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Assessment of urate-lowering therapies on lipid metabolism and kidney function in non-dialysis chronic kidney disease patients: 12 months multicenter cohort study

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Background and objectives: Urate lowering therapies (ULTs) are primarily used to manage hyperuricemia (HUA), which refers to an increase in serum uric acid (SUA) levels. SUA is an important marker for assessing kidney function in patients complicated with chronic kidney disease (CKD). Recent studies revealed a close relationship between SUA and lipid metabolism. We aim to investigate the impact of ULTs on kidney function and lipid profiles in CKD patients, and further explore the sex-specific ULTs effects on lipid profiles.

Method: We conducted a multicenter, prospective observational cohort study, enrolled n=200 patients aged between 20 and 80 years old with stages 3/4 CKD. Patients were divided into two groups: the ULT group (n=94) who were receiving febuxostat or allopurinol, and the Non-ULT group (n=106) who were receiving their conventional CKD therapy, the study employed clinically indicated allocation. ULT initiation was based on physician judgment per guidelines persistent HUA with SUA ≥7 mg/dL in males and ≥6 mg/dL in females with CKD progression risk factors. Models adjusted for all collected confounders, renal function including estimated glomerular filtration rate (eGFR), serum creatinine (Scr), blood urea nitrogen (BUN), and SUA, and lipid profiles including high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglyceride (TG), and total cholesterol (TC). Results remained consistent in sensitivity analyses stratifying by baseline characteristics. Subgroups were further analyzed based on sex, to evaluate sex-specific differences in lipid metabolism related to ULTs. All participants went through clinical assessment before and after treatment and were followed for 12 consecutive months.

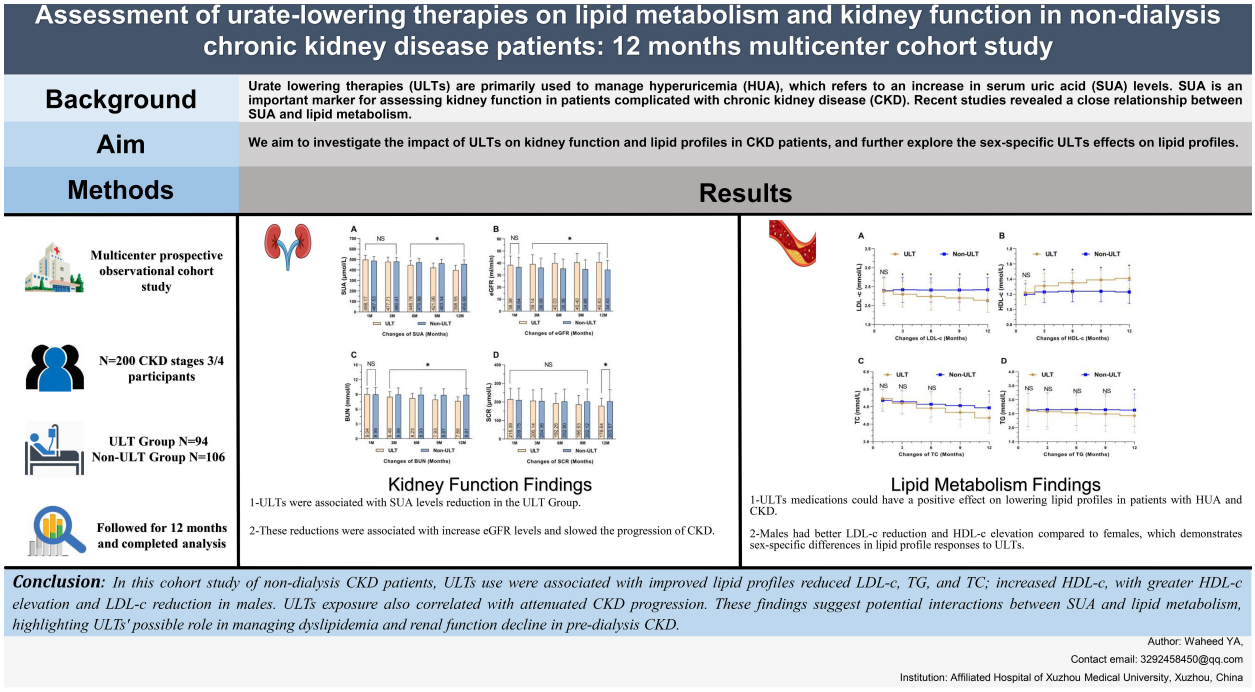
Results: LDL-c significantly decreased in the ULT group compared to the Non-ULT group after 12 months of observation (2.14 ± 0.32 vs. 2.42 ± 0.32 [95% CI: -0.36 to -0.18], *P<0,001*). Similarly, TC and TG were significantly decreased in the ULT group compared to the Non-ULT group after 12 months of observation (4.18 ± 0.44 vs.

