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ORIGINAL RESEARCH

Nonlinear Association Between the Liver Fat Content and the Risk of Hyperuricemia in Prediabetic Individuals: Evidence from Cross-Sectional Health Screening Data in China

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Purpose: The impact of hepatic lipid accumulation on hyperuricemia presents an intriguing research avenue, particularly in light of existing studies linking obesity with hyperuricemia. Nevertheless, there remains a scarcity of quantitative investigations into the correlation between liver fat content (LFC) and hyperuricemia among prediabetic cohorts, notably within the Chinese demographic.

Patients and Methods: This cross-sectional study was conducted at the Health Management Center of Henan Provincial People's Hospital between January 2019 and December 2023, involving 2,950 pre-diabetic participants. Participants were categorized into groups based on diagnostic criteria for hyperuricemia. LFC was assessed using computed tomography. Statistical analyses included multivariate logistic regression, limited cubic spline regression models, and subgroup analyses to explore the association between LFC and hyperuricemia among individuals with pre-diabetes.

Results: The prevalence of hyperuricemia among the 2,950 prediabetic individuals was observed to be 22.20%. Prediabetic individuals with hyperuricemia exhibited higher levels of LFC compared to those without hyperuricemia. This association persisted even after adjusting for other variables, indicating a heightened risk of hyperuricemia among prediabetic individuals with elevated LFC [Q4 vs Q1: odds ratio (OR 2.70), 95% confidence interval (CI) 1.93–3.79, $P < 0.001$; $P_{\text{for trend}} < 0.001$]. Importantly, a nonlinear relationship between LFC and hyperuricemia risk was identified in the prediabetic individuals, showing a significant increase in hyperuricemia risk when LFC exceeded 8.4% (OR per standard deviation = 1.05, 95% CI: 1.02–1.08, $P < 0.001$).

Conclusion: In individuals with prediabetes, a higher LFC is associated with an elevated risk of hyperuricemia, especially when LFC exceeds 8.4%.

Keywords: hyperuricemia, LFC, prediabetes, Chinese adults

Introduction

Uric acid, as the end product of human purine metabolism, exhibits antioxidant properties determined by its chemical microenvironment, which may confer protective effects. However, it can also act as a pro-oxidant and is associated with the occurrence of various diseases.[1] The body typically maintains a dynamic equilibrium between uric acid production and excretion. However, dietary shifts, particularly the widespread adoption of high-purine diets, lead to a notable surge in uric acid production, consequently elevating serum uric acid levels.[2] Global epidemiological data indicate a rising

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prevalence of hyperuricemia, particularly among middle-aged and elderly populations. In a recent survey of Chinese adults, the prevalence of hyperuricemia escalated to 14.0% from 11.1% between 2015–2016 and 2018–2019, respectively.[3] A United States-based study focusing on kidney disease and gout revealed a higher prevalence of hyperuricemia among men compared to women.[4] This disparity was closely linked with factors such as obesity and metabolic syndrome (MetS). Notably, Han et al[5] has underscored insulin resistance (IR) as a key pathological mechanism in hyperuricemia, potentially escalating the risk of hyperuricemia by fostering inflammation, oxidative stress, and exacerbating IR. A comprehensive systematic review and meta-analysis investigating the correlation between hyperuricemia and diabetes mellitus indicated a notably higher prevalence of hyperuricemia in individuals with prediabetes compared to those with normal glucose levels.[6] This indicates that hyperuricemia may function as a pertinent biomarker in identifying prediabetic states. Hence, early detection and management of hyperuricemia could hold substantial importance in averting prediabetes and impeding its progression to type 2 diabetes mellitus (T2DM).

The pathophysiological progression of liver fat content (LFC) is intricately linked to a spectrum of metabolic disorders. Elevated LFC levels compromise liver function, precipitating the onset of fatty liver, liver fibrosis, and potentially cirrhosis.[7] Research indicates a significant correlation between increased LFC and the onset and progression of diverse conditions such as MetS, T2DM, and cardiovascular disease (CVD).[8] Among middle-aged and elderly cohorts, heightened LFC levels have been closely tied to the emergence of hyperuricemia and its associated maladies.[9] In a Chinese study, Huang et al[10] also observed that 23.5% of non-alcoholic fatty liver disease (NAFLD) patients concurrently exhibited hyperuricemia, with markedly elevated serum uric acid levels compared to non-NAFLD counterparts. Furthermore, Gesteiro et al[11] also demonstrated a robust link between augmented visceral fat, liver fat accumulation, and the development of hyperuricemia, showcasing distinct risk profiles across genders and age brackets. Nonetheless, the dose-response relationship between LFC and the risk of hyperuricemia remains inadequately explored, and given the reciprocal influences of hyperuricemia and prediabetes, the existing research landscape on LFC and hyperuricemia within prediabetic individuals appears insufficient.

In this study, computer tomography (CT) scans were used to quantify hepatic fat content, with the primary aim of investigating the correlation between LFC and hyperuricemia in prediabetic patients. This research aims to provide targeted guidance for the prevention and treatment of hyperuricemia and to reveal the potential pathophysiological pathways underlying the coexistence of prediabetes and hyperuricemia.

