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Associations between non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio and hyperuricemia: a cross-sectional study

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Abstract

Background and objective The value of the non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) assessment in the context of metabolic abnormalities is growing in importance. Nevertheless, the relationship between NHHR and hyperuricemia (HUA) is unknown. This study seeks to investigate the relationship between NHHR and HUA.

Methods The data derived from the 2017–2020 National Health and Nutrition Examination Survey (NHANES) included 7,876 adult participants. The multivariable logistic regression model, subgroup analysis and smooth fitting curve were utilized in order to investigate the association between NHHR and HUA.

Results In the fully adjusted model 3, NHHR was significantly associated with HUA. Specifically, participants in the highest quartile of NHHR had 1.95 times higher odds of HUA prevalence compared to those in the lowest quartile [2.95 (2.39, 3.64), $P < 0.0001$]. Although the overall trend suggested a positive association, further analysis using smooth fitting curves and threshold effect analysis indicated that this association was nonlinear, with an inflection point at 5.8. The positive association persisted across different HUA definitions and after removing outliers. Subgroup analysis showed significant interactions between NHHR and HUA in different races and diabetes statuses. The odds of HUA prevalence were higher among non-diabetic participants [1.40 (1.32, 1.49), $P < 0.0001$] compared to diabetic participants [1.18 (1.06, 1.32), $P = 0.0031$]. Mexican Americans had the lowest odds of HUA prevalence [1.09 (0.92, 1.27), $P = 0.2413$] compared to other races.

Conclusions There is a significant positive association between NHHR and HUA, indicating that NHHR may serve as a potential risk assessment maker for HUA, although further prospective studies are needed for validation.

Keywords Hyperuricemia, Cross-sectional study, Non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

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Background

Hyperuricemia (HUA) is a metabolic disorder which is characterized by an elevation in the levels of uric acid. The prevalence of HUA is 20% among women and 20.2% among men in the United States. The incidence of HUA has shown an increasing trend globally in recent years [1, 2]. The deposition of uric acid and urate in the human body can result in a number of complications, including as gout, kidney damage, and kidney stones [3, 4]. Increasing evidence suggests that HUA is linked to a wide range of diseases, including chronic kidney disease, metabolic syndrome, and cardiovascular diseases [5–8]. HUA poses a serious threat to human health and quality of life, imposing a substantial economic burden on global public health [9].

Lipid metabolism dysregulation in the body is linked to the onset and progression of various cardiovascular diseases. Moreover, the relationship between uric acid and metabolic syndrome is bidirectional and complex. This complex interplay suggests that uric acid is both a marker and a mediator of metabolic disturbances [10]. Compared to traditional assessments of body lipid indicators, the value of the non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) assessment in the context of metabolic abnormalities is growing in importance. Studies have shown that NHHR holds significant importance in the research of cardiovascular diseases and metabolic syndrome [11, 12]. Elevated NHHR levels also have significant clinical value in the risk assessment of diseases in particular breast cancer, abdominal aortic aneurysm, depression, and kidney stones [13–16]. Obesity and insulin resistance are becoming global health issues and are also risk factors for HUA. These conditions are inextricably linked to dysregulation of lipid metabolism in the body [17–19]. Dysregulation of lipid metabolism can alter the body's metabolic patterns and affect disease progression in patients with HUA [20, 21]. However, the relationship between NHHR, as a novel lipid indicator, and HUA remains unclear.

Therefore, we utilized sample data from the National Health and Nutrition Examination Survey (NHANES) of American adults to investigate the association between NHHR and HUA. This study may provide a novel insight into the pathogenesis of HUA for future research.

Methods

Study population

NHANES, a significant epidemiological survey project led by the National Center for Health Statistics (NCHS), is for the purpose of evaluating the health and nutrition of Americans, Providing critical data on the health status of Americans to policymakers, researchers, and the public [22]. From the 15,560 participants in NHANES 2017–2020, we excluded 6,373 participants who lacked serum

uric acid data and were under 18 years of age, and 1,311 participants who lacked NHHR data. Ultimately, 7,876 participants who met the study criteria were included (Fig. 1).

Definition of outcome and exposure variables

The outcome variable in this study is HUA, which is diagnosed based on serum uric acid levels. HUA is diagnosed when a serum uric acid concentration reaches a level of ≥ 6 mg/dL in females and ≥ 7 mg/dL in males [23]. Sensitivity analysis was conducted using different definitions of HUA, including serum uric acid concentration ≥ 6.8 mg/dL [24], to ensure the robustness of the study findings. Serum uric acid levels were measured by professionals using the Roche Cobas 6000 analyzer (c501 module).