4.47 ± 0.39 [95% CI: -0.40 to -0.16], *P<0,001*) for TC, and (2.43 ± 0.62 vs. 2.63 ± 0.58 [95% CI: -0.37 to -0.03], *P<0,016*) for TG. Moreover, HDL-c increased significantly in the ULT group compared to the Non-ULT group (1.41 ± 0.13 vs. 1.23 ± 0.15 [95% CI: 0.13 to 0.21], *P<0.001*). The sex-specific ULT on lipid profiles exhibited a greater reduction in LDL-c in males by (-0.28 mmol/L [95% CI: -0.32 to -0.14], *P<0.001*), and a more pronounced increase in HDL-c levels by (+0.23 mmol/L [95% CI: 0.07 to 0.18], *P<0.001*). A significant correlation was observed Pre- and Post-treatment between SUA and LDL-c/HDL-c, Post-treatment LDL-c (R=0.2942, R^2=0.2639, 95% CI: [0.0974 to 0.4689], *P<0.0040)*, Post-treatment HDL-c (R=-0.3935, R^2=0.1548, 95% CI: [-0.5521 to -0.2074], *P<0.0001*). SUA significantly decreased in the ULT group compared to the Non-ULT group after 12 months of treatment (398.55 ± 45.48 vs. 456.66 ± 38.23 [95% CI: -69.78 to -46.42], *P<0.001).* Similarly, eGFR slightly improved in the ULT group compared to the Non-ULT after 12 months of treatment (40.83 ± 7.50 vs. 34.43 ± 7.68 [95% CI: 4.32 to 8.51], *P<0.001).* These results indicate the renoprotective effects of ULTs in CKD patients.

Conclusion: In this cohort study of non-dialysis CKD patients, ULT use was associated with improved lipid profiles reduced LDL-c, TG, and TC; increased HDL-c, with greater HDL-c elevation and LDL-c reduction in males. ULTs exposure also correlated with attenuated CKD progression. These findings suggest potential interactions between SUA and lipid metabolism, highlighting ULTs' possible role in managing dyslipidemia and renal function decline in pre-dialysis CKD.

KEYWORDS

serum uric acid, chronic kidney disease, urate-lowering therapy, hyperuricemia, dyslipidemia, cardiovascular risk



GRAPHICAL ABSTRACT

1 Introduction

Chronic kidney disease (CKD) is a significant public concern, not only in China but worldwide, affecting a large and growing proportion of the population. CKD is characterized by gradual loss of kidney function over time. CKD, if left untreated, not only will lead to end-stage kidney disease (ESKD) but also contribute to a heightened risk of developing cardiovascular disease (CVD) and overall mortality (1). Many factors can influence the progression of CKD, and these can be termed traditional factors, such as hypertension (HTN), and diabetes and nontraditional factors, such as inflammation, oxidative stress, and mineral bone disorders (2). As CKD is known to be a significant health burden with several dimensions, it is important to discover new treatment targets or strategies that would slow down the CKD progression and improve the overall prognosis. This explains why such high-persistent diseases should draw the attention of early diagnosis and intervention for effective management.

The end-product of purine metabolism is serum uric acid (SUA), produced in the liver and ultimately excreted via the kidneys throughout the body (3–5). Mostly, it is formed by endogenous synthesis with less being sourced externally (6). Abnormalities in either excessive production or under-excretion define the causes behind hyperuricemia (HUA). The definition for HUA diagnosis in China states the cut-off value for SUA concentration > 420 μmol/L, specifically applied to male and female patients (7). According to one meta-analysis, the estimated aggregated prevalence of HUA in mainland China was found to be 13.3% (95% CI: 11.9-16.4%) (8). SUA is a critical factor in CKD progression through multiple pathways: it has independent associations with the risk of decline in renal function, all-cause mortality, and cardiovascular events, especially in the later stages of CKD (5). Both high and very low SUA concentrations exhibit U-shaped relationships with mortality with inflection points of (311.65 μmol/L all-cause and 392.34 μmol/L CVD) (9). HUA, >420 μmol/L in China is associated with tubulointerstitial damage, faster estimated glomerular filtration rate (eGFR) decline, and coronary calcification in early CKD (10, 11). Mechanisms and metabolism of SUA and HUA have been previously published in our reviews in greater detail (4, 5).