Materials and Methods

Participants and Criteria for Inclusion

Ethical approval for this study was granted by the Ethics Committee of Henan Provincial People's Hospital (Approval No. 115, 2022). All participants provided informed consent after receiving detailed information regarding the study's objectives and procedures.

Data for this study were collected from individual health records of participants who underwent comprehensive physical assessments at the Health Management Center of Henan Provincial People's Hospital from 2019 to 2023. The criteria for participant inclusion were defined as follows: (1) individuals aged 20 to 80 years diagnosed with prediabetes; (2) individuals who underwent a complete hematological examination and provided questionnaire data; (3) individuals who underwent LFC assessment. Exclusion criteria comprised: (1) any history of cancer; (2) current or past history of diabetes or use of hypoglycemic agents; (3) history of hepatic resection, hepatic space-occupying lesions (excluding benign small cysts and small liver calcifications), cirrhosis, or alcoholic fatty liver disease; and (4) current or past history of other metabolic disease such as primary hyperaldosteronism, pheochromocytoma, or thyroid dysfunction. Baseline data, including age, gender, nationality, medical history, and medication history, were collected by trained personnel. Details of the participant selection process are depicted in Figure 1.

Laboratory Tests

To ensure data accuracy and reliability, all investigators underwent standardized training in survey methodology prior to study initiation. Comprehensive participant data were obtained through a detailed questionnaire, and measurements of

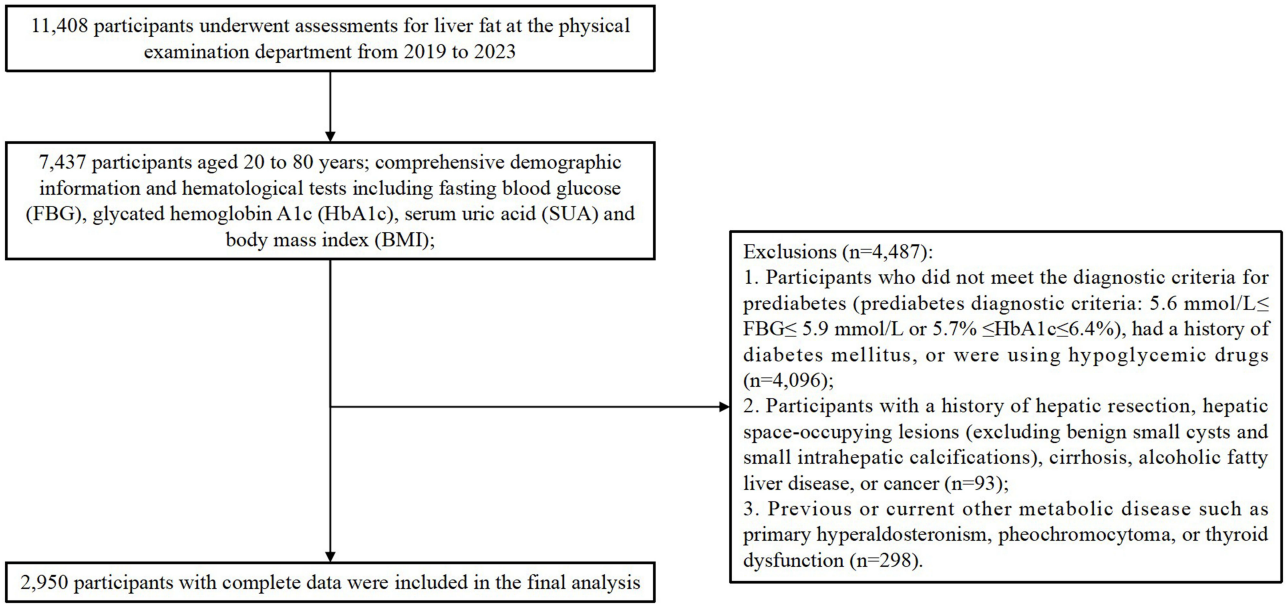

Figure 1 Flowchart of participants selection.

height, weight, blood pressure, and other relevant indicators were documented. To minimize potential errors, each measurement was conducted twice, and the mean of the two readings was adopted as the final value.

Fasting blood samples were obtained from participants at 8 a.m., and various laboratory parameters were assessed, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), hemoglobin (Hb), total protein (TP), total bilirubin (TB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), serum uric acid (SUA), serum creatinine, fasting blood glucose (FBG) and glycated hemoglobin A1c (HbA1c). An Olympus® AU 5400 automated biochemistry analyzer was used for lipid and blood glucose evaluations, while standard laboratory methods were employed for the analysis of the remaining variables.

