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Exploring the associations and potential mediators between lipid biomarkers and the risk of developing gout: NHANES 2007–2018

Yuzhe Huang[1,2], Ying Li[1,2], Zhounan Wu[1,2], Yuhang Liang[1,2] and Jinshen He[1*]

Abstract

Background Gout stands as a prevailing manifestation of inflammatory arthritis. While it is linked to several well-established risk factors, the associations between lipid profiles and the risk of gout remain unclear.

Methods This research involved National Health and Nutrition Examination Survey data (2007–2018). The cardiometabolic index, which incorporates the Triglycerides (TG)/High-density lipoprotein cholesterol (HDL) ratio and waist to height ratio (WHtR), was used to assess lipid profiles and metabolic health. Multivariate logistic regression analysis, propensity score matching, and mediation analyses were utilized to evaluate the associations of lipid profiles and the cardiometabolic index with the risk of developing gout.

Results Among 11,032 participants, each 1-unit increase in TG levels was associated with a 65% increase in the odds of developing gout before matching [1.65 (1.15–2.38), $P=0.007$] and a 155% increase in the odds of developing gout after matching [2.55 (1.59–4.09), $P=0.007$]. Each 1-unit increase in the cardiometabolic index was linked to an 81% increase in the odds of developing gout before matching [1.81 (1.22–2.70), $P=0.004$] and a 215% increase in the odds of developing gout after matching [3.15 (1.84–5.40), $P<0.001$]. The participants with HDL levels in the third quartile presented a 35% reduction in gout risk relative to those with HDL levels in the first quartile before matching [0.65 (0.46–0.92), $P=0.014$] and a 51% reduction in gout risk after matching [0.49 (0.32–0.75), $P<0.001$]. Mediation analyses revealed that BMI, WHtR, and homeostatic model assessment for insulin resistance (HOMA-IR) mediated the relationships between TG levels and the risk of developing gout at 18.75%, 24.28%, and 5.35%, respectively. For the association between HDL levels and the risk of developing gout, the mediating effects of BMI, WHtR, leukocytes, γ-glutamyltransferase (in those with HDL < 56 mmol/L), and HOMA-IR were 57.98%, 69.03%, 8.77%, 5.18%, and 11.14%, respectively.

Conclusion This study reveals the relationship between lipid profiles and the risk of developing gout. Regularly checking TG and HDL levels and actively managing obesity, insulin resistance, oxidative stress and inflammation are important for lowering the risk of developing gout.

Keywords Dyslipidaemia, Gout, Hyperuricaemia, National Health and Nutrition Examination Survey, Cross-sectional study

*Correspondence:
Jinshen He
jinshen.he@hotmail.com

[1]Department of Orthopaedic Surgery, the Third Xiangya Hospital of Central South University, 138 Tongzipo Road, Hexi Yuelu District, Changsha, Hunan 410013, China
[2]Xiangya School of Medicine, Central South University, Changsha 410013, China

Introduction

Gout is marked by the deposition of urate crystals in tissues. The onset of acute gout is marked by sudden and intense pain in the affected joint, especially at night or in the early morning. In contrast, chronic gout may manifest as recurrent episodes that ultimately result in joint damage and dysfunction [1]. In 2019, global gout cases reached 53 million, and this number is projected to surpass 120 million by 2035, positioning it as a commonly encountered type of inflammatory arthritis in the West [2]. Patients with recurrent gout experience annual medical costs of approximately $27,000. Given the high prevalence of gout, it exerts a substantial economic strain on healthcare recipients and the medical system [3].

Dyslipidaemia, featuring the abnormalities of low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides (TG), and total cholesterol (TC) [4], is a pathophysiological condition closely associated with various clinical disorders. With the advancement of social and economic conditions, it has emerged as a significant threat to human health, particularly cardiovascular disease, which is becoming the leading cause of mortality worldwide [5, 6]. Additionally, dyslipidaemia has also been observed to be associated with metabolic diseases and autoimmune disorders [7–9]. Several risk factors are well-established contributors to gout, including hyperuricaemia (HUA), obesity, hypertension, diuretic use, and alcohol consumption [1]. However, the associations between dyslipidaemia and gout still lack clarity. Several cross-sectional studies conducted in China and South Korea have suggested a correlation between dyslipidaemia and HUA [10–13]. Nevertheless, due to ethnic geographical variations and limited sample size, there is a need for further systematic investigation into the associations and underlying mechanisms between lipid profiles and uric acid metabolism, gout, along with the differential effects of lipids on HUA and gout in a large American population sample.

To further explore the associations between blood lipid biomarkers and gout, utilization of the cardiometabolic index (CMI) was also incorporated into our investigation. Ichiro Wakabayashi initially designed CMI to function as a visceral adipose tissue dysfunction marker. Meanwhile, It can additionally indicate the individual blood lipid profiles level [14]. It combines the TG/HDL ratio and waist to height ratio (WHtR), which reflect insulin resistance and obesity, respectively. Both indices are strongly linked to metabolic processes. Recent research has identified a robust association between CMI and conditions including hypertension, kidney dysfunction, and diabetes [15–17], highlighting CMI's critical role in metabolic disease.

In summary, the study drew upon the National Health and Nutrition Examination Survey (NHANES) data to assess the associations involving blood lipid profiles and gout. In contrast to previous studies, the current investigation utilized a robust dataset derived from a large American population to conduct its analysis. Moreover, the incorporation of propensity score matching (PSM) and mediation analysis methodologies enhanced the elucidation of the intricate relationships between the variables of interest. Notably, there is a paucity of research examining the connection between CMI and gout. Exploring the association between CMI and gout not only facilitates a deeper understanding of the interplay between lipid metabolism and gout but also sheds light on the dynamics of uric acid metabolism. Such insights could significantly contribute to the advancement of strategies for the management and prevention of gout. It was hypothesized that lipid biomarkers and CMI are significantly associated with gout among adults in America.

Methods and materials

Study population

The information gathered between 2007 and 2018 originates from the NHANES. All participants are aged 20 years or above. The participant exclusion procedure is illustrated in Fig. 1.

Lipid biomarkers

The lipid biomarkers include TG, TC, HDL and LDL. The data was analyzed using samples from participants who had fasted for a minimum of 8.5 h and a maximum of 24 h. The TC, TG, LDL, and HDL concentrations were assessed through an enzymatic technique. The information can be accessed through the comprehensive sample collection and processing protocols on the NHANES website. All lipid biomarkers were measured by the same method in all patients over the period. The CMI was derived mathematically by the equation: CMI = TG (mmol/L)/HDL (mmol/L)×WHtR. WHtR is the ratio of waist circumference (WC) to height. The exposure variables were TG, TC, HDL, LDL, and CMI.

Definition of hyperuricaemia and gout

In the context of NHANES, serum urate levels were quantified using the timed endpoint assay facilitated by the DxC800 analytical platform. The threshold for HUA diagnosis was delineated at serum urate concentrations exceeding or equal to 7.0 mg/dl in the male cohort and 6.0 mg/dl in the female cohort. Gout diagnosis was determined derived from self-reported responses.