The exposure variable is NHHR. This is calculated by dividing non-high-density lipoprotein cholesterol (total cholesterol minus high-density lipoprotein cholesterol) by high-density lipoprotein cholesterol [25].

Covariables

To more accurately understand the relationship between HUA and NHHR, We included potential confounding covariables including demographic factors (gender, race, age, education level, family income-to-poverty ratio (PIR), marital status), lifestyle factors (physical activity status, drink status, smoking status), clinical measurements (glycated hemoglobin, total bilirubin, fasting blood glucose, serum creatinine, urinary albumin, serum urea nitrogen, aspartate aminotransferase, alanine aminotransferase, waist circumference, body mass index (BMI), systolic and diastolic blood pressure and medical history (diabetes, hyperlipidemia, high blood pressure, and kidney stones). The definitions of these covariables can be found in Supplementary Table 1. Missing values for covariables are replaced by medians for continuous variables and plurals for categorical variables.

Statistical analysis

All statistical analyses were performed using Empower software (www.empowerstats.com) and R version 4.1.3. The appropriate NHANES sampling weights, as prescribed in the guidelines established by the Centers for Disease Control and Prevention (CDC), were duly applied. In the case of continuous data variables, variance-weighted analysis was employed, while in the case of categorical variables, weighted chi-square tests were used to assess differences between NHHR quartiles. In constructing multivariable analyses, we employed three different models to evaluate the association between NHHR and HUA. Model 1 is not adjusted to account for any variables. Model 2 was adjusted for demographic factors (including race, age, and gender). Model