LFC Measurements

Utilizing a Lightspeed VCT 64-row CT scanner (General Electric), the study adhered to the standard low-dose chest CT scan protocol, with the tube voltage set to 120 kV and tube current at 100 mA. The scanning parameters included a defined scanning field of 500 mm×500 mm, with a slice thickness of 5 mm and a pitch of 0.984. Quantitative computed tomography (QCT) of liver fat was performed using the Measure Liver Fat module scanning analysis software, a specialized tissue measurement application. During this process, three circular regions of interest (ROIs) were positioned in the anterior and posterior segments of the left and right lobes, each with a cross-sectional area of 290–310 mm². The ROIs were positioned in the subcapsular area of the liver, avoiding bile ducts and blood vessels. If the left lobe of the liver was too small to be visualized on the section, the slice with the largest visible area of the left lobe was utilized for measurement. The final liver fat percentage was determined as the mean of three measurements. All analyses using the QCT software were conducted by specially trained radiologists. Importantly, a previous publication confirmed the suitability of this technique for individuals of Chinese descent.[12]

Definition

The body mass index (BMI) was determined by dividing the individual's weight by their height squared (kg/m²). Hypertension was characterized by a prior diagnosis of the condition or the current use of antihypertensive medications, or two consecutive daily blood pressure readings indicating elevated levels. Diagnosis of prediabetes is based on FBG and HbA1c levels: FPG levels ranging from 5.6 to 6.9 mmol/L or HbA1c levels ranging from 5.7% to 6.4%.

Hyperuricemia is defined as SUA ≥ 420 μmol/L in males and ≥ 360 μmol/L in females, or a history of previous and current uric acid-lowering medications.[13]

Variables

In this study, LFC was considered the independent variable, with hyperuricemia serving as the dependent variable. The collected covariates encompassed: (1) demographic data such as age, sex, and ethnicity; (2) physical examination parameters including BMI, systolic and diastolic blood pressure; (3) medical history including diabetes, cancer, and other clinical conditions; and (4) Laboratory indicators such as TC, TG, LDL-C, HDL-C, Hb, TP, TB, AST, ALT, GGT, ALP, SUA, and serum creatinine. Notably, BMI categories were defined based on specific thresholds: individuals with a BMI of 24 kg/m² were classified as overweight, while those with a BMI of 28 kg/m² or higher were categorized as obese.

Statistical Analysis

Statistical analysis was performed using EmpowerStats (X&Y Solutions, Inc., Boston, MA, USA) and R software (version 4.2.0). The data underwent normality assessment. Continuous variables were expressed as mean ± standard deviation if normally distributed, or as medians if non-normally distributed. Categorical variables were described using appropriate scales. Statistical significance across groups was determined using Chi-square tests and ANOVA. Initially, a univariate logistic regression model assessed each variable's impact on hyperuricemia risk, calculating odds ratios (ORs) with corresponding 95% confidence intervals (CIs). To mitigate potential confounding factors, a stepwise regression multivariate logistic analysis explored the relationship between LFC and hyperuricemia among individuals with prediabetes. The initial model (Crude model) did not include covariate adjustments. Model 1 adjusted for age, sex, ethnicity, and BMI, while Model 2 encompassed all covariates. Furthermore, LFC was categorized into quartiles with the lowest quartile as reference to evaluate its association with hyperuricemia. A restricted cubic spline analysis investigated potential nonlinear associations between LFC and hyperuricemia risk. Lastly, stratified analysis and cross-validation were conducted according to Model II to elucidate additional factors influencing LFC and hyperuricemia development.

Results

Prediabetic Individuals Baseline Characteristics

The study recruited 2,950 prediabetic individuals, including 1,107 women and 1,843 men, from the Health Management Center of Henan Provincial People's Hospital. The prevalence of hyperuricemia was 22.20% in the prediabetic individuals studied. Figure 2 illustrates that the LFC was significantly higher in the hyperuricemia group compared to the non-hyperuricemia group ($P < 0.001$). Table 1 provides an overview of baseline characteristics in individuals with prediabetes, classified by hyperuricemia diagnosis. The hyperuricemia group of prediabetic individuals is mainly composed of males, higher BMI and hypertension. In addition, the hyperuricemia group had higher indicators in a number of indicators, including TC, TG, LDL-C, Hb, TP, TB, AST, ALT, GGT, serum creatinine, and LFC. Notably, participants in the hyperuricemia group exhibited lower age, HDL-C levels compared to non-hyperuricemia individuals ($P < 0.001$).

Relationship Between LFC and Hyperuricemia in Prediabetic Individuals According to the Different Models

Table 2 presents findings from univariate logistic regression, revealing a notable link between LFC and hyperuricemia in individuals with prediabetes. The analysis yielded an OR of 1.11 (95% CI: 1.10–1.13, $P < 0.001$), signifying a significant association. Subsequent multiple logistic regression models further validated the independent correlation between LFC and hyperuricemia within this cohort. Both Model I (OR = 1.07, 95% CI: 1.05–1.09, $P < 0.001$) and Model II (OR = 1.06, 95% CI: 1.04–1.08, $P < 0.001$) emphasized the independent relationship between elevated LFC and heightened risk of hyperuricemia, even after adjusting for confounding factors. Stratification based on quartiles of increasing LFC levels demonstrated a stronger association with hyperuricemia in individuals within the highest quartile (Q4) compared to those in the lowest quartile (Q1). Specifically, individuals in Q4 exhibited a 2.70-fold increase in hyperuricemia risk for every 1%

