Never drinker. Physical activity was defined as: (1) Active: engaging in sustained physical activity $ $10 minutes per week; (2) Inactive: <10 minutes per week.

Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula based on serum creatinine [15]: For women: if Cr $\leq$ 0.7 mg/L, eGFR = 144 $\times$ (Cr/0.7)^(-0.329) $\times$ 0.993^{age}; if Cr > 0.7 mg/L, eGFR = 144 $\times$ (Cr/0.7)^(-1.209) $\times$ 0.993^{age}. For men: if Cr $\leq$ 0.9 mg/L, eGFR = 141 $\times$ (Cr/0.9)^(-0.411) $\times$ 0.993^{age}; if Cr > 0.9 mg/L, eGFR = 141 $\times$ (Cr/0.9)^(-1.209) $\times$ 0.993^{age}.

Statistical Analysis

Statistical analysis was performed using SPSS 25.0 software. Normally distributed continuous variables were expressed as mean $\pm$ standard deviation, compared between two groups using independent samples t-test and among multiple groups using one-way ANOVA. Non-normally distributed continuous variables were expressed as median (P25, P75), compared between two groups using Mann-Whitney U test and among multiple groups using Kruskal-Wallis H test. Categorical variables were described using frequencies and percentages, with inter-group comparisons using ^{2} test and trend analysis using ^{2} trend test. Pearson correlation analysis examined associations between UHR and metabolic indicators. Multivariate logistic regression analysis explored the relationship between UHR and MS. ROC curves were constructed for the overall population and by gender to assess UHR's predictive value for MS risk, with AUC calculated to identify optimal cutoff values. Statistical significance was set at P<0.05.

Results

Participant Characteristics

Participants were divided into non-MS (n=7,006) and MS (n=2,227) groups. Additionally, they were stratified by UHR quartiles: Q1 (UHR $\leq$ 7.32%, n=2,308), Q2 (7.32% < UHR $\leq$ 9.45%, n=2,307), Q3 (9.45% < UHR $\leq$ 12.20%, n=2,310), and Q4 (UHR > 12.20%, n=2,308).

Among 9,233 participants aged 45-102 years (mean age 60.3 $\pm$ 9.6 years), no significant differences were observed between MS and non-MS groups in physical activity, marital status, or serum creatinine (P>0.05). The MS group had significantly higher proportions of females, older individuals, urban residents, and those with hypertension, diabetes, dyslipidemia histories, and lipid-lowering medication use. The MS group also showed higher levels of glycated hemoglobin, C-reactive protein, TG, TC, FPG, SUA, SBP, DBP, BMI, WC, and UHR, while

HDL-C, LDL-C, and eGFR were significantly lower. Education level, smoking, and alcohol consumption also differed significantly between groups ($P<0.05$) .

MS Detection and Clinical Indicators Across UHR Levels

As UHR levels increased from Q1 to Q4, detection rates of MS, central obesity, hyperglycemia, hypertension, hypertriglyceridemia, and low HDL-C increased significantly (P-trend <0.01). Significant differences across Q1-Q4 groups were observed for BMI, WC, SBP, DBP, TG, HDL-C, LDL-C, TC, FPG, eGFR, and C-reactive protein ($P<0.01$) .

Correlation Analysis Between UHR and Metabolic Indicators

Pearson correlation analysis showed UHR was positively correlated with TG, FPG, DBP, SBP, BMI, and WC ($P<0.01$) and negatively correlated with HDL-C ($P<0.01$). After gender stratification, both males and females exhibited the same correlation patterns ($P<0.01$) .

Multivariate Logistic Regression Analysis of UHR Levels and MS

Using MS status (no=0, yes=1) as the dependent variable and UHR quartile groups (Q1=1, Q2=2, Q3=3, Q4=4) as the independent variable, gender-stratified multivariate logistic regression was performed. Model 1 adjusted for age, residence type, education, and marital status, showing increased MS risk in Q2-Q4 groups compared to Q1 ($P<0.05$). Model 2 additionally adjusted for smoking, alcohol consumption, physical activity, and histories of hypertension, diabetes, dyslipidemia, and lipid-lowering medication use, with Q2-Q4 groups showing increased MS risk ($P<0.05$). Model 3 further adjusted for SBP, DBP, BMI, and WC, revealing increased MS risk in male Q4 and female Q4 groups compared to Q1 ($P<0.01$). Model 4 additionally adjusted for TG, TC, LDL-C, FPG, eGFR, glycated hemoglobin, and C-reactive protein, confirming increased MS risk in both male Q4 and female Q4 groups ($P<0.05$) .