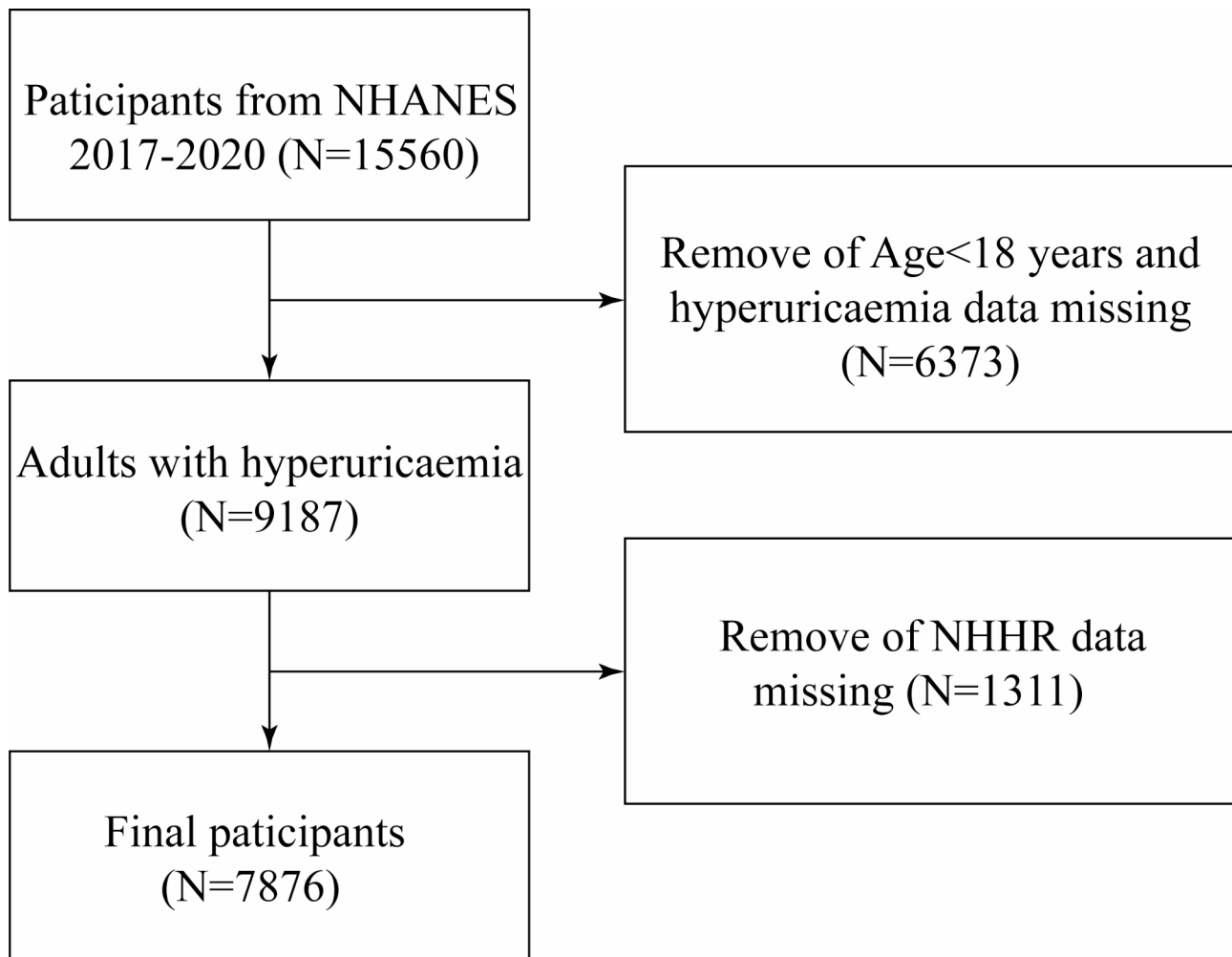


Fig. 1 Flow chart of participants selection

3 incorporated all covariable adjustments. To deal with potential outliers in the NHHR distribution, we examined the data for abnormal truncated tail values. Outliers were defined as values greater than three standard deviations from the mean. These outliers were removed and the analyses repeated to assess the robustness of the association between NHHR and HUA. We performed linear trend tests by converting NHHR levels into quartile categorical variables. To examine the nonlinear relationship and inflection points between NHHR and HUA, a smooth fitting curve and threshold effect analysis were utilised. Finally, subgroup analyses were performed to identify any statistically significant differences between the various subgroups, including race, gender, age, BMI, diabetes, high blood pressure and estimated glomerular filtration rate (eGFR). We decided that the p -value of less than 0.05 was statistically significant.

Results

Baseline characteristics

The weighted distributions of all clinical characteristics for participants are shown in Table 1 across the quartiles of the NHHR. This study included 7,876 adults with a mean age of 48.43 ± 17.32 years. The study population consisted of 48.29% male and 51.71% female participants. The mean NHHR was 2.72 ± 1.23 , and the NHHR range for the 1st to 4th quartiles was 0.28–1.80, 1.80–2.50, 2.50–3.35, and 3.35–11.9, respectively. The overall prevalence of HUA was 17.28%, with quartile-specific prevalence rates of 10.96% in the 1st quartile, 12.75% in the 2nd quartile, 19.29% in the 3rd quartile, and 25.78% in the 4th quartile. Significant differences were observed across NHHR quartiles in terms of race, gender, age, drink status, glycosylated hemoglobin, systolic and diastolic blood pressure, fasting blood glucose, PIR, education level, marital status, smoking status, serum creatinine, urinary albumin, aspartate aminotransferase, total bilirubin, alanine aminotransferase, and the prevalence of