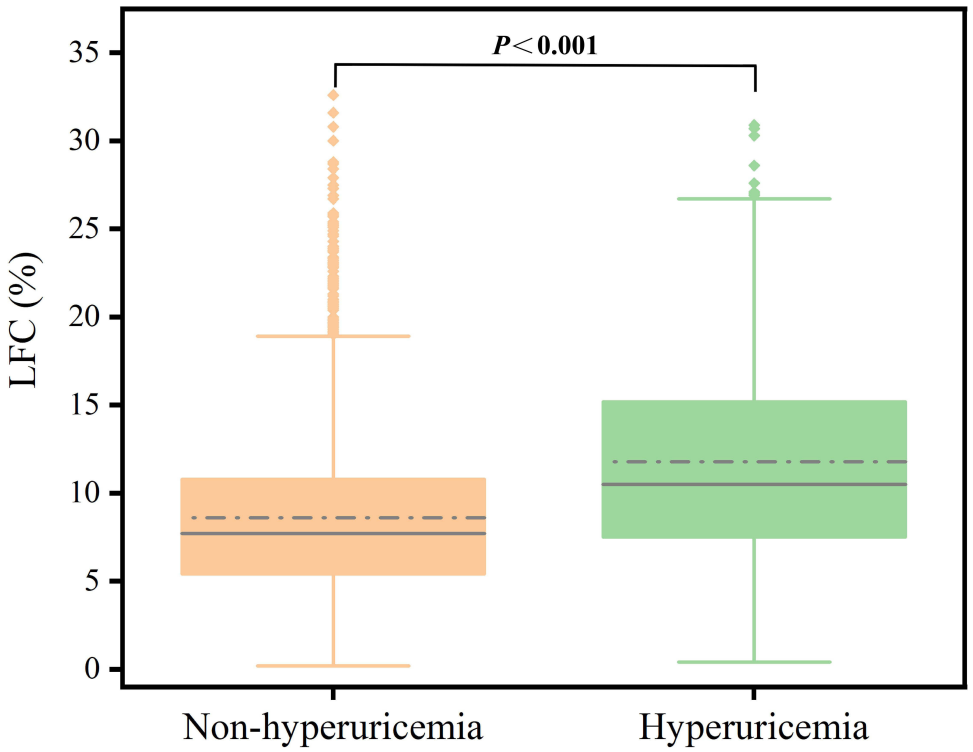

Figure 2 LFC in the non-hyperuricemia and hyperuricemia groups in the prediabetic population.
Notes: *P* <0.001, as compared with non-hyperuricemia group.

rise in LFC. The unadjusted model revealed an OR of 1.41 (95% CI: 1.01–1.96, $P < 0.05$, $P_{\text{for trend}} < 0.001$). In Model I, the OR was 1.78 (95% CI: 1.29–2.46, $P < 0.001$, $P_{\text{for trend}} < 0.001$), while Model II showed an OR of 2.70 (95% CI: 1.93–3.79, $P < 0.001$, $P_{\text{for trend}} < 0.001$). Table 3.

Table 1 Baseline Characteristics of Prediabetic Participants by Hyperuricemia Status

Variables	Overall	Non-Hyperuricemia	Hyperuricemia	*P* value
N	2,950	2,295	655	
Age (years)	52.73±10.37	53.47±10.04	50.15±11.05	<0.001
Gender [n (%)]				<0.001
Female	1,107 (37.53%)	977 (42.57%)	130 (19.85%)	
Male	1,843 (62.47%)	1,318 (57.43%)	525 (80.15%)	
Nationality [n (%)]				0.628
Non-Han nationality	31 (1.05%)	23 (1.00%)	8 (1.22%)	
Han nationality	2,919 (98.95%)	2,272 (99.00%)	647 (98.78%)	
BMI (kg/m^2)	25.43±3.15	25.07±3.07	26.70±3.10	<0.001
Hypertension [n (%)]				<0.001
No	918 (31.12%)	677 (29.50%)	241 (36.79%)	
Yes	2,032 (68.88%)	1,618 (70.50%)	414 (63.21%)	
TC (mmol/L)	5.07±0.97	5.03±0.95	5.20±1.03	<0.001
TG (mmol/L)	1.93±1.38	1.78±1.24	2.46±1.69	<0.001
LDL-C (mmol/L)	3.05±0.80	3.01±0.78	3.19±0.86	<0.001
HDL-C (mmol/L)	1.29±0.29	1.31±0.30	1.20±0.24	<0.001
Hb (g/L)	143.18±15.00	141.57±15.26	148.83±12.56	<0.001
TP (g/L)	71.51±4.12	71.26±4.12	72.40±4.00	<0.001

(*Continued*)

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Table 1 (Continued).

Variables	Overall	Non-Hyperuricemia	Hyperuricemia	*P* value
TB (g/L)	11.55±4.77	11.39±4.80	12.09±4.63	<0.001
AST (U/L)	21.00 (17.80–25.30)	20.70 (17.55–24.60)	22.30 (18.90–27.30)	<0.001
ALT (U/L)	20.90 (15.40–30.00)	20.00 (14.80–28.10)	25.20 (18.30–35.95)	<0.001
GGT (U/L)	24.70 (17.60–37.40)	22.60 (16.70–34.20)	32.00 (23.70–49.90)	<0.001
ALP (U/L)	71.49±19.96	71.67±20.36	70.83±18.49	0.338
Serum creatinine (μmol/L)	65.35±15.04	63.22±13.09	72.81±18.64	<0.001
LFC (%)	9.29±5.19	8.59±4.82	11.77±5.68	<0.001

Abbreviations: BMI, body mass index; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; Hb, hemoglobin; TP, total protein; TB, total bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, glutamyl transpeptidase; ALP, alkaline phosphatase.