Mediators and covariates

The mediators in this study included various indices of obesity, inflammation, oxidative stress, and insulin resistance. Obesity indexes consisted of body mass index (BMI) and WHtR to capture two different aspects of obesity. Compared to BMI, WHtR places greater emphasis

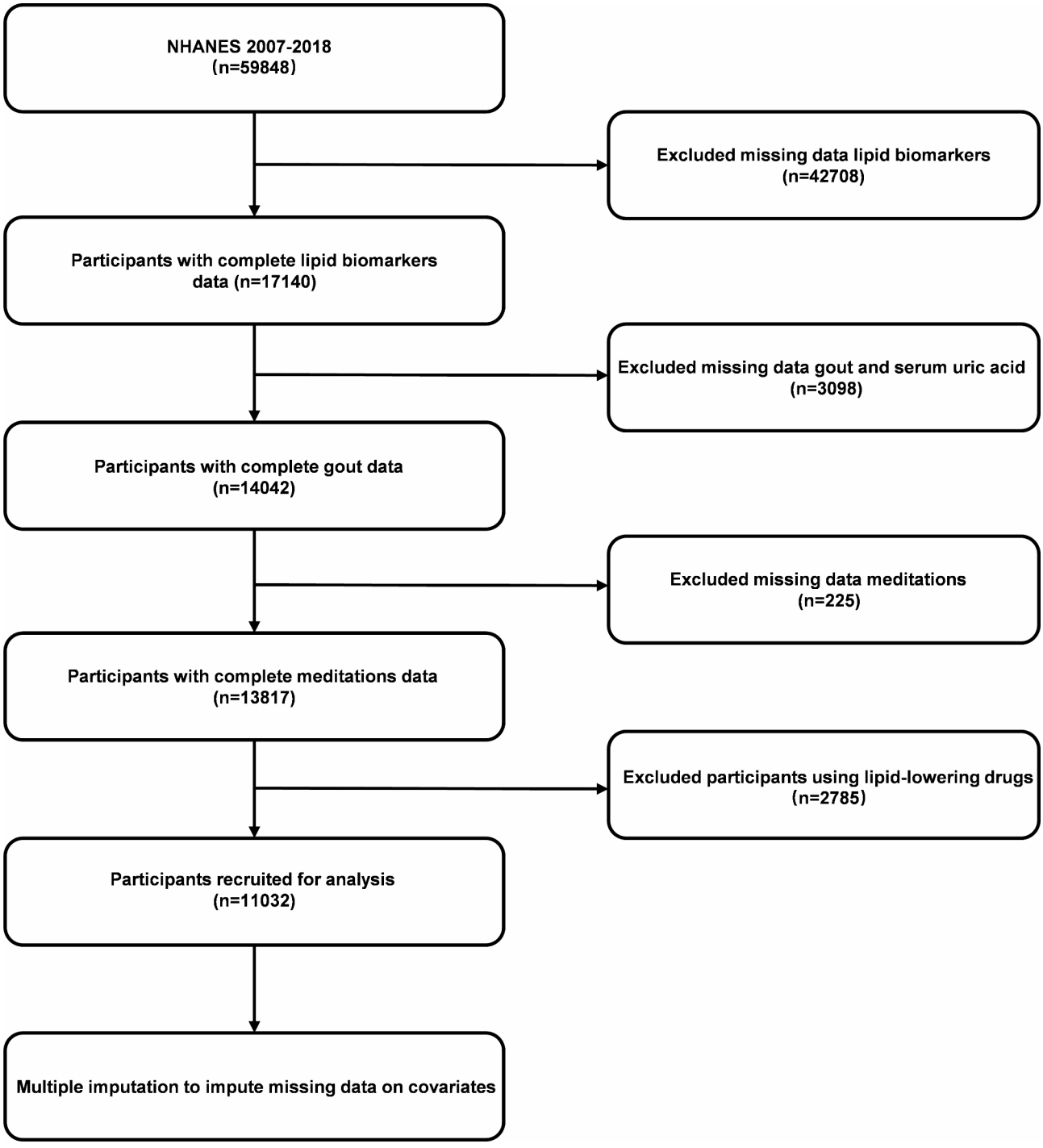

Fig. 1 Flow chart of sample selection from the NHANES 2007–2018 ($n = 11,032$). NHANES, National Health and Nutrition Examination Survey

on the distribution of the body and the assessment of central obesity in individuals [18]. Inflammation indexes included leukocyte, lymphocyte counts, neutrophil to lymphocyte ratio (NLR), and systemic immune inflammation index (SII). SII is derived from the multiplication of the platelet count and NLR. This index serves as a comprehensive marker of systemic inflammation and immune response. The oxidative stress index was represented byγ-glutamyltransferase (GGT). Insulin resistance index included homeostasis model assessment of insulin resistance (HOMA-IR). Covariates encompassed sex, age, ethnicity, education attainment, BMI, income to poverty ratio, alcohol intake, cigarette use, hypertension, diabetes, estimated glomerular filtration rate (eGFR),

HOMA-IR, and the release cycle of the NHANES. The definitions of covariates and mediators were listed in the Supplementary instruction.

Statistical analysis

This study employed multiple imputations to fill in missing data, computed Cronbach's coefficient to assess the internal consistency of the imputed datasets, and ultimately selected the dataset with the highest Cronbach's coefficient for analysis. Quantitative variables are reported as means and analyzed using the two-sample t-test, while qualitative variables are expressed as percentages and assessed with the chi-squared test. The associations between lipid biomarkers and gout were assessed using multivariable logistic regression models across three different analyses. In Model I, sex, age, ethnicity, and BMI were accounted for. Model II incorporated supplementary considerations for education attainment, income-to-poverty ratio, alcohol, cigarette use, diabetes, hypertension, eGFR, and release cycle. Model III was fine-tuned for BMI and HOMA-IR in accordance with the adjustments made in Model II. PSM was meticulously applied to account for potential confounders, employing a 1:2 nearest-neighbor matching algorithm to establish cohorts with and without gout and HUA. Smooth curve fitting was employed to examine the possible nonlinear associations between the lipid biomarkers and gout. Analyses of subgroups and interactions were performed based on gender, BMI, race, cigarette smoking status, and alcohol consumption. Mediation analyses incorporated obesity, insulin resistance, inflammation, and oxidative stress indices. The results delineated the extent of the indirect pathway effect, the relative contribution of the mediating impact, and the *P*-value associated with the statistical significance of these mediators. All analyses were performed employing EmpowerStats software (version 4.0) and the R project (version 4.3.1) for computational purposes. $P<0.05$ signified statistical relevance.

Results

Population characteristics

Table 1 offered a compilation of the essential features of the 11,032 individuals from NHANES 2007–2018, with gout as a column stratification variable. Among the participants enrolled in this analysis, a subset of 358 individuals was identified as suffering from gout. Significant disparities in baseline characteristics were observed between patients with gout and those without. In comparison to individuals without gout, those with gout were generally older in age, male, non-Hispanic white, smokers. Additionally, they had higher rates of HUA, hypertension, and diabetes. Moreover, the gout participants exhibited higher levels of BMI, WHtR, uric acid, TG, TC, CMI, GGT, HOMA-IR, leukocytes, lymphocytes, NLR, and SII, while eGFR, HDL were lower than those non-gout participants.

Associations between lipid biomarkers and gout, hyperuricaemia

The associations between lipid biomarkers and gout, HUA were shown in Table 2. In the analysis of lipid profiles related to gout, participants in the third HDL quartile revealed significantly lowest likelihood of developing gout relative to individuals in the lowest HDL quartile in the three models. The odds ratios (OR) were 0.58 (95% CI: 0.41–0.81, $P=0.001$), 0.56 (95% CI: 0.40–0.80, $P=0.001$), and 0.65 (95% CI: 0.46–0.92, $P=0.014$), respectively. Conversely, a markedly elevated likelihood of gout was witnessed in the highest TG quartile in contrast to the first TG quartile in the three models, with OR of 1.94 (95% CI: 1.37–2.73, $P<0.001$), 1.97 (95% CI: 1.38–2.81, $P<0.001$), and 1.65 (95% CI: 1.15–2.38, $P=0.007$), respectively. However, the associations between LDL, TC by quartile, and gout are insignificant across the three models. For HUA, four lipid profiles were significantly associated with HUA, excluding the second and third quartiles of LDL and the second quartile in TC. Moreover, the analysis revealed a constant association between TG and gout, as the smooth curve fitting indicated. (shown in Supplementary Fig. 1 and Supplement Table 1).