Due to the inability of the kidneys to metabolize and eradicate lipids in CKD patients, this process will lead to the deposition of atherogenic lipoproteins; dyslipidemia in CKD is characterized by highly augmented serum low-density lipoprotein cholesterol (LDL-c) and oxidized LDL (OX-LDL) levels. The accumulated levels of LDL-c are indicative of dyslipidemia related to CKD. OX-LDL is simply a modified form of LDL-c, with great detrimental effects due to its inductive properties for inflammation and the formation of foam cells in renal blood vessels (12). The modified lipoprotein is taken up by the scavenger receptors on macrophages, with foam cell formation, culminating in glomerular damage (13). Hypertriglyceridemia is also a common occurrence in the CKD population, due simply to impaired lipoprotein lipase activity and increased triglyceride-rich lipoproteins harboring insulin resistance, which is often prevalent in CKD patients (14, 15). Furthermore, there is a low level of high-density lipoproteins cholesterol (HDL-c) in CKD patients, thereby overturning its protective effects against inflammation, oxidative damage, and cholesterol accumulation. HDL-cin CKD patients is dysfunctional, compared to those without kidney disease which arrests the reverse transport of cholesterol and ameliorates oxidative stress (16). In sum, these various lipid disorders provide services to set a stage for inflammatory and oxidative processes most conducive to renal injury and cause CKD to progress rapidly. The condition of dyslipidemia in CKD can lead to the activation of the renin-angiotensin-aldosterone system (RAAS), a major contributor to renal impairment. Angiotensin II, a dominant component of the RAAS, can promote vasoconstriction, sodium retention, and the release of pro-fibrotic elements such as transforming growth factor-beta (TGF-β) (17). These results can initiate glomerular sclerosis and tubulointerstitial fibrosis, which can significantly speed the progression of CKD (18). The dyslipidemia-RAAS interaction sets up a deleterious cycle that aggravates renal impairment (19).

During the last decade, the pharmacological mechanisms of urate-lowering therapies (ULTs) are well established, by means of pharmacological interventions, thereby establishing their efficacy in lowering SUA concentration (20). Although strong evidence has additionally been revealed that ULTs can effectively decrease SUA concentrations particularly (febuxostat and allopurinol) (21, 22), their role in slowing CKD progression remains controversial (23, 24). Few clinical trials have been conducted over the last decade to investigate the renal protective role of these medications in CKD patients, with varying results (25–27). Patients with CKD are more often treated with ULTs compared with those with no CKD (28). New clinical and epidemiological findings indicate that HUA may also be related to the increased prevalence of dyslipidemia in this population (29). Basic research indicated that ULTs can effectively lower lipid levels in animal studies (30, 31). Furthermore, it has been reported that ULTs could potentially reduce LDL-c levels in patients with mild CKD (32, 33). However, ULTs, SUA, and lipid profile associations are scanty and warrant future research. Understating the relationship between SUA, lipid profiles, and the effects of ULTs is essential for developing new targeted therapeutic and measurement strategies.

Patients with non-dialysis CKD experience a significant burden of HUA, which intensifies as renal function deteriorates. Research indicates that the prevalence of HUA increases from 19.9% in CKD stage 1 to over 75% in stage 5 (34). This demographic finds itself at a pivotal moment where interventions such as ULTs may effectively postpone the need for dialysis by alleviating renal impairment. ULTs are being investigated as a protective approach to delay the onset of dialysis (35). Factors associated with CKD progression, such as hypertension and dyslipidemia, are mechanistically related to SUA and lipid dysregulation. Specifically, dyslipidemia increases inflammation, which is a good predictor of eGFR decline, while uremic toxins in advanced CKD disrupt normal mitochondrial lipid metabolism, exacerbating oxidative stress and endothelial dysfunction. This chain of evidence is further supported by interventions such as SGLT2 inhibitors, which reduce eGFR decline by 1.50 mL/min/1.73m^2/year in non-diabetes, non-proteinuric CKD, thereby confirming that addressing SUA and

dyslipidemia in pre-dialysis patients helps maintain renal function (36).