Table 1 Baseline characteristics of the study population

Quartiles of NHHR					
Characteristic	Q1 (0.28–1.80) N= 1967	Q2 (1.80–2.50) N= 1971	Q3 (2.50–3.35) N= 1969	Q4 (3.35–11.9) N= 1969	P- value
Age (years)	47.89±19.35	49.24±17.88	49.58±16.45	47.02±15.30	<0.0001
Ratio of family income to poverty	3.23 (1.78 ,5.00)	3.22 (1.79 ,5.00)	2.92 (1.58 ,4.81)	3.08 (1.73 ,5.00)	0.0133
Glycohemoglobin (%)	5.40 (5.10 ,5.70)	5.50 (5.20 ,5.80)	5.50 (5.30 ,5.90)	5.60 (5.30 ,5.90)	<0.0001
Fasting glucose (mg/dL)	99.00 (92.00 ,107.00)	101.10 (95.00 ,110.00)	104.00 (97.00 ,113.00)	107.19 (100.00 ,118.00)	<0.0001
Alanine aminotransferase (U/L)	19.00 (16.00 ,23.00)	19.00 (16.00 ,23.00)	19.00 (16.00 ,24.00)	20.00 (16.00 ,25.00)	0.0169
Aspartate aminotransferase (U/L)	15.00 (12.00 ,21.00)	17.00 (13.00 ,24.00)	18.00 (14.00 ,27.00)	22.00 (16.00 ,32.00)	<0.0001
Total bilirubin (mg/dL)	0.40 (0.30 ,0.60)	0.40 (0.30 ,0.60)	0.40 (0.30 ,0.60)	0.40 (0.30 ,0.50)	0.0014
Serum creatinine (mg/dL)	0.80 (0.69 ,0.94)	0.82 (0.70 ,0.97)	0.85 (0.72 ,1.00)	0.88 (0.76 ,1.01)	0.0088
Blood urea nitrogen (mg/dL)	14.00 (11.00 ,18.00)	14.00 (11.00 ,17.00)	14.00 (12.00 ,18.00)	14.00 (12.00 ,17.00)	0.8585
Systolic pressure(mmHg)	120.76±18.62	122.38±17.78	121.99±16.57	123.06±16.35	0.0004
Diastolic pressure(mmHg)	71.56±10.62	73.67±10.79	74.82±10.32	76.97±10.44	<0.0001
Waist circumference (cm)	89.44 (77.30 ,101.70)	89.41 (74.70 ,101.70)	89.74 (77.30 ,104.00)	89.53 (74.10 ,102.20)	0.5943
Albumin, urine (ug/mL)	8.00 (4.20 ,16.00)	7.30 (3.60 ,15.50)	8.30 (4.30 ,15.90)	8.80 (4.40 ,18.00)	0.1551
Body mass index(kg/m ²)	26.47 (22.00 ,30.10)	26.33 (20.60 ,30.20)	26.42 (21.60 ,30.30)	26.40 (21.10 ,29.60)	0.6677
eGFR (ml/min/1.73 m ²)	103.89±24.36	100.88±22.20	98.94±21.97	98.82±21.87	<0.0001
Gender (%)					<0.0001
Male	727 (33.69)	846 (41.59)	979 (51.63)	1255 (65.53)	
Female	1240 (66.31)	1125 (58.41)	990 (48.37)	714 (34.47)	
Race (%)					<0.0001
Mexican American	176 (6.68)	206 (7.31)	260 (9.21)	305 (10.73)	
Other Hispanic	154 (6.56)	210 (7.36)	210 (7.57)	257 (9.11)	
Non-Hispanic White	683 (63.97)	721 (64.44)	688 (62.76)	685 (61.83)	
Non-Hispanic Black	649 (14.52)	527 (11.47)	468 (9.80)	358 (7.43)	
Other Race	305 (8.26)	307 (9.41)	343 (10.67)	364 (10.90)	
Education level (%)					<0.0001
Less than high school	298 (8.02)	325 (10.29)	397 (11.70)	459 (13.94)	
High school	492 (25.39)	459 (24.91)	479 (28.80)	467 (28.61)	
More than high school	1177 (66.60)	1187 (64.79)	1093 (59.50)	1043 (57.45)	
Marriage (%)					<0.0001
Yes	1023 (57.58)	1128 (59.61)	1179 (63.41)	1234 (67.44)	
No	944 (42.42)	843 (40.39)	790 (36.59)	735 (32.56)	
Smoking (%)					<0.0001
Yes	806 (39.67)	769 (41.72)	818 (40.97)	905 (48.64)	
No	1161 (60.33)	1202 (58.28)	1151 (59.03)	1064 (51.36)	
Drink (%)					<0.0001
Yes	294 (12.14)	280 (12.47)	317 (14.35)	330 (16.77)	
No	1161 (87.86)	1691 (87.53)	1625 (85.65)	1639 (83.23)	
Moderate work activity (%)					0.5429
Yes	876 (48.49)	844 (49.48)	835 (47.54)	894 (49.54)	
No	1091 (51.51)	1127 (50.52)	1134 (52.46)	1075 (50.46)	
High blood pressure (%)					0.0001
Yes	744 (28.97)	750 (31.90)	775 (34.67)	768 (34.99)	
No	1223 (71.03)	1221 (68.10)	1194 (65.33)	1201 (65.01)	
Diabetes (%)					0.0278
Yes	287 (10.71)	298 (10.43)	319 (13.10)	316 (12.19)	
No	1680 (89.29)	1673 (89.57)	1650 (86.90)	1653 (87.81)	
Hypertriglyceridemia (%)					<0.0001
Yes	558 (24.85)	678 (33.36)	715 (35.29)	876 (44.86)	
No	1409 (75.15)	1293 (66.64)	1254 (64.71)	1093 (55.14)	
kidney stone (%)					0.0035
Yes	150 (8.32)	177 (9.54)	218 (11.73)	206 (10.57)	

Table 1 (continued)

Quartiles of NHHR					
Characteristic	Q1 (0.28–1.80) N= 1967	Q2 (1.80–2.50) N= 1971	Q3 (2.50–3.35) N= 1969	Q4 (3.35–11.9) N= 1969	P-value
No	1817 (91.68)	1794 (90.46)	1751 (88.27)	1763 (89.43)	
Hyperuricaemia (%)					< 0.0001
Yes	249 (10.96)	289 (12.75)	407 (19.29)	516 (25.78)	
No	1718 (89.04)	1682 (87.25)	1562 (80.71)	1453 (74.22)	