Subgroup analyses

The associations between lipid biomarkers and gout were further examined in Table 3, using subgroup analysis categorized by gender, BMI, race, cigarette use, and alcohol intake. All concomitant variables were adjusted for in each subgroup analysis model, excluding the stratification variable. No substantial interactions were detected across all subgroups. (all interaction *P* values exceeded 0.05). In addition, the associations between LDL, TC, and gout in different subgroups were not statistically significant (shown in Supplementary Tables 2–3).

Potential mediators between lipid biomarkers and gout

Furthermore, mediation analyses were undertaken to assess the potential mediations between TG, HDL, and gout (shown in Table 4). The results indicated that obesity indices like BMI and WHtR mediated the association between TG and gout, contributing to 20.42% and 26.09% of the risk, respectively. For HOMA-IR, the proportion of mediator was found to be 5.39%. Regarding HDL, the analysis revealed that the leukocytes mediated the association, resulting in an 8.62% increased risk. GGT mediated the association at -7.08%. Moreover, the study conducted a comprehensive analysis using smooth curve fitting to detect the association between HDL and GGT. It indicated a nonlinear association between HDL and GGT. Additionally, segmented regression

Table 1 Baseline characteristics from NHANES 2007–2018

	Control Group ($n=10674$)	Gout ($n=358$)	*P* value
Age(years)	45.32 ± 16.48	60.69 ± 13.79	< 0.001*
Gender			< 0.001*
male	4955 (46.42%)	237 (66.20%)	
female	5719 (53.58%)	121 (33.80%)	
Race/ethnicity			< 0.001*
Mexican American	1784 (16.71%)	36 (10.06%)	
Other Hispanic	1231 (11.53%)	24 (6.70%)	
Non-Hispanic White	4162 (38.99%)	165 (46.09%)	
Non-Hispanic Black	2144 (20.07%)	80 (22.35%)	
Other Race	1355 (12.69%)	53 (14.80%)	
Body mass index(kg/m2)	28.64 ± 6.81	30.99 ± 7.00	< 0.001*
WHtR	0.58 ± 0.10	0.63 ± 0.10	< 0.001*
Income to poverty ratio			0.423
< 1	24,449 (22.94%)	91 (25.42%)	
1–3	4426 (42.40%)	153 (42.74%)	
≥ 3	3699 (34.70%)	114 (31.84%)	
Education level			0.042*
Less than high school	2584 (24.21%)	89 (24.86%)	
High school	2344 (21.96%)	97 (27.09%)	
More than high school	5746 (53.83%)	172 (48.04%)	
Smoking status			< 0.001*
No	6213 (58.21%)	147 (41.06%)	
Yes	4461 (41.79%)	211 (58.94%)	
Alcohol consumption			0.528
No	6352 (59.51%)	219 (61.17%)	
Yes	4322 (40.49%)	139 (38.83%)	
Hypertension			< 0.001*
No	8211 (76.93%)	143 (39.94%)	
Yes	2463 (23.07%)	215 (60.06%)	
Diabetes			< 0.001*
No	9257 (86.72%)	240 (67.04%)	
Yes	1417 (13.28%)	118 (32.96%)	
Hyperuricemia			< 0.001*
No	8753 (82.00%)	158 (44.13%)	
Yes	1921 (18.00%)	200 (55.87%)	
Uric acid	5.36 ± 1.37	6.81 ± 1.79	< 0.001*
eGFR	99.94 ± 21.38	78.88 ± 25.27	< 0.001*
HDL	54.68 ± 16.14	51.17 ± 15.62	< 0.001*
LDL	117.92 ± 34.97	119.84 ± 37.19	0.311
TG	112.61 ± 64.48	142.75 ± 76.28	< 0.001*
TC	195.12 ± 40.13	199.55 ± 42.40	0.041*
CMI	1.45 ± 1.26	2.17 ± 2.12	< 0.001*
GGT	27.96 ± 36.78	44.08 ± 66.62	< 0.001*
HOMA-IR	3.45 ± 4.91	5.48 ± 9.76	< 0.001*
Leukocytes	6.73 ± 2.25	7.35 ± 3.46	< 0.001*
Lymphocytes	2.06 ± 0.78	2.18 ± 2.40	0.006*
NLR	2.06 ± 1.11	2.43 ± 1.60	< 0.001*
SII	505.20 ± 407.58	555.02 ± 414.12	0.023*
Release cycle			< 0.001*
2007–2008	1866 (17.48%)	63 (17.60%)	
2009–2010	2036 (19.07%)	57 (15.92%)	
2011–2012	1735 (16.25%)	53 (14.80%)	
2013–2014	1826 (17.11%)	37 (10.34%)	

Table 1 (continued)

	Control Group ($n=10674$)	Gout ($n=358$)	*P* value
2015–2016	1588 (14.88%)	55 (15.36%)	
2017–2018	1623 (15.22%)	93 (25.98%)	

Mean ± SD for continuous variables: *P* value was calculated by the t-test; % for categorical variables, *P* value was calculated by the chi-square test

* Signifcant at the $P<0.05$ level

BMI: Body mass index, WHtR: waist-to-height ratio, HOMA-IR: Homeostatic model assessment for insulin resistance, GGT: γ-glutamyltransferase, NLR: neutrophil lymphocyte ratio, SII: The systemic immune inflammation index, eGFR: Estimated glomerular filtration, CMI: Cardiometabolic Index

analysis identified a significant turning point for HDL at 56 mmol/L, supported by a log-likelihood ratio *P*-value of less than 0.05, thus validating this inflection point's statistical significance (Supplementary Tables 4 and Supplementary Fig. 1). In individuals with HDL levels below 56 mmol/L, GGT mediated the association at 5.35%, whereas this mediation was not significant in those with HDL levels exceeding 56 mmol/L. The proportion of mediators was noted to be 11.14%. Regarding obesity indexes such as BMI and WHtR, it was found that both BMI and WHtR mediated the association between HDL and gout at the risks of 57.81% and 68.80%, respectively. Notably, the statistical analysis did not demonstrate a significant direct impact of HDL on gout., suggesting that HDL's impact was mainly mediated through BMI and WHtR. Other outcomes were not significant. The mediation models were shown in supplementary Figs. 2–4.

Association between CMI and gout, hyperuricaemia

The association between CMI and gout was presented in the Supplementary Table 4. It was observed that participants in the top CMI quartile revealed a notably highest risk of gout compared with the lowest CMI quartile in the three models, with OR of 2.15 (95% CI: 1.46–3.15, $P<0.001$), 2.50 (95% CI: 1.72–3.62, $P<0.001$), and 1.81 (95% CI: 1.22–2.70, $P=0.004$), respectively. In relation to HUA, significant associations were observed across all three quartiles of CMI. To further investigate the possible nonlinear association between CMI and gout, a smooth curve fitting analysis was performed, revealing a linear correlation between CMI and gout (shown in Supplementary Table 5). Furthermore, the study conducted a subgroup analysis (shown in Supplementary Table 6). No notable interactions were detected within any of the subgroups (all interaction *P* values exceeded 0.05).