Sex stratification was methodologically essential in our study due to fundamental biological differences in CKD progression and SUA metabolism between males and females (37). Androgen-mediated pathways, such as urate transporter 1 (URAT1) upregulation and HDL-c suppression, accelerate renal decline in males, whereas estrogen-dependent mechanisms promote urate excretion but increase tubular vulnerability in females. These inherent differences introduce sex-specific confounders that could obscure ULTs efficacy if unaccounted for.

To the best of our knowledge, no studies have specifically observed the effects of ULTs on lipid profiles in patients complicated with CKD and HUA. Investigating this relationship can facilitate a better understanding and provide new clues and insights for the field. Henceforth, we initiated our study to examine and observe how ULTs can impact lipid profiles in non-dialysis CKD hyperuricemic patients.

2 Methods

2.1 Study design and participant eligibility

This is a multicenter, prospective observational cohort study involving 200 non-dialysis stages 3/4 CKD patients enrolled from December 2021- to March 2025 (Figure 1). We performed comparisons of baseline characteristics and outcomes across the participating centers and found no significant differences in lipid profiles and SUA. Heterogeneity was formally assessed with Cochran's Q test statistic values, with low variability suggested. We used mixed-effects models to account for center effects, demonstrating that our results were robust. Throughout sensitivity analyses, which included the three centers, we consistently found that our results were similar. While we cannot discount the possibility of residual heterogeneity based on regional treatment practices, our stratified and adjusted analyses support our conclusions. Eligible patients were divided into ULT group n=96 and Non-ULT group n=106. HUA was defined as SUA more than 420 µmol/L in males and 360 µmol/L in females which is a widely accepted criterion for diagnosis (38, 39), CKD stages were determined according to participants' eGFR levels calculated according to the Chronic Kidney Disease Epidemiology Collaboration formula CKD-EPI based on serum creatinine levels, sex, and age at the time of enrolment (40). Patients were classified as diabetic if they had fasting blood glucose (FBG) ≥ 7.0 mmol/L (41). Participants with systolic blood pressure (SBP) ≥ 140 mmHg and diastolic blood pressure (DBP) ≥ 90 mmHg were diagnosed with HTN (42). Patients initiating ULTs with (allopurinol or febuxostat) were enrolled in the ULT group. All participants must have documented follow-up data for at least 12 months to assess the outcomes, including SUA levels and lipid profiles. Inclusion criteria