Mean±standard deviation for normally distributed continuous variables, median and interquartile range for non-normally distributed continuous variables; the P value was calculated by the weighted linear regression model; (%) for categorical variables: the P value was calculated by the weighted chi-square test, n=unweighted sample size; % = weighted percentage. Abbreviation: NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio; eGFR, estimated glomerular filtration rate

Table 2 Associations between NHHR and hyperuricemia

Characteristic	Model 1 OR (95%CI) N= 7876	Model 2 OR (95%CI) N= 7876	Model 3 OR (95%CI) N= 7876
Primary Definition (≥ 6/7 mg/dL)			
NHHR	1.28 (1.22, 1.33)	1.33 (1.27, 1.40)	1.36 (1.28, 1.44)
Categories			
Q1	1.0	1.0	1.0
Q2	1.19 (0.99, 1.42)	1.22 (1.02, 1.47)	1.25 (1.03, 1.52)
Q3	1.80 (1.51, 2.14)	1.92 (1.61, 2.28)	2.01 (1.66, 2.44)
Q4	2.45 (2.07, 2.89)	2.82 (2.37, 3.36)	2.95 (2.39, 3.64)
NHHR group trend	1.42 (1.34, 1.51) <0.0001	1.50 (1.41, 1.60) <0.0001	1.52 (1.41, 1.64) <0.0001
Alternative Definition (≥ 6.8 mg/dL)			
NHHR	1.21 (1.16, 1.27)	1.19 (1.13, 1.24)	1.20 (1.14, 1.26)
Categories			
Q1	1.0	1.0	1.0
Q2	1.08 (0.90, 1.29)	1.06 (0.89, 1.27)	1.10 (0.92, 1.32)
Q3	1.44 (1.21, 1.71)	1.38 (1.16, 1.64)	1.46 (1.22, 1.75)
Q4	1.87 (1.59, 2.21)	1.73 (1.46, 2.05)	1.79 (1.49, 2.16)
NHHR group trend	1.29 (1.21, 1.36) <0.0001	1.25 (1.17, 1.33) <0.0001	1.26 (1.18, 1.35) <0.0001

Model 1: no covariables were adjusted. Model 2: age, gender, and race were adjusted. Model 3: gender, age, race, family income-to-poverty ratio, education level, physical activity status, marital status, drink status, smoking status, systolic blood pressure, diastolic blood pressure, glycated hemoglobin, total bilirubin, fasting blood glucose, serum creatinine, serum urea nitrogen, urinary albumin, aspartate aminotransferase, alanine aminotransferase, body mass index, waist circumference, and history of diabetes, high blood pressure, hyperlipidemia, and kidney stones were adjusted. Abbreviation: NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

diabetes, hyperlipidemia, high blood pressure, kidney stones, and HUA ($p < 0.05$).

indicates that the inflection points for NHHR and HUA were 5.8.

Elevated NHHR levels are linked to a higher odds of HUA Prevalence

Table 2 shows a positive association between NHHR and HUA across all three models, all of which were statistically significant. When NHHR was treated as a quartile variable, the highest quartile of NHHR participants exhibited a 1.95 times greater odds of HUA prevalence compared to the lowest quartile [2.95 (2.39, 3.64), $P < 0.0001$]. When different definitions of HUA were used, this similar association has also been observed in this instance. The results of Supplementary Table 2 indicate that this positive association remained statistically significant even after the exclusion of the outliers. The findings of the smooth fitting curve showed a nonlinear relationship between NHHR and HUA (Fig. 2). Table 3

Subgroup analysis

Table 4 shows the different associations between NHHR and HUA across various subgroups. A positive association between NHHR and HUA was identified in each subgroup. Additionally, we observed significant interactions between NHHR and HUA in the race and diabetes subgroups ($p < 0.05$). The odds of HUA prevalence were higher among non-diabetic participants [1.40 (1.32, 1.49), $P < 0.0001$] compared to diabetic participants [1.18 (1.06, 1.32), $P = 0.0031$]. Among the different races, Mexican Americans had the lowest odds of HUA prevalence [1.09 (0.92, 1.27), $P = 0.2413$] compared to other races.