Association between lipid biomarkers, CMI, and gout, hyperuricaemia after matching

To rigorously mitigate confounding factors, PSM was applied for gout and HUA (shown in Table 5). Multivariate logistic regression analysis post-PSM was conducted to ensure a more precise estimation of the associations. The baseline characters after matching for gout and HUA were shown in Supplementary Tables 7–8. In participants matched for gout, those in the third HDL quartile revealed significantly lowest risk of gout relative to individuals in the lowest HDL quartile in the three models. The OR were 0.53 (95% CI: 0.35–0.80, $P=0.002$), 0.43 (95% CI: 0.29–0.66, $P<0.001$), and 0.49 (95% CI: 0.32–0.75, $P<0.001$), respectively. Conversely, those in the topmost TG quartile demonstrated a heightened likelihood of gout relative to individuals in the lowest TG quartile, with OR of 2.32 (95% CI: 1.47–3.64 $P<0.001$), 2.98 (95% CI: 1.88–4.72, $P<0.001$), and 2.55 (95% CI: 1.59–4.09, $P<0.001$), respectively. Participants in the third and highest CMI quartile revealed notably the highest risk of gout relative to the minimal CMI quartile in the three models. For the third quartile, the ORs were 1.96 (95% CI: 1.21–3.19, $P=0.007$), 2.58 (95% CI: 1.61–4.13, $P<0.001$), and 2.19 (95% CI: 1.32–3.61, $P=0.002$), respectively. In the highest quartile, ORs were 2.76 (95% CI: 1.65–4.60, $P<0.001$), 3.89 (95% CI: 2.38–6.36, $P<0.001$), and 3.15 (95% CI: 1.84–5.40, $P<0.001$). The outcome of CMI in the third quartile was not significant before PSM. Concerning HUA, the outcomes were consistent across the five exposures, except for the second HDL quartile, which was not significantly associated with HUA post-matching.

Discussion

In this large-scale observational study recruiting 11,042 participants in America, the study investigated the associations between lipid biomarkers, CMI and gout, alongside their potential mediating pathways. It was found that TG was directly associated with gout. HDL was inversely associated with gout. Besides, it was witnessed that BMI, WHtR, and HOMA-IR mediated the association between TG and gout at 20.42%, 26.09%, and 5.39%, respectively. While BMI, WHtR, leukocytes, GGT, and HOMA-IR functioned as mediators at 57.81%, 68.80%, 8.62%, and 5.35% (in individuals with HDL levels below 56 mmol/L), and 9.12%, respectively. Subsequently, CMI was implemented to demonstrate better the association between blood lipid biomarkers and gout. It was witnessed that CMI was significantly correlated with gout. Further post-matching multivariate logistic regression also supported the mentioned outcomes.

Previous observational investigations have reported that dyslipidaemia is a prevalent condition in individuals with gout [19, 20]. HUA is a critical determinant in

Table 2 Association between lipid profiles and gout, hyperuricemia

Exposure	Model I	Model II	Model III
Gout			
HDL			
Continuous	0.9913 (0.9833, 0.9994) 0.035	0.9892 (0.9815, 0.9969) 0.006	0.9957 (0.9877, 1.0037) 0.295
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	0.83 (0.62, 1.10) 0.193	0.86 (0.645, 1.17) 0.324	0.92 (0.68, 1.23) 0.567
Q3	0.58 (0.41, 0.81) 0.001	0.56 (0.40, 0.80) 0.001	0.65 (0.46, 0.92) 0.014
Q4	0.82 (0.59, 1.13) 0.230	0.77 (0.55, 1.06) 0.109	1.01 (0.72, 1.42) 0.951
TG			
Continuous	1.0046 (1.0031, 1.0061) < 0.001	1.0045 (1.0030, 1.0061) < 0.001	1.0039 (1.0024, 1.0055) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	0.94 (0.64, 1.38) 0.748	0.94 (0.64, 1.38) 0.750	0.88 (0.59, 1.30) 0.511
Q3	1.25 (0.87, 1.79) 0.220	1.29 (0.90, 1.87) 0.168	1.15 (0.79, 1.66) 0.472
Q4	1.94 (1.37, 2.73) < 0.001	1.97 (1.38, 2.81) < 0.001	1.65 (1.15, 2.38) 0.007
LDL			
Continuous	0.9979 (0.9947, 1.0010) 0.184	0.9993 (0.9962, 1.0025) 0.678	0.9989 (0.9957, 1.0021) 0.496
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.02 (0.74, 1.40) 0.911	1.09 (0.79, 1.51) 0.580	1.07 (0.78, 1.48) 0.671
Q3	0.83 (0.60, 1.14) 0.245	0.96 (0.70, 1.34) 0.828	0.92 (0.66, 1.27) 0.597
Q4	0.83 (0.61, 1.14) 0.247	0.96 (0.70, 1.32) 0.798	0.90 (0.66, 1.25) 0.539
TC			
Continuous	1.0001 (0.9973, 1.0028) 0.968	1.0006 (0.9979, 1.0034) 0.646	1.0009 (0.9981, 1.0036) 0.543
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.01 (0.72, 1.41) 0.960	1.06 (0.76, 1.49) 0.717	1.06 (0.75, 1.49) 0.734
Q3	1.07 (0.78, 1.48) 0.663	1.22 (0.88, 1.70) 0.240	1.21 (0.87, 1.68) 0.267
Q4	1.03 (0.75, 1.42) 0.858	1.11 (0.79, 1.54) 0.555	1.11 (0.80, 1.55) 0.532
Hyperuricemia			
HDL			
Continuous	0.9875 (0.9836, 0.9913) < 0.001	0.9763 (0.9726, 0.9800) < 0.001	0.9893 (0.9853, 0.9933) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	0.73 (0.63, 0.83) < 0.001	0.68 (0.60, 0.79) < 0.001	0.75 (0.66, 0.86) < 0.001
Q3	0.64 (0.55, 0.74) < 0.001	0.51 (0.44, 0.59) < 0.001	0.67 (0.58, 0.78) < 0.001
Q4	0.55 (0.46, 0.64) < 0.001	0.36 (0.30, 0.42) < 0.001	0.59 (0.50, 0.70) < 0.001
TG			
Continuous	1.0055 (1.0047, 1.0062) < 0.001	1.0065 (1.0058, 1.0073) < 0.001	1.0053 (1.0045, 1.0061) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.77 (1.49, 2.10) < 0.001	1.93 (1.62, 2.29) < 0.001	1.72 (1.44, 2.05) < 0.001
Q3	2.12 (1.79, 2.51) < 0.001	2.56 (2.16, 3.04) < 0.001	2.05 (1.73, 2.45) < 0.001
Q4	3.26 (2.76, 3.85) < 0.001	4.19 (3.54, 4.97) < 0.001	3.12 (2.62, 3.72) < 0.001
LDL			
Continuous	1.0029 (1.0015, 1.0044) < 0.001	1.0045 (1.0031, 1.0059) < 0.001	1.0034 (1.0019, 1.0048) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.03 (0.89, 1.20) 0.675	1.18 (1.01, 1.37) 0.037	1.06 (0.91, 1.25) 0.438
Q3	1.08 (0.93, 1.26) 0.283	1.35 (1.16, 1.56) < 0.001	1.14 (0.98, 1.33) 0.101
Q4	1.32 (1.15, 1.53) < 0.001	1.61 (1.39, 1.86) < 0.001	1.38 (1.19, 1.61) < 0.001
TC			
Continuous	1.0040 (1.0027, 1.0052) < 0.001	1.0042 (1.0029, 1.0054) < 0.001	1.0043 (1.0030, 1.0056) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.17 (1.01, 1.37) 0.042	1.26 (1.08, 1.47) 0.003	1.20 (1.03, 1.41) 0.021

Table 2 (continued)

Exposure	Model I	Model II	Model III
Q3	1.24 (1.06, 1.44) 0.006	1.38 (1.19, 1.61) < 0.001	1.31 (1.12, 1.53) < 0.001
Q4	1.64 (1.41, 1.90) < 0.001	1.73 (1.49, 2.01) < 0.001	1.70 (1.45, 1.98) < 0.001

The data: OR (95% CI) *P* value

Model I: gender, age, race, BMI were adjusted

Model II: gender, age, race, education level, Income to poverty ratio, alcohol, smoke, diabetes, hypertension, eGFR and release cycle were adjusted;

Model III: gender, age, race, BMI, education level, Income to poverty ratio, alcohol, smoke, diabetes, hypertention, eGFR, HOMA-IR and release cycle were adjusted

OR: Odds ratio, *BMI*: Body mass index, *eGFR*: Estimated glomerular filtration, *HOMA-IR*: Homeostatic model assessment for insulin resistance

Given that some of our results did not clearly indicate a relationship, we have retained four decimal places for precision

the development of gout, as most gout patients exhibit elevated uric acid levels. However, the two conditions are not synonymous. Some individuals with HUA remain asymptomatic and never develop gout, while a subset of gout patients may present with normouricemia [1, 21, 22]. Several cross-sectional studies conducted in China and South Korea have suggested a correlation between dyslipidaemia and HUA [10–13]. Two retrospective studies in China have found that TG emerged as a standalone determinant in the development of HUA.