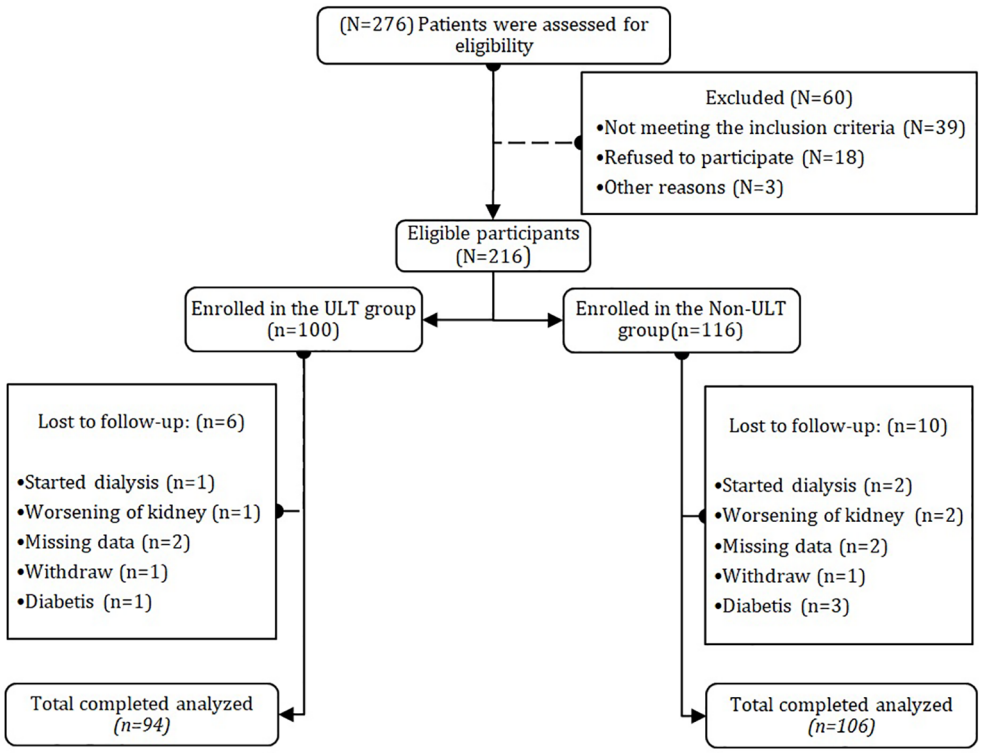


FIGURE 1
Flow chart of the current study. N=200 chronic kidney disease patients were evaluated and assessed for eligibility, patients who met the inclusion criteria were assigned according to urate-lowering therapy to the ULT Group or the Non-ULT Group. Participants were followed for 12 months to observe the impact of urate-lowering therapy on lipid markers and kidney function. Patients with missing data were excluded from the study.

were as follows: 1- patients who have resided in the Xuzhou area for at least 12 months, 2- participants aged between 20 and 80, 3- patients diagnosed with CKD stages 3/4, 4- had not received any medical intervention for lipid profiles such as statins in the past 3 months, 5- no history of severe cardiac events. Exclusion criteria were: 1- patients undergoing dialysis therapy, due to dialysis therapy can alter the level of SUA and lipid profiles, 2- pregnancy and lactation period, 3- patients with severe cardiovascular and neurological complications, 4- patients with gout 5- severe liver disease, 6- patients with missing data on SUA and lipid profiles and those who are not fit to participate in the study. Participants in the study were receiving their conventional therapy for CKD and no interference with their medication administration. Each investigator conducted the study in compliance with the local or regional regulatory requirements and with the ethical standards of the participating hospitals. The study protocol was approved by the scientific research ethics committee at the Faculty of Nephrology, Xuzhou Medical University, and the participating hospitals, and the project ethics number (XYFY2024-KL642-01) and was registered on the Chinese Clinical Trial Registry (ChiCTR2500096252). All participants enrolled in the study gave written informed consent.

2.2 Sample size calculation

A total of 276 patients were Screened during the observational period, with 76 excluded per predefined criteria. The final cohort comprised 200 participants. *Post hoc* power analysis PASS v3.1 determined the adequacy of our sample size to detect intergroup differences in 12-month lipid profiles. For a moderate effect size Cohen's d = 0.5, a two-tailed independent t-test with $\alpha = 0.05$ and sample sizes of 94 (ULT) and 106 (non-ULT) achieved 80% power ($\beta = 0.20$). Although participant numbers were limited by eligibility constraints, this cohort size and group balance aligns with comparable observational studies of longitudinal lipid changes (43).

2.3 Data collection

The patients' basic information, demographic data, and medical records were collected by our department medical staff at the time of the visit. Clinical variables include age, past and current medical history, medication administration, and etiology of CKD, CVD such as (HTN, atherosclerosis, heart failure, and myocardial infarction) and other diseases, were also collected and confirmed by the medical staff of our department. An automated biochemical analyzer Roche cobas8000 (Basel, Switzerland) was utilized to analyze the blood samples and laboratory variables to assess; lipid profiles included; total cholesterol (TC) mmol/L, triglyceride (TG) mmol/L, HDL-c mmol/L, and LDL-c mmol/L, renal function variables included; SUA μmol/L, eGFR ml/min/1.73m^2, blood urea nitrogen (BUN) mmol/L, and serum creatinine (Scr) μmol/L. Echocardiographs were also obtained from participants and were performed by our hospital specialists, who are experienced technicians using standardized methods to ensure patients has no severe cardiovascular conditions, tests included left ventricular ejection fraction (LVEF), left ventricular end-diastolic dimension (LVEDD), and left ventricular posterior wall (LVPW) to confirm the absence of severe cardiovascular lesions (defined as LVEF<30%, severe valvular disease, or ventricular aneurysms). The variables were collected and measured according to the American Society of Echocardiography guidelines (44, 45). Renal function decline was operationally defined as any reduction in eGFR from baseline observed during the study period. No minimum threshold for decline magnitude was applied. This approach captures all longitudinal eGFR deterioration events. Patients were followed for 12 months with the expectation of 5 visits to observe the ULT effects on the kidney function and lipid markers.