Table 2 Univariate Logistic Analysis for Predicting Hyperuricemia in Prediabetic Populations

Variables	Statistics	OR (95% CI)	*P* value
Age (years)	52.73±10.37	0.97 (0.96, 0.98)	<0.001
Gender [n (%)]			<0.001
Female	1,107 (37.53%)	1.0	
Male	1,843 (62.47%)	2.99 (2.43, 3.69)	
Nationality [n (%)]			0.628
Non-Han nationality	31 (1.05%)	1.0	
Han nationality	2,919 (98.95%)	0.82 (0.36, 1.84)	
BMI (kg/m^2)	25.43±3.15	1.18 (1.15, 1.21)	<0.001
Hypertension [n (%)]			<0.001
No	2,032 (68.88%)	1.0	
Yes	918 (31.12%)	1.39 (1.16, 1.67)	
TC (mmol/L)	5.07±0.97	1.19 (1.09, 1.30)	<0.001
TG (mmol/L)	1.93±1.38	1.38 (1.30, 1.48)	<0.001
LDL-C (mmol/L)	3.05±0.80	1.31 (1.17, 1.46)	<0.001
HDL-C (mmol/L)	1.29±0.29	0.21 (0.15, 0.30)	<0.001
Hb (g/L)	143.18±15.00	1.04 (1.03, 1.04)	<0.001
TP (g/L)	71.51±4.12	1.07 (1.05, 1.09)	<0.001
TB (g/L)	11.55±4.77	1.03 (1.01, 1.05)	0.001
AST (U/L)	21.00 (17.80–25.30)	1.01 (1.01, 1.02)	<0.001
ALT (U/L)	20.90 (15.40–30.00)	1.02 (1.01, 1.02)	<0.001
GGT (U/L)	24.70 (17.60–37.40)	1.01 (1.01, 1.01)	<0.001
ALP (U/L)	71.49±19.96	1.00 (0.99, 1.00)	0.338
Serum creatinine (μmol/L)	65.35±15.04	1.05 (1.04, 1.06)	<0.001
LFC (%)	9.29±5.19	1.11 (1.10, 1.13)	<0.001

Abbreviations: BMI, body mass index; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; Hb, hemoglobin; TP, total protein; TB, total bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, glutamyl transpeptidase; ALP, alkaline phosphatase; OR, Odds ratio; CI, Confidence interval.

A Nonlinear Relationship Between LFC and Hyperuricemia in Prediabetic Individuals

Figure 3 illustrates a nonlinear relationship between LFC and hyperuricemia risk in prediabetic individuals even after adjusting for confounders (*P* for nonlinear = 0.017). Segmentation analysis revealed an OR per standard deviation (SD) of 1.07 (95% CI: 0.98–1.18, $P = 0.149$) for individuals with LFC below 8.4%. Importantly, the risk of hyperuricemia significantly increased when LFC exceeded 8.4% (OR per SD = 1.05, 95% CI: 1.02–1.08, $P < 0.001$).

Table 3 Relationship Between LFC and Hyperuricemia in Prediabetic Populations in Different Models

	Crude Model		Model I		Model II	
	OR (95% CI)	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
LFC	1.12 (1.10, 1.13)	<0.001	1.07 (1.05, 1.09)	<0.001	1.06 (1.04, 1.08)	<0.001
Q1	Reference		Reference		Reference	
Q2	1.65 (1.21, 2.25)	0.002	1.45 (1.06, 2.00)	0.022	1.41 (1.01, 1.96)	0.042
Q3	2.74 (2.04, 3.68)	<0.001	1.95 (1.43, 2.67)	<0.001	1.78 (1.29, 2.46)	<0.001
Q4	5.57 (4.19, 7.39)	<0.001	3.27 (2.39, 4.48)	<0.001	2.70 (1.93, 3.79)	<0.001
P for trend		<0.001		<0.001		<0.001

Notes: Crude model: no covariates were adjusted. Model I: Age, gender, nationality and BMI were adjusted. Model II: Age, gender, nationality, BMI, hypertension, TC, TG, LDL-C, HDL-C, TP, TB, AST, ALT, GGT, ALP and serum creatinine were adjusted.

Abbrviations: OR, Odds ratio; CI, confidence interval.

Subgroup Analysis

The consistency of the association between LFC and hyperuricemia in the prediabetic individuals was demonstrated in subgroup analyses, as shown in Figure 4 and Supplementary Figure 1. When stratified by Age, gender, nationality, BMI, hypertension, TC, TG, LDL-C, HDL-C, TP, TB, AST, ALT, GGT, ALP and serum creatinine, the interaction was not significant ($P_{\text{for interaction}} > 0.05$). These findings confirm the robust association of LFC with hyperuricemia in the prediabetic individuals.