Drawing on our research, which includes a large American sample, the development and progression of gout are intertwined with disturbances in lipid metabolism. In multivariable logistic regression analysis of TG, HDL, and gout, discrepancies were observed between Model 1 and Model 2 outcomes. When assessing Model 3 in relation to Model 2, the OR for the association between TG and gout was 0.32 lower, while the OR for the association between HDL and gout was 0.09 higher. This difference may be attributed to the additional adjustment for HOMA-IR and BMI in Model 3. To further explore the mediating roles of HOMA-IR, BMI, and other potential factors, the study conducted a mediation analysis. The analysis provided deeper insights into the complex interplay between lipid profiles, obesity, insulin resistance, and inflammatory processes in gout development. Specifically, BMI and WHtR, as markers of obesity, were significant mediators of the relationship between TG and gout, explaining 20.42% and 26.09% of the association, respectively. The mediating effect size of WHtR exceeded that of BMI, indicating that central obesity, in comparison to general adiposity, had a more pronounced influence on the pathogenesis of gout. HOMA-IR, a marker of insulin resistance, also mediated 5.39% of the association, underscoring the metabolic disturbances that link lipid abnormalities and gout. These outcomes align with prior studies demonstrating that insulin resistance and obesity lead to increased serum urate levels and heighten the likelihood of gout. In the context of HDL, BMI, and WHtR accounted for 57.81% and 68.80% of the association between HDL and gout, revealing the significance of central obesity. In terms of analyzing the role of GGT, it was hypothesized that an increase in HDL levels would reduce the concentration of GGT, thereby mitigating oxidative stress and subsequently lowering the risk of gout. However, contrary to this hypothesis, GGT was found to mediate the association between HDL and gout at a negative proportion of -7.10%. This unexpected result prompted further investigation, leading to the stratification of participants based on an HDL threshold of 56 mmol/L, which was used as a critical point to assess differential mediation effects. In individuals with HDL concentrations below 56 mmol/L, GGT mediated the association at 5.18%, aligning with our hypothesis. Conversely, this mediating effect was not statistically significant in those with HDL levels above 55 mmol/L, and the indirect mediation of GGT was $\beta = 0.0008$ (95% CI = 0.0003–0.0012, $P < 0.001$). The anticipated protective influence of HDL on GGT may diminish or even reverse. This may be attributable to the increased particle sizes and detrimental subspecies in the demographic exhibiting elevated HDL levels. Under these conditions, changes in the protein makeup of HDL particles may result in functional impairment, potentially leading to a shift from an anti-inflammatory to a pro-inflammatory state [23–26]. In the multiple logistic regression analysis of the top quartile of HDL and gout, a similar pattern emerged, with the protective effect of HDL no longer observed. The quandary may stem from statistical imbalances within the study population. In the baseline characteristics, it could be found that there were pronounced disparities in anthropometric measurements, demographics, and concurrent health issues. It was thought that age emerged as the predominant confounding variable. In the geriatric population, a propensity for reduced levels of HDL may ensue, potentially culminating in an insufficient HDL-mediated protective effect against gout. Discrepancies were also observed in the multivariable logistic regression results before and after PSM, likely attributable to the influence of confounders.

Mechanically, the correlation between hyperlipidemia and gout is complex. As shown in Fig. 2, TG and HDL may exert convergent effects on the pathogenesis of gout. Both of them are pivotal in modulating obesity. It is one of the most vital factors influencing the progression of gout. Elevated TG levels increase the circulation

Table 3 Subgroup analyses for the associations between TG, HDL and gout

Subgroups	Q1	Q2	Q3	Q4	*P* for interaction
TG					
Gender					0.429
Male	ref	0.73 (0.45, 1.20) 0.219	1.15 (0.73, 1.81) 0.542	1.48 (0.95, 2.32) 0.084	
Female	ref	1.16 (0.61, 2.23) 0.649	1.08 (0.56, 2.08) 0.827	2.03 (1.07, 3.85) 0.029	
Body mass index(kg/m2)					0.575
< 25	ref	1.08 (0.53, 2.20) 0.829	1.37 (0.68, 2.77) 0.374	2.42 (1.18, 4.93) 0.016	
25–30	ref	0.44 (0.21, 0.92) 0.029	0.95 (0.50, 1.77) 0.862	1.12 (0.60, 2.11) 0.720	
≥ 30	ref	1.26 (0.65, 2.46) 0.495	1.22 (0.64, 2.35) 0.543	1.83 (0.97, 3.46) 0.062	
Race					0.893
Mexican American	ref	2.66 (0.46, 15.24) 0.272	2.25 (0.43, 11.74) 0.337	3.35 (0.67, 16.65) 0.140	
Other Hispanic	ref	0.15 (0.02, 1.07) 0.059	0.50 (0.11, 2.28) 0.375	0.68 (0.16, 2.98) 0.610	
Non-Hispanic White	ref	0.86 (0.46, 1.62) 0.642	0.95 (0.52, 1.73) 0.872	1.61 (0.91, 2.84) 0.101	
Non-Hispanic Black	ref	0.85 (0.44, 1.63) 0.627	1.38 (0.73, 2.64) 0.319	1.24 (0.58, 2.68) 0.579	
Other Race	ref	1.30 (0.42, 4.05) 0.650	1.57 (0.54, 4.51) 0.407	2.33 (0.86, 6.33) 0.094	
Smoking status					0.559
No	ref	0.88 (0.49, 1.59) 0.674	0.92 (0.52, 1.65) 0.790	1.67 (0.96, 2.93) 0.071	
Yes	ref	0.89 (0.53, 1.50) 0.661	1.30 (0.793, 2.11) 0.301	1.61 (0.99, 2.61) 0.053	
Alcohol consumption					0.467
No	ref	0.98 (0.61, 157) 0.936	1.06 (0.67, 1.67) 0.800	1.52 (0.97, 2.37) 0.070	
Yes	ref	0.70 (0.35, 1.42) 0.321	1.28 (0.67, 2.45) 0.451	1.83 (0.98, 3.43) 0.058	
HDL					
Gender					0.103
Male	ref	0.86 (0.60, 1.22) 0.388	0.60 (0.39, 0.93) 0.022	1.35 (0.89, 2.05) 0.164	
Female	ref	0.97 (0.55, 1.72) 0.928	0.68 (0.37, 1.24) 0.203	0.72 (0.40, 1.32) 0.290	
Body mass index(kg/m2)					0.113
< 25	ref	0.81 (0.37, 1.81) 0.612	0.38 (0.16, 0.92) 0.031	1.04 (0.50, 2.14) 0.924	
25–30	ref	0.62 (0.35 1.08) 0.090	0.82 (0.47, 1.43) 0.485	0.70 (0.37, 1.30) 0.021	
≥ 30	ref	1.22 (0.82, 1.80) 0.326	0.63 (0.37, 1.08) 0.092	1.18 (0.67, 2.06) 0.564	
Race					0.524
Mexican American	ref	0.91 (0.39, 2.14) 0.695	0.37 (0.12, 1.19) 0.10	0.46 (0.13, 1.68) 0.239	
Other Hispanic	ref	1.83 (0.66, 5.12) 0.248	0.61 (0.11, 3.27) 0.561	0.54 (0.09, 3.13) 0.496	
Non-Hispanic White	ref	0.78 (0.50, 1.23) 0.283	0.80 (0.49, 1.30) 0.368	1.14 (0.69, 1.90) 0.607	
Non-Hispanic Black	ref	1.05 (0.50, 2.19) 0.895	0.84 (0.38, 1.84) 0.660	1.32 (0.63, 2.76) 0.461	
Other Race	ref	0.73 (0.34, 1.58) 0.428	0.35 (0.13, 0.91) 0.032	0.63 (0.24 1.69) 0.358	
Smoking status					0.689
No	ref	0.82 (0.52, 1.32) 0.413	0.61 (0.36, 1.05) 0.007	0.84 (0.49, 1.44) 0.533	
Yes	ref	1.03 (0.70, 1.51) 0.882	0.68 (0.43, 1.07) 0.098	1.12 (0.72, 1.75) 0.620	
Alcohol consumption					0.470
No	ref	1.03 (0.70, 1.51) 0.898	0.81 (0.53, 1.26) 0.356	1.15 (0.73, 1.79) 0.547	
Yes	ref	0.79 (0.50, 1.26) 0.324	0.45 (0.25, 0.80) 0.006	0.86 (0.50, 1.47) 0.579	