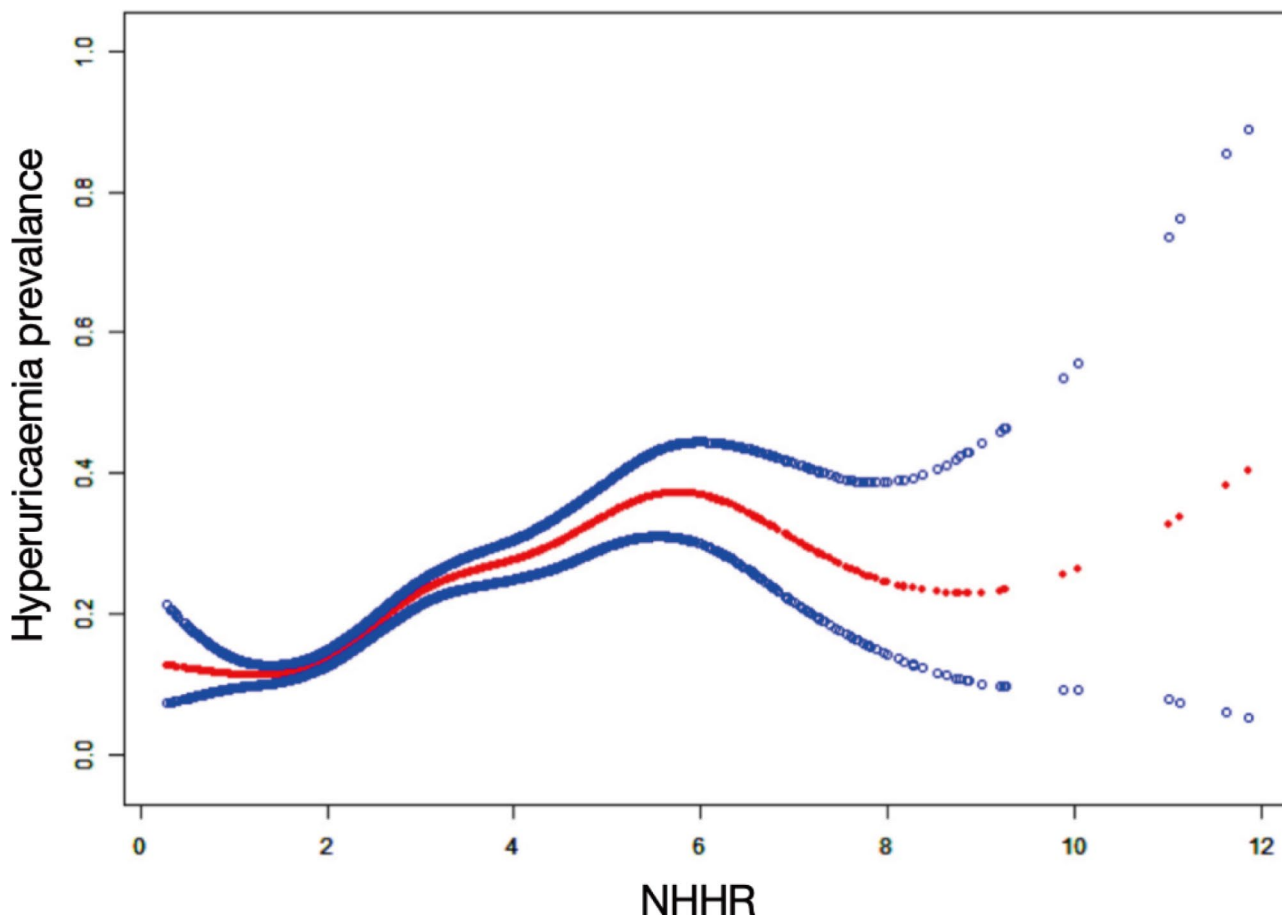


Fig. 2 The nonlinear associations between NHHR and hyperuricemia

Table 3 Threshold effect analysis of NHHR on hyperuricemia using a two-piecewise linear regression model

Model	OR (95%CI)	P-value
Inflection point (K)	5.8	
Fitting by two-piecewise linear model		
NHHR ≤ 5.8	1.44 (1.36, 1.52)	< 0.0001
NHHR > 5.8	0.69 (0.52, 0.91)	0.0102
Log-likelihood ratio		< 0.001

gender, age, race, family income-to-poverty ratio, education level, physical activity status, marital status, drink status, smoking status, systolic blood pressure, diastolic blood pressure, glycated hemoglobin, total bilirubin, fasting blood glucose, serum creatinine, serum urea nitrogen, urinary albumin, aspartate aminotransferase, alanine aminotransferase, body mass index, waist circumference, and history of diabetes, high blood pressure, hyperlipidemia, and kidney stones were adjusted. Abbreviation: NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

Discussion

In this study of 7,876 U.S. adults, the results demonstrated the positive association between NHHR and the odds of HUA prevalence, which persisted across three different models. This remains the case even when different HUA definitions are employed and outliers are removed. The results of the smooth fitting curve indicated a nonlinear positive association between NHHR

and HUA. The threshold effect analysis showed an inflection point at 5.8. Furthermore, subgroup analysis revealed significant interactions between different races, diabetes status, and NHHR levels, affecting the odds of HUA prevalence.