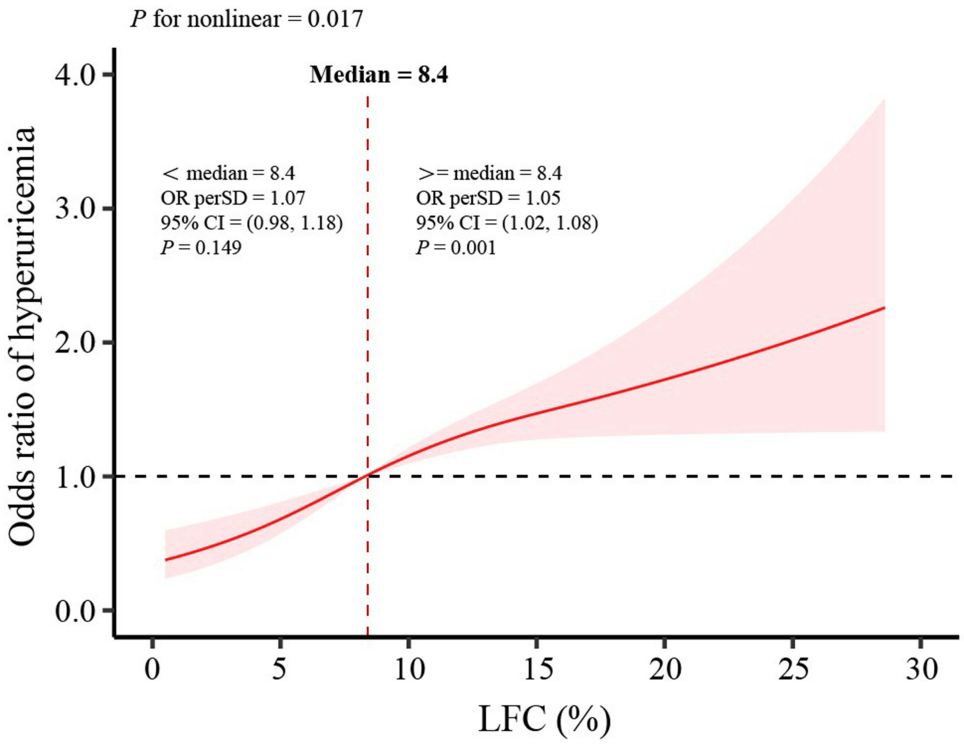

Figure 3 Odds ratio of hyperuricemia according to LFC in the prediabetic population. A nonlinear association was found (*P* for nonlinearity = 0.017) between LFC and risk of hyperuricemia in a restricted cubic spline regression model.

Notes: The solid line and shadow represented the odds ratio of hyperuricemia and 95% CI, respectively. Dashed vertical line indicated the threshold (LFC = 8.4%) with the lowest risk of hyperuricemia. All covariates were adjusted in this model.

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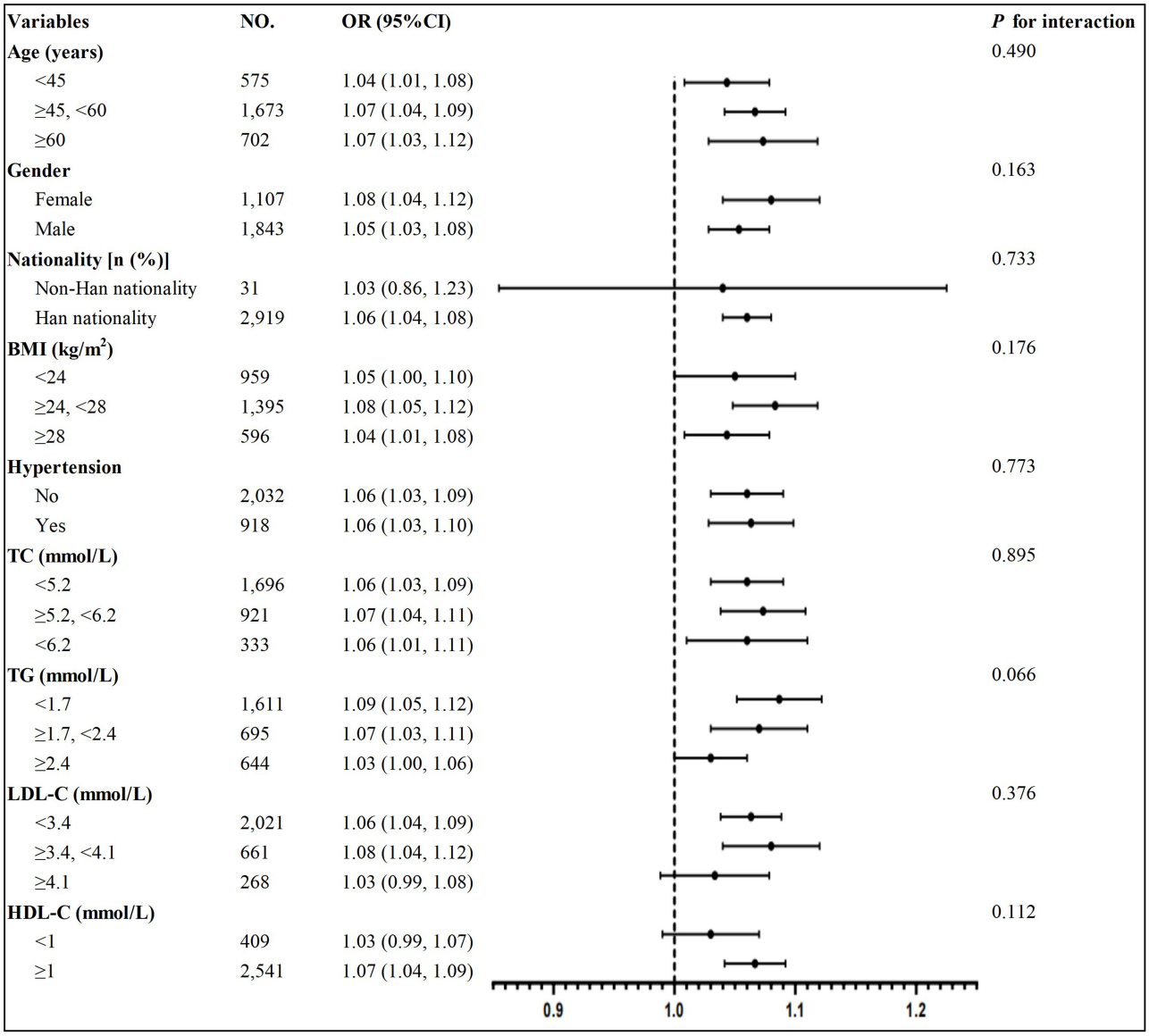