The data: OR (95% CI) *P* value

The analysis was based on Model III

Model III: gender, age, race, BMI, education level, Income to poverty ratio, alcohol, smoke, diabetes, hypertention, eGFR, HOMA-IR and release cycle were adjusted

of free fatty acid (FFA), which are re-esterified in the liver and released via VLDL, promoting fat accumulation, particularly in the abdominal region, contributing to obesity. HDL, by contrast, can contribute to helping maintain healthy lipid profiles and reducing excessive fat buildup. Obesity can enhance nucleic acid metabolism, increasing uric acid synthesis. Additionally, cytokines associated with obesity, including adiponectin and leptin, play a role in the onset of HUA [27, 28]. Elevated TG levels or diminished HDL can precipitate insulin resistance, thereby augmenting serum urate concentrations [29–31]. Insulin resistance also plays a particularly essential and multifaceted role in blood lipid profiles and gout. It can upregulate xanthine oxidoreductase production in fatty tissue and augment the excretion of serum urate by modulating metabolic processes, thereby contributing to the pathogenesis of HUA [32]. It also activates the renin-angiotensin-aldosterone system,

Table 4 Analysis of the potential mediators of the associations of TG and HDL with gout

	Mediation effect (95% CI), *P* value			
	Total effect	**Indirect effect**	**Direct effect**	**Mediation**
TG				
BMI	0.009 (0.006, 0.012) $P<0.001$	0.002 (0.001, 0.003) $P<0.001$	0.008 (0.004, 0.011) $P<0.001$	20.42%
WHtR	0.010 (0.006, 0.013) $P<0.001$	0.003 (0.002, 0.003) $P<0.001$	0.007 (0.004, 0.010) $P<0.001$	26.09%
HOMA-IR	0.009 (0.006, 0.012) $P<0.001$	0.0005 (0.0001, 0.0010) $P=0.022$	0.008 (0.005, 0.011) $P<0.001$	5.39%
HDL				
BMI	-0.007 (-0.011, -0.002) $P=0.006$	-0.0038(-0.005, -0.003) $P<0.001$	-0.003 (-0.007, 0.002) $P=0.216$	57.81%
WHtR	-0.007 (-0.011, -0.002) $P=0.004$	-0.0046(-0.006, -0.003) $P<0.001$	-0.002 (-0.007, 0.002) $P=0.368$	68.80%
Leukocytes	-0.006 (-0.011, -0.002) $P=0.008$	-0.0005(-0.00141, -0.00008) $P=0.020$	-0.006 (-0.011, -0.001) $P=0.016$	8.62%
Lymphocytes	-0.006 (-0.011, -0.002) $P=0.012$	-0.0003(-0.0009, 0.0001) $P=0.090$	-0.006 (-0.011, -0.002) $P=0.018$	5.08%
NLR	-0.006 (-0.011, -0.002) $P=0.006$	0.00002(-0.00003, 0.00010) $P=0.562$	-0.006 (-0.011, -0.002) $P=0.006$	-0.27%
SII	-0.006 (-0.011, -0.002) $P=0.006$	-0.000005(-0.00009, 0.00010) $P=0.842$	-0.006 (-0.011, -0.002) $P=0.006$	0.08%
HOMA-IR	-0.007 (-0.012, -0.002) $P=0.006$	-0.0006(-0.0014, -0.0002) $P=0.006$	-0.006 (-0.011, -0.002) $P=0.006$	9.12%
GGT overall	-0.007 (-0.011, -0.002) $P=0.006$	0.0005(0.0002, 0.0008) $P<0.001$	-0.007 (-0.012, -0.003) $P=0.004$	-7.08%
HDL < 56 mmol/L	-0.009 (-0.014, -0.002) $P=0.014$	-0.0005(-0.0010, -0.0001) $P=0.012$	-0.008 (-0.015, -0.002) $P=0.022$	5.35%
HDL ≥ 56 mmol/L	-0.001 (-0.006, 0.003) $P=0.510$	0.0007(0.0003, 0.0012) $P=0.006$	-0.002 (-0.007, 0.002) $P=0.324$	-53.50%

The analysis was based on the Model II

Model II: gender, age, race, education level, Income to poverty ratio, alcohol, smoke, diabetes, hypertension, eGFR and release cycle were adjusted;

BMI: Body mass index, WHtR: waist-to-height ratio, HOMA-IR: Homeostatic model assessment for insulin resistance, GGT: γ-glutamyltransferase, NLR: neutrophil to lymphocyte ratio, SII: The systemic immune inflammation index

exacerbating renal dysfunction and impairing uric acid regulation [33]. Regarding distinct TG and HDL mechanisms, FFA, the lipolysis products of TG, can contribute to acute gouty arthritis by upregulating pro-IL-1β transcription, resulting in increased IL-1β in monosodium urate crystal-induced joint inflammation [34, 35]. HDL's inverse association with gout may be attributed to its role in inflammation reduction and oxidative stress mitigation. HDL downregulates pro-inflammatory cytokines and diminishes the levels of adhesion molecules such as vascular cell adhesion molecule 1, intercellular adhesion molecule 1, and E-selectin, thereby inhibiting leukocyte activation and endothelial adhesion. HDL also contains antioxidant enzymes, including paraoxonase-1 and glutathione peroxidase, which protect against LDL oxidation and foam cell formation [36–39].

Based on current findings, this research represents the inaugural attempt to assess the association between CMI and gout. CMI is currently a clinical indicator that combines TG/HDL and WHtR. It reflected visceral adipose tissue distribution and individual blood lipid levels [40]. TG/HDL ratio was considered the predictor for insulin resistance assessment [41]. Prior studies have documented a correlation between the TG/HDL ratio and HUA [13, 42, 43]. WHtR is an efficient predictor of abdominal obesity. Research has demonstrated that obesity is significantly associated with a heightened gout risk among men [44]. Besides, Body measurement indices, including BMI, WC, and WHtR, are found to be highly associated with the likelihood of gout [45, 46]. Both ratios are closely related to serum uric acid content and gout. Besides, earlier investigations also identified an association between CMI and HUA [47, 48]. Given that CMI integrates TG/HDL and WHtR, it may serve as a novel predictor for elucidating the association and mediators between blood lipid levels and gout.