HUA is associated with the onset and development of various chronic diseases and has become a significant health issue that cannot be ignored, imposing a heavy burden on public health [1, 5, 26, 27]. The relationship between uric acid and metabolic syndrome is bidirectional and complex; elevated uric acid levels are not only a consequence of metabolic syndrome but can also exacerbate its components, such as insulin resistance, obesity, and lipid metabolism dysregulation. Conversely, insulin resistance can increase uric acid reabsorption in the kidneys, further elevating uric acid levels [10]. Therefore, identifying risk factors for HUA is crucial for guiding clinical prevention and treatment. Increasing research indicates that lipid metabolism is vital in the development of HUA. A study carried out in Northwest China showed that dyslipidemia increases the odds of HUA prevalence, with higher triglyceride levels and total cholesterol levels identified as risk factors for HUA [28]. A retrospective

Table 4 Subgroup analysis of the association between NHHR and hyperuricemia

Characteristic	Model OR (95%CI)	P- value	P for interaction
Stratified by age (years)			0.0548
20–40	1.54 (1.40, 1.69)	< 0.0001	
40–60	1.27 (1.17, 1.38)	< 0.0001	
60–80	1.32 (1.21, 1.44)	< 0.0001	
Stratified by gender			0.9568
Male	1.36 (1.27, 1.46)	< 0.0001	
Female	1.36 (1.25, 1.47)	< 0.0001	
Stratified by race			0.0247
Mexican American	1.09 (0.94, 1.27)	0.2413	
Other Hispanic	1.44 (1.24, 1.66)	< 0.0001	
Non-Hispanic White	1.40 (1.28, 1.53)	< 0.0001	
Non-Hispanic Black	1.40 (1.27, 1.55)	< 0.0001	
Other Race	1.37 (1.22, 1.53)	< 0.0001	
Stratified by BMI			0.6434
Normal weight	1.37 (1.26, 1.48)	< 0.0001	
Overweight	1.32 (1.21, 1.44)	< 0.0001	
Obese	1.39 (1.27, 1.53)	< 0.0001	
Stratified by Diabetes			0.0031
Yes	1.18 (1.06, 1.32)	0.0031	
No	1.40 (1.32, 1.49)	< 0.0001	
Stratified by High blood pressure			0.1741
Yes	1.31 (1.21, 1.41)	< 0.0001	
No	1.40 (1.30, 1.50)	< 0.0001	
Stratified by eGFR			0.0847
eGFR ≥ 90	1.49 (1.27, 1.74)	< 0.0001	
90 < eGFR ≤ 60	1.25 (1.16, 1.36)	< 0.0001	
eGFR < 60	1.37 (1.28, 1.46)	< 0.0001	

gender, age, race, family income-to-poverty ratio, education level, physical activity status, marital status, drink status, smoking status, systolic blood pressure, diastolic blood pressure, glycated hemoglobin, total bilirubin, fasting blood glucose, serum creatinine, serum urea nitrogen, urinary albumin, aspartate aminotransferase, alanine aminotransferase, body mass index, waist circumference, and history of diabetes, High blood pressure, hyperlipidemia, and kidney stones were adjusted. Abbreviation: NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio, BMI, body mass index, eGFR, estimated glomerular filtration rate

study involving 3,884 subjects found that triglycerides are risk factor for HUA. Individuals with hypertriglyceridemia have a 2.353 times higher odds of HUA prevalence compared to those with normal triglyceride levels [29]. A large-scale cohort study conducted in China by Liu et al [30], over a period of four years involving 15,198 subjects demonstrated that a higher triglyceride to high-density lipoprotein cholesterol ratio is positively correlated with the odds of HUA prevalence. Another study also showed a positive association between residual cholesterol and HUA in Americans, which is similar to what we found, but the association was stronger in those without diabetes [31].