Figure 4 The relationship between LFC and hyperuricemia in different subgroups of prediabetic populations.
Abbreviations: BMI, body mass index; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Discussion

Prediabetes refers to a metabolic condition characterized by elevated blood glucose levels that do not meet the diagnostic criteria for diabetes mellitus. Its pathophysiology involves a complex interplay between IR and inadequate insulin secretion. IR, commonly linked to factors such as obesity, particularly abdominal adiposity, chronic inflammation, and MetS, contributes to aberrant glucose metabolism, leading to hyperglycemia.[14] While patients in this stage may be asymptomatic, their underlying metabolic dysregulation poses a potential risk to cardiovascular health. Hsu et al[15] indicates that prediabetes serves not only as a precursor to diabetes but also as a significant predictor for various chronic conditions, including CVD and renal diseases. Furthermore, individuals with prediabetes often exhibit impaired insulin secretion. Although the pancreas initially compensates for this deficiency by increasing insulin production, this compensatory mechanism eventually falters, resulting in further glucose elevation.[16] Research has demonstrated a robust association between hyperuricemia and prediabetes, where increased serum uric acid levels are linked with MetS, obesity, and IR. Krishnan et al[17] have observed heightened uric acid levels in prediabetic individuals, possibly due to decreased

renal excretion caused by IR, leading to uric acid accumulation. Moreover, uric acid is recognized as a pro-inflammatory agent that may exacerbate IR by inciting an inflammatory cascade, creating a detrimental feedback loop.[18,19] Notably, elevated uric acid levels not only contribute to the onset of prediabetes but also serve as a significant risk factor for progressing to T2DM.[20,21] Therefore, managing uric acid levels could represent a crucial preventive measure against prediabetes progression, particularly in high-risk cohorts. Early interventions aimed at controlling uric acid levels may enhance insulin sensitivity and mitigate the incidence of diabetes. This study examined individuals with hyperuricemia within the prediabetic cohort, offering novel perspectives for subsequent investigations in the field.

Hyperuricemia, a prevalent metabolic disorder, has exhibited a notable global upsurge in recent years. Increasing evidence points to intricate interplays among dietary patterns, obesity, and various metabolic indicators with hyperuricemia, underscoring the necessity for deeper investigations into the underlying mechanisms and intervention strategies.[22,23] The research cohort comprised 2,950 subjects from the Health Management Center at Henan Provincial People's Hospital, with LFC was quantified using computed tomography. Notably, the study revealed a significantly elevated LFC in prediabetic individuals with hyperuricemia compared to those without. Following adjustment for potential confounders, a substantial correlation between LFC and hyperuricemia risk in the prediabetic individuals was established. Furthermore, a positive correlation between LFC and hyperuricemia was evident across all subgroups. Noteworthy findings from restricted cubic spline analysis unveiled a nonlinear relationship between LFC and hyperuricemia in the prediabetic cohort, indicating a markedly heightened hyperuricemia risk when LFC exceeded 8.4% (P for nonlinearity = 0.017). By delving into the inflection point of this nonlinear curve, the study sheds light on the pathophysiological pathways linking prediabetes and hyperuricemia, offering valuable insights for primary care physicians to proactively identify hyperuricemia risk in individuals with prediabetes.