Strengths and limitations

The study had some noteworthy advantages. First, the study extended the associations to a more extensive and diverse American sample group, broadening the applicability of the results and strengthening the evidence linking lipid profiles with gout and HUA. Moreover, the study further explores the potential mediators and proportions between blood lipid biomarkers and gout, which helped to gain a deeper insight into the intricate associations between lipid files and gout. Based on these analyses, CMI, which serves as an indicator of metabolic dysregulation and its application in predicting gout risk, offered a crucial foundation for health promotion and gout prevention strategies.

The study also had several limitations. First of all, as a cross-sectional study, it was not capable of determining causal associations between HDL, TG, CMI, and gout. Second, Specific data were gathered through self-reported questionnaires by participants. This bias could potentially distort the accuracy of the data collected and impact the reliability of our findings. The potential for recall bias must be acknowledged in this study. Third, the study could not incorporate data on all covariates influencing gout and lipid biomarkers to maintain an adequately sized sample due to database constraints. Thus, PSM was utilized to address confounding factors in the analysis. The results are consistent, thereby

Table 5 Associations between lipid profiles and hyperuricemia, gout using propensity score weighted regression

Exposure	Model I	Model II	Model III
Gout			
HDL			
Continuous	0.9909 (0.9814, 1.0004) 0.0610	0.9835 (0.9741, 0.9929) < 0.001	0.9883 (0.9786, 0.9982) 0.0206
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	0.96 (0.66, 1.42) 0.854	0.89 (0.60, 1.31) 0.546	0.91 (0.62, 1.35) 0.646
Q3	0.53 (0.35, 0.80) 0.002	0.43 (0.29, 0.66) < 0.001	0.49 (0.32, 0.75) < 0.001
Q4	0.83 (0.54, 1.27) 0.391	0.61 (0.40, 0.93) 0.022	0.75 (0.48, 1.17) 0.205
TG			
Continuous	1.0045 (1.0025, 1.0065) < 0.001	1.0054 (1.0033, 1.0075) < 0.001	1.0048 (1.0027, 1.0070) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.14 (0.73, 1.79) 0.563	1.29 (0.82, 2.02) 0.276	1.20 (0.76, 1.90) 0.434
Q3	1.42 (0.90, 2.22) 0.128	1.69 (1.07, 2.65) 0.024	1.50 (0.94, 2.38) 0.086
Q4	2.32 (1.47, 3.64) < 0.001	2.98 (1.88, 4.72) < 0.001	2.55 (1.59, 4.09) < 0.001
LDL			
Continuous	1.0015 (0.9977, 1.0053) 0.453	1.0018 (0.9979, 1.0056) 0.373	1.0009 (0.9969, 1.0048) 0.671
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.52 (0.99, 2.31) 0.052	1.61 (1.05, 2.46) 0.028	1.53 (0.99, 2.36) 0.051
Q3	1.35 (0.88, 2.06) 0.170	1.42 (0.93, 2.18) 0.107	1.28 (0.83, 1.98) 0.266
Q4	1.28 (0.84, 1.94) 0.251	1.36 (0.89, 2.08) 0.154	1.21 (0.79, 1.86) 0.382
TC			
Continuous	1.0025 (0.9992, 1.0059) 0.142	1.0021 (0.9987, 1.0055) 0.228	1.0018 (0.9983, 1.0052) 0.314
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.38 (0.91, 2.11) 0.131	1.39 (0.91, 2.14) 0.128	1.34 (0.87, 2.06) 0.185
Q3	1.52 (1.01, 2.29) 0.047	1.52 (1.00, 2.32) 0.049	1.40 (0.92, 2.15) 0.120
Q4	1.45 (0.96, 2.17) 0.078	1.43 (0.94, 2.17) 0.090	1.34 (0.88, 2.05) 0.168
CMI			
Continuous	1.19 (1.08, 1.32) < 0.001	1.28 (1.16, 1.42) < 0.001	1.22 (1.09, 1.36) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.36 (0.85, 2.19) 0.201	1.56 (0.97, 2.51) 0.064	1.42 (0,87, 2.30) 0.161
Q3	1.96 (1.21, 3.19) 0.007	2.58 (1.61, 4.13) < 0.001	2.19 (1.32, 3.61) 0.002
Q4	2.76 (1.65, 4.60) < 0.001	3.89 (2.38, 6.36) < 0.001	3.15 (1.84, 5.40) < 0.001
Hyperuricemia			
HDL			
Continuous	0.9918 (0.9873, 0.9964) 0.0005	0.99 (0.98, 0.99) < 0.001	0.9927 (0.9880, 0.9974) 0.002
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	0.87 (0.74, 1.03) 0.109	0.84 (0.71, 1.00) 0.051	0.90 (0.76, 1.07) 0.221
Q3	0.75 (0.63, 0.89) < 0.001	0.67 (0.67, 0.80) < 0.001	0.77 (0.64, 0.92) 0.003
Q4	0.61 (0.50, 0.74) < 0.001	0.49 (0.41, 0.59) < 0.001	0.63 (0.52, 0.77) < 0.001
TG			
Continuous	1.0051 (1.0041, 1.0060) < 0.001	1.0065 (1.0058, 1.0073) < 0.001	1.0053 (1.0045, 1.0061) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.71 (1.42, 2.06) < 0.001	1.79 (1.49, 2.16) < 0.001	1.70 (1.41, 2.05) < 0.001
Q3	2.00 (1.66, 2.41) < 0.001	2.20 (1.83, 2.66) < 0.001	2.00 (1.66, 2.42) < 0.001
Q4	2.89 (2.40, 3.48) < 0.001	3.32 (2.75, 4.01) < 0.001	2.90 (2.39, 3.52) < 0.001
LDL			
Continuous	1.0036 (1.0019, 1.0053) < 0.001	1.0041 (1.0024, 1.0058) < 0.001	1.0035 (1.0017, 1.0052) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.12 (0.94, 1.33) 0.217	1.15 (0.97, 1.38) 0.108	1.11 (0.93, 1.32) 0.260
Q3	1.25 (1.05, 1.49) 0.013	1.35 (1.13, 1.61) < 0.001	1.23 (1.03, 1.47) 0.025
Q4	1.44 (1.21, 1.72) < 0.001	1.53 (1.28, 1.82) < 0.001	1.42 (1.19, 1.69) < 0.001
TC			
Continuous	1.0047 (1.0032, 1.0062) < 0.001	1.0046 (1.0031, 1.0061) < 0.001	1.0046 (1.0031, 1.0062) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)

Table 5 (continued)

Exposure	Model I	Model II	Model III
Q2	1.23 (1.03, 1.47) 0.021	1.25 (1.04, 1.49) 0.015	1.22 (1.023, 1.46) 0.031
Q3	1.34 (1.12, 1.60) 0.001	1.40 (1.17, 1.67) < 0.001	1.34 (1.12, 1.60) < 0.001
Q4	1.76 (1.47, 2.10) < 0.001	1.76 (1.47, 2.10) < 0.001	1.73 (1.45, 2.07) < 0.001
CMI			
Continuous	1.22 (1.17, 1.29) < 0.001	1.31 (1.25, 1.38) < 0.001	1.23 (1.17, 1.30) < 0.001
Q1	Reference (1.00)	Reference (1.00)	Reference (1.00)
Q2	1.48 (1.22, 1.78) < 0.001	1.63 (1.35, 1.96) < 0.001	1.45 (1.20, 1.76) < 0.001
Q3	1.83 (1.51, 2.22) < 0.001	2.21 (1.83, 2.66) < 0.001	1.86 (1.53, 2.26) < 0.001
Q4	2.69 (2.21, 3.28) < 0.001	3.41 (2.82, 4.12) < 0.001	2.70 (2.20, 3.32) < 0.001