2.4 Statistical processing

The study data were analyzed using SPSS 24.0 software on Windows 11. Q-Q plots were used to check whether the residuals were normally distributed. Normally distribution data were expressed as means ± SD, and independent sample t-tests were utilized for comparison between groups. Non-normally distributed data were expressed as medians and interquartile ranges. The enumeration data were expressed as percentages, and the Chi-square (χ^2) test was used to compare groups. Mixed effects repeated measures model was utilized to analyze the mean changes from baseline in kidney biomarkers, and lipid profiles over 12 months. Spearman correlation analysis was utilized to confirm the association between SUA and lipid profiles pre- and post-treatment in the ULT group. P-values less than ($P<0.05$) were considered statistically significant. In addition, GraphPad Prism 9 was utilized to generate figures.

3 Results

3.1 The baseline characteristics of participants according to ULTs

From December 2021 to March 2025, 200 participants completed the 12-month follow-up. Participants were divided into two groups: hyperuricemic patients who started taking urate-lowering therapies were assigned to the ULT group (n=94), and hyperuricemic patients without intervention for HUA were assigned to the Non-ULT group (n=106). The mean SUA was 498.17 ± 42.52 μmol/L in the ULT group versus 487.53 ± 40.30 μmol/L in the Non-ULT group ($P=0.071$). The mean age was 54.24 ± 13.62 years in the ULT group and 53.34 ± 13.95 years in the Non-ULT group. BMI was 24.43 ± 1.80 kg/m^2 in the (ULT) and 24.55 ± 2.45 kg/m^2 in the (Non-ULT). Demographic and clinical markers are summarized in (Table 1). At baseline, no significant differences existed between groups except systolic BP (ULT: 136 ± 13 mmHg vs. Non-ULT: 132 ± 10 mmHg; $P=0.011$) and diastolic BP (ULT: 91 ± 10 mmHg vs. Non-ULT: 88 ± 7 mmHg; $P=0.029$).

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TABLE 1 Baseline characteristics of the study population stratified according to Urate-lowering therapies.

Characteristics	All groups	ULT group	Non-ULT group	t/χ^2	*P value*
Patients No.	N=200	n=94	n=106		
Demographical					
Age Years	53.77 ± 13.77	54.24 ± 13.62	53.34 ± 13.95	0.463	0.644
Body weight kg	71.53 ± 10.38	71.60 ± 9.96	71.46 ± 10.79	0.090	0.928
Height cm	170.49 ± 8.70	170.78 ± 8.63	170.24 ± 8.79	0.438	0.662
BMI kg/m²	24.49 ± 2.16	24.43 ± 1.80	24.55 ± 2.45	-0.176	0.685
Etiology of CKD (%)					
Hypertension Nephropathy	80 (40)	43 (21.5)	37 (18.5)	2.443	0.118
Diabetic Nephropathy	0 (0)	0 (0)	0 (0)	N/A	N/A
Chronic Glomerular Nephritis	100 (50)	48 (24)	52 (26)	0.080	0.776
Other	20 (10)	11 (5.5)	9 (4.5)	0.570	0.450
Laboratory Markers					
SUA µmol/L	492.53 ± 41.59	498.17 ± 42.52	487.53 ± 40.30	1.816	0.071
TG mmol/L	2.62 ± 0.63	2.61 ± 0.69	2.63 ± 0.59	-0.229	0.819
TC mmol/L	4.70 ± 0.30	4.73 ± 0.27	4.68 ± 0.31	1.200	0.232
LDL-c mmol/L	2.39 ± 0.36	2.38 ± 0.38	2.39 ± 0.34	-0.206	0.837
HDL-c mmol/L	1.21 ± 0.15	1.22 ± 0.16	1.20 ± 0.14	0.878	0.381
FBG mmol/L	5.37 ± 0.70	5.41 ± 0.82	5.35 ± 0.58	0.593	0.554
Hgb g/L	116.18 ± 12.49	116.16 ± 12.95	116.20 ± 12.12	-0.022	0.983
[Æ]eGFR ml/min per 1.73m²	37.46 ± 7.85	38.38 ± 7.42	36.64 ± 8.16	1.567	0.119
Scr µmol/L	212.40 ± 61.46	215.39 ± 58.52	209.75 ± 64.12	0.648	0.518
BUN mmol/L	9.01 ± 1.32	9.04 ± 1.21	8.99 ± 1.41	0.276	0.783
C-cys mg/L	1.71 ± 0.53	1.75 ± 0.60	1.66 ± 0.45	1.179	0.231
Hs-CRP mg/L	12.13 ± 5.67	12.90 ± 5.73	11.45 ± 5.56	1.809	0.072
TnT ng/L	9.19 ± 3.14	8.86 ± 3.06	9.47 ± 3.20	-1.379	0.169
CK u/L	74.07 ± 13.73	74.44 ± 14.27	73.75 ± 13.30	0.354	0.691
CK-MB ng/mL	1.56 ± 0.31	1.59 ± 0.33	1.54 ± 0.29	1.234	0.219
[a]LVEF %	50.68 ± 4.17	50.91 ± 3.33	50.46 ± 4.80	0.764	0.446
[a]LVEDD mm	55.13 ± 3.04	55.47 ± 3.10	54.83 ± 2.98	1.482	0.140
[a]LVPW mm	9.89 ± 1.39	9.86 ± 1.41	9.91 ± 1.37	-0.222	0.824
Systolic BP mmHg	134 ± 11	136 ± 13	132 ± 10	2.578	0.011
Diastolic BP mmHg	90 ± 9	91 ± 10	88 ± 7	2.198	0.029
Medications (%)					
Antiplatelet agent	74 (37)	35 (17.5)	39 (19.5)	0.004	0.949
Diuretics	113 (56.5)	61 (30.5)	52 (26)	5.081	0.024
ACEI/ARB	139 (69.5)	72 (36)	67 (33.5)	4.213	0.041
β-blocker	39 (19.5)	18 (9)	21 (10.5)	0.013	0.910
CCB	26 (13)	14 (7)	12 (6)	0.562	0.453