The aberrant buildup of liver fat not only correlates significantly with the onset of MetS, T2DM, and CVD but also poses grave risks such as hepatic cirrhosis, failure, and hepatocellular carcinoma.[24] Research indicates a close association between heightened liver fat and pathophysiological processes like IR, inflammatory cascades, and lipid metabolism irregularities, collectively fostering the progression of hepatic steatosis and its associated complications.[25,26] Hence, the surveillance and assessment of liver fat hold paramount importance in the prompt detection and management of these maladies. This investigation employs QCT technology to directly appraise liver fat in individuals with prediabetes, aiming to elucidate its impact on hyperuricemia. Given its pragmatic nature, tolerability, efficiency, and cost-effectiveness in gauging liver fat, QCT emerges as a viable tool for large-scale populace screening and comprehensive evaluation of liver fat accumulation.

In recent years, the correlation between hepatic lipid accumulation and hyperuricemia has garnered significant attention. Research has indicated a close association between liver fat deposition and the onset of hyperuricemia. Hyperuricemia is recognized as a pivotal element of MetS, with metabolic fatty liver disease representing a prevalent manifestation of this syndrome. Investigations have unveiled a positive correlation between elevated LFC and increased serum uric acid levels, implying a potential pivotal role of liver fat in the pathogenesis of hyperuricemia.[27,28] Specifically, the buildup of hepatic fat may impact uric acid metabolism through diverse mechanisms, such as enhancing uric acid synthesis within the liver and diminishing its excretion. Moreover, heightened hepatic fat levels could exacerbate hyperuricemia by fostering IR and inflammation.[29] Significantly, earlier animal studies have identified a rate-limiting enzyme in the liver, xanthine oxidase (XO), which catalyzes the conversion of hypoxanthine to xanthine, a precursor of uric acid. This enzymatic pathway potentially elucidates the interplay linking NAFLD with hyperuricemia, presenting XO as a promising therapeutic target for managing these interconnected conditions, which is also a potential mechanism present.[30] The interplay of these mechanisms may culminate in a sustained elevation of uric acid levels, heightening the susceptibility to gout and related conditions. In a prior cross-sectional investigation involving 801 male participants undergoing health evaluations, computed tomography measurements revealed significant associations between visceral fat, liver fat, and hyperuricemia. These associations remained robust even after controlling for potential confounders such as age and lifestyle factors.[31] However, the study's limitation primarily stemmed from its exclusive focus on male subjects. Moreover, Bai et al[32] in a study involving 3,683 participants from China, also corroborated these findings concerning the relationship between liver fat accumulation and hyperuricemia. Yang et al[33] conducted a cross-sectional study to investigate the combined relationship between SUA, serum ALT, and NAFLD prevalence in older Chinese adults. Their findings indicate a significant association between SUA levels and the prevalence of mild and severe steatosis. Moreover, the study highlights that older adults with higher SUA levels

exhibit a notably increased prevalence of NAFLD, being 2.74 times higher in men and 4.60 times higher in women compared to those with the lowest SUA levels. The outcomes of this investigation furnish supplementary support to the aforementioned research. This study analysis encompassing 2,950 prediabetic individuals, a substantial positive correlation between LFC and hyperuricemia was observed, persisting even after accounting for additional confounding variables. Notably, this study identified a non-linear relationship between LFC and hyperuricemia through direct LFC measurement, with liver fat surpassing 8.40% significantly heightening the hyperuricemia risk. These findings suggest a plausible link between hepatic lipid accumulation and the pathophysiology of hyperuricemia. Furthermore, the exploration of the special individuals of prediabetes also provides innovative perspectives and avenues for the subsequent studies of prediabetes and hyperuricemia.

This study explored factors associated with the prevalence of hyperuricemia among individuals with prediabetes, contributing novel epidemiological evidence specific to this population. Utilizing multivariate logistic regression analysis, the study provided robust statistical validation. Notably, it quantified liver fat and conducted subgroup analyses to ensure reliable outcomes across diverse prediabetic cohorts, aspects seldom addressed in prior research. Moreover, the QCT technique are employed for the quantification of liver fat, a modality that avoids additional scanning time and radiation exposure, facilitating the large-scale population application of liver fat screening. Despite efforts to address inherent confounding factors in cross-sectional designs, certain limitations warrant acknowledgment. Retrospective studies are limited in establishing the causal relationship between LFC and hyperuricemia among individuals with prediabetes. Additionally, covariates such as dietary habits, smoking and alcohol use history, and physical activity were not fully accounted for, although participants with alcoholic fatty liver disease were excluded based on medical records. Notably, considering the potential impact of antihypertensive medications on serum uric acid levels, the use of different medications should also be considered as a confounding factor in subsequent studies. Lastly, being a single-center study focused on health screening, generalizability to broader populations is restricted. These limitations underscore the necessity for further investigation to elucidate the association between LFC and hyperuricemia risk in prediabetic cohorts.

Conclusion

This study uncovered a notable correlation linking higher LFC (exceeding 8.4%) with an elevated likelihood of hyperuricemia. Significantly, a nonlinear association between LFC and hyperuricemia was noted in prediabetic individuals undergoing health evaluations. To investigate causal mechanisms, thorough prospective studies are essential to mitigate the risk of hyperuricemia and enhance metabolic health outcomes in individuals with prediabetes.

Data Sharing Statement

The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study protocol adhered to the Declaration of Helsinki and received approval from the Ethics Committee of Henan Provincial People's Hospital (Approval No. 115, 2022). Informed consent was obtained from all participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests in this work.

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