The data: OR (95%CI) *P* value

Model I: gender, age, race, BMI were adjusted

Model II: gender, age, race, education level, Income to poverty ratio, alcohol, smoke, diabetes, hypertension, eGFR and release cycle were adjusted;

Model III: gender, age, race, BMI, education level, Income to poverty ratio, alcohol, smoke, diabetes, hypertention, eGFR, HOMA-IR and release cycle were adjusted

OR: Odds ratio, *BMI*: Body mass index, *eGFR*: Estimated glomerular filtration, *HOMA-IR*: Homeostatic model assessment for insulin resistance

Given that some of our results did not clearly indicate a relationship, we have retained four decimal places for precision

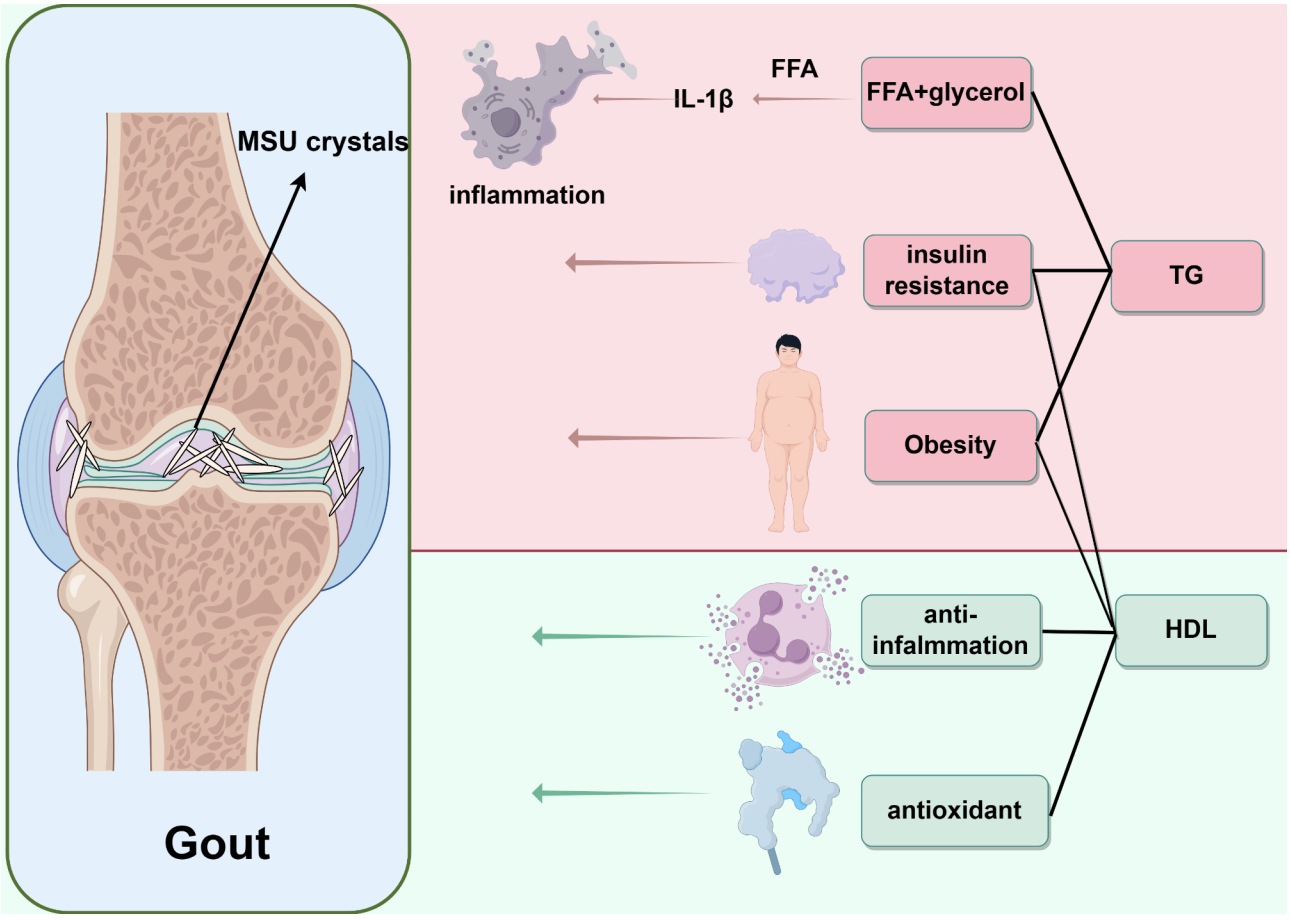

Fig. 2 Potential mechanisms of TG and HDL leading to gout. TG broke down into free fatty acids and glycerol. Free fatty acids contribute to the disease mechanism by influencing the transcription of pro-IL-1β. This process may result in the substantial production of bioactive IL-1β molecules, particularly in the context of joint inflammation induced by monosodium urate crystals. TG can contribute to the development of gout by promoting obesity and insulin resistance. In terms of HDL, it may reduce the risk of gout by mitigating obesity and decreasing insulin resistance. Meanwhile, HDL acted as roles in anti-inflammatory and antioxidant functions which reduce the risk of gout. MSU: monosodium urate

substantiating the reliability of the conclusions drawn. Nevertheless, the current associations between lipid biomarkers, CMI, and gout remain robust enough to address the impact of unaccounted variables.

Conclusion

To summarize, the study illustrated significant associations between HDL, TG, and gout, independent of key confounding factors. Besides, it was witnessed that BMI, WHtR, and HOMA-IR mediated the association between TG and gout. While BMI, WHtR, leukocytes, GGT, and HOMA-IR mediated between HDL and gout. CMI was strongly associated with gout, which provided an understanding of the associations between lipid biomarkers and gout and uric acid metabolism. Closely monitoring TG and HDL levels and proactively addressing obesity, insulin resistance, oxidative stress and inflammation are crucial for lowering the risk of gout. Nonetheless, further extensive prospective studies are essential to corroborate these findings.

Abbreviations

HUA	Hyperuricaemia
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
TC	Total cholesterol
TG	Triglyceride
WHtR	Waist-to-height ratio
WC	Waist circumference
CMI	Cardiometabolic index
BMI	Body mass index
NHANES	National Health and Nutrition Examination Survey
PSM	Propensity score matching
eGFR	Glomerular filtration rate
PIR	Household poverty-to-income ratio
HOMA-IR	Homeostatic model assessment for insulin resistance
GGT	γ-glutamyltransferase
NLR	Neutrophil lymphocyte ratio
SII	The systemic immune inflammation index
NCHS	National Center for Health Statistics

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02346-z.

Supplementary Material 1

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Author contributions

JH was responsible for the design of this study and performed the experiments. YH analyzed/interpreted the results and wrote the manuscript. YL, ZW and YL revised the English writing. All authors participated in the review of the manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. The detailed information on the data is available at https://wwwn.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate

The research involving human subjects underwent evaluation and approval by the NCHS Ethics Review Board. Written consent to participate in this study was furnished by the legal guardian/next of kin of the participants. Additionally, written consent was obtained from the individual(s) for the publication of any potentially identifiable images or data contained within this article.

Consent for publication

Not Applicable.

Conflict of interest

The authors assert that the research was conducted without any affiliations or financial arrangements that could potentially give rise to a conflict of interest.

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