NHHR, as a newly developed lipid indicator, has been shown to have significant predictive value for the risk of

kidney stones and diabetes [15, 32]. An elevated NHHR indicates dysregulation of lipid metabolism. The pathogenesis between NHHR and HUA remains unclear. Our study results suggest that elevated NHHR levels are positively associated with the odds of HUA prevalence. Based on existing studies, we propose several possible theoretical explanations: (1) Elevated lipid metabolism levels are closely related to insulin resistance [33, 34]. Insulin resistance is associated with increased expression of Urate transporter 1, which promotes uric acid reabsorption and inhibits the function of adenosine triphosphate-binding cassette subfamily G member 2, reducing uric acid excretion [35], this consequently resulted in elevated serum uric acid levels. Anti-diabetic medications such as pioglitazone and metformin, which improve insulin resistance, can reduce serum uric acid levels [36, 37]. (2) Low serum high-density lipoprotein cholesterol (HDL-C) levels can lead to decreased glomerular filtration function, thereby increasing serum uric acid levels. Low serum HDL-C levels are key factors in atherosclerosis and are major causes of renal artery stenosis and decreased glomerular filtration function [38]. A body of evidence indicates that a low serum HDL-C level represents a risk factor associated with the advancement of chronic kidney disease [39]. (3) High triglyceride levels can lead to increased oxidation of free fatty acids, producing more acetyl-CoA. The liver utilizes free fatty acids to synthesize more purines, resulting in elevated uric acid levels [40]. (4) HDL-C has anti-inflammatory properties. Low levels of HDL-C can weaken antioxidant and anti-inflammatory effects [41]. Low levels of HDL-C trigger inflammatory responses and oxidative stress in the body, promoting purine metabolism and increasing uric acid production [40, 42]. Therefore, we have reason to infer that elevated NHHR levels are associated with HUA.

In the diabetes subgroup of this study, we found that among participants with different NHHR levels, non-diabetic participants had a higher odds of HUA prevalence compared to diabetic participants. This may be because non-diabetic participants might have higher insulin resistance, whereas diabetic patients receive medication to control blood glucose and insulin levels and are often treated with lipid-lowering drugs. Some glucose-controlling and lipid-lowering medications have been shown to reduce serum uric acid levels [36, 37, 43]. Recent studies have highlighted Sodium-Glucose Co-Transporter 2 inhibitors facilitate increased renal excretion of uric acid by inhibiting its reabsorption in the renal proximal tubules [44, 45]. We also found that among participants with different NHHR levels, a lower odds of HUA prevalence was observed in Mexican Americans compared to other racial groups. This may be due to genetic factors, dietary habits, and lifestyle differences [46].

The strengths of our study include utilizing NHANES data, overseen by the CDC, which ensures the rigour and authenticity of the data through a nationally representative survey methodology. Admittedly, our study has certain limitations. Since our study design is cross-sectional, we cannot accurately infer the causal relationship between NHHR and HUA. Although we included many confounding factors that influence NHHR and HUA, there are still some potential confounders that we could not include, such as genetic factors, the use of glucose-controlling and lipid-lowering medications, and the consumption of high-purine foods.

Conclusion

The study results indicate that higher NHHR levels are positively associated with the odds of HUA prevalence, especially when NHHR levels are below the inflection point of 5.8. Early intervention and treatment for individuals with specific NHHR levels may reduce the occurrence of HUA and related complications. Based on these findings, NHHR is expected to become a new indicator for assessing lipid levels in HUA, providing new insights into the link between lipid metabolism disorders and the formation of HUA. Consequently, to substantiate these findings, large-scale prospective studies are required.

Abbreviations

HUA	Hyperuricemia
NHHR	Non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio
NHANES	National Health and Nutrition Examination Survey
NCHS	National Center for Health Statistics
CDC	Centers for Disease Control and Prevention
PIR	Family income-to-poverty ratio
BMI	Body Mass Index
HDL-C	High-density lipoprotein cholesterol
eGFR	Estimated glomerular filtration rate

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12944-024-02269-9>.

Supplementary Material 1

Supplementary Material 2

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Author contributions

ZJ, XZ, and FS designed the research. ZJ, XZ, HJ, XW, and DZ collected, analyzed the data, and drafted the manuscript. ZJ and FS revised the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability

The survey data are publicly available on the internet for data users and researchers throughout the world (www.cdc.gov/nchs/nhanes/).

Declarations

Ethics approval and consent to participate

The portions of this study involving human participants, human materials, or human data were conducted in accordance with the Declaration of Helsinki and were approved by the NCHS Ethics Review Board. The patients/participants provided their written informed consent to participate in this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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