ROC Curve Analysis of UHR for Predicting MS Risk

ROC analysis showed UHR predicted MS with an AUC of 0.735 [95%CI (0.723-0.746)] in the overall population, with an optimal cutoff of 10.17%, sensitivity 0.687, and specificity 0.659. In males, the AUC was 0.773 [95%CI (0.757-0.790)], cutoff 11.04%, sensitivity 0.816, specificity 0.605. In females, the AUC was 0.750 [95%CI (0.735-0.766)], cutoff 8.86%, sensitivity 0.715, specificity 0.664 [Figure 1: see original paper].

Discussion

In recent years, with global economic development, lifestyle changes, and population aging, MS prevalence has continuously risen and shows a trend toward younger age groups [16]. This study found a 24.1% MS detection rate among Chinese adults aged 45 and older, higher than the 15.2% reported in Guangzhou' s population aged 50+ [17] but lower than the 31.59% in Hebei' s population aged 40+ [18], indicating regional variations in MS prevalence among middle-aged and elderly Chinese.

SUA is the primary end product of purine metabolism. Previous studies have shown SUA exhibits pro-inflammatory and pro-oxidant effects, closely linking it to MS development [19]. HDL-C comprises a group of anti-atherogenic lipoproteins with anti-inflammatory, antioxidant, and insulin resistance-improving properties, serving as an important MS diagnostic component [20]. Given the antagonistic relationship between SUA and HDL-C, the UHR metric derived from these two indicators may more precisely reflect metabolic disturbance severity [21]. This study demonstrated that as UHR levels increased, detection rates of MS and its components—including central obesity, hyperglycemia, hypertension, hypertriglyceridemia, and low HDL-C—also increased. Pearson correlation analysis confirmed UHR was positively correlated with WC, BMI, SBP, DBP, FPG, and TG, and negatively correlated with HDL-C in both genders, consistent with previous findings [22]. The underlying mechanism likely involves chronic metabolic disturbance and inflammatory states.

ROC curve analysis revealed UHR had diagnostic value for MS in both genders (AUC>0.70), suggesting UHR is a good predictive indicator for MS in middle-aged and elderly populations.

Currently, few studies have examined the UHR-MS association. KOCAK et al. [23] found UHR was positively associated with MS and predicted MS risk in type 2 diabetes patients. YAZDI et al. [24] reported that high UHR levels increased MS risk 2.9-fold in community residents, with elevated UHR significantly correlating with higher MS prevalence. After adjusting for confounders, our multivariate logistic regression showed that compared with Q1, both male and female Q4 groups had significantly elevated MS risk, confirming a clear positive association between UHR and MS risk in middle-aged and elderly Chinese, consistent with these previous studies.

The potential mechanisms linking UHR and MS remain unclear. MS is a metabolic disorder syndrome centered on insulin resistance (IR) and chronic low-grade inflammation, with pathogenesis primarily involving oxidative stress and inflammatory responses [25-26]. Studies have shown elevated SUA has pro-oxidant effects, causing endothelial dysfunction and increased oxidative stress by inhibiting endothelial nitric oxide (NO) bioavailability, leading to chronic insulin resistance [27]. Other research indicates high SUA has pro-inflammatory effects, stimulating vascular endothelial oxidative stress and inducing inflammatory responses mediated by C-reactive protein, tumor necrosis factor-α, and interleukins, maintaining chronic low-grade inflammation [28]. Additionally, HDL-C has anti-inflammatory and antioxidant properties [29]. Therefore, high UHR levels may exacerbate lipid metabolism disorders through pro-inflammatory and pro-oxidant effects, thereby inducing MS, consistent with previous findings [30].

This study has several limitations. First, SUA is influenced by dietary factors, which were not included due to objective constraints and should be incorporated in future research. Second, as a cross-sectional study, it cannot establish causality between UHR and MS, necessitating prospective cohort studies for validation.

In conclusion, this study demonstrates that UHR is closely associated with MS in Chinese middle-aged and elderly populations, with significantly increased MS risk as UHR levels rise. UHR shows good predictive value for MS, suggesting it may be a risk factor for MS in this demographic. Therefore, regular monitoring, assessment, and control of UHR should be emphasized for early MS prevention in middle-aged and elderly populations, which is important for preventing or delaying MS and related diseases.

Author Contributions

Wu Ruipeng: conceptualization, design, data collection, statistical analysis, results interpretation, manuscript writing. Peng Cheng and Yuan Bingkun: manuscript revision, supervision. Zhang Mengjun: literature/data/figure organization. Li Wenyuan: project implementation, feasibility analysis, quality control, and manuscript review.

Conflict of Interest: The authors declare no conflict of interest.

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Received: April 4, 2023
Revised: August 8, 2023
Edited by: Zou Lin

Note: Figure translations are in progress. See original paper for figures.