(Continued)

TABLE 1 Continued

Characteristics	All groups	ULT group	Non-ULT group	t/χ^2	*P value*
Medications (%)					
Insulin	0 (0)	0 (0)	0 (0)	N/A	N/A
Lipid lowering drugs	0 (0)	0 (0)	0 (0)	N/A	N/A
Urate-lowering drugs	94 (47)	94 (47)	0 (0)	N/A	N/A
Coexisting conditions (%)					
Smoking	93 (46.5)	45 (22.5)	48 (24)	0.134	0.715
Alcohol use	121 (60.5)	57 (28.5)	64 (32)	0.001	0.969

Measurement data are given as mean ± SD or number (%). $P < 0.05$ was deemed statistically significant.
Chi-Square analysis χ^2 was utilized for comparison of number (%) values, and Student-T test for mean ± SD values.
[&]eGFR (ml/min per 1.73m^2) was calculated with the according to the Chronic Kidney Disease Epidemiology Collaboration formula CKD-EPI
[a]Variables were measured according to the American Society of Echocardiography guideline
BMI, body mass index; SUA, serum uric acid; TG, triglyceride; TC, total cholesterol; LDL-c low density lipoprotein cholesterol; HDL-c, high density lipoprotein cholesterol; FBG, fasting blood glucose; Hgb, hemoglobin; eGFR, estimated glomerular filtration rate; Scr, serum creatinine; BUN, blood urea nitrogen; C-cys, Cystin C; Hs-CRP, High-sensitivity C-reactive protein; TnT troponin T; CK creatine kinase; CK-MB, creatine kinase MB; LVEF left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; LVPW, left ventricular posterior wall; ACEI/ARB, angiotensinogen converting enzyme inhibitor/angiotensin receptor blocker; CCB, calcium channel blocker; CKD, chronic kidney disease; N/A, not applicable

3.2 ULTs effects on kidney function

The visual inspection of the Q-Q plot showed that SUA, eGFR, and other kidney markers were approximately normally distributed. Therefore, a student t-test was utilized to measure the differences between groups. The mean baseline of SUA was (498.17 ± 42.52 µmol/L in the ULT group vs. 487.53 ± 40.30 µmol/L in the Non-ULT group, *P<0.071*). SUA levels in the ULT group and the Non-ULT group were reduced from baseline to 6, 9, and 12 months. However, the SUA levels were significantly lower in the ULT group compared to the Non-ULT group with a statistical difference (*P<0.001*). Detailed values for each time point are listed in (Table 2). The mean changes in SUA levels were higher in the ULT group than in the Non-ULT group after 12 months of observation (*P<0.001*) (Figure 2A).

The baseline of eGFR was comparable between the ULT group and the Non-ULT group (38.38 ± 7.42 ml/min/1.73m^2 vs. 36.64 ± 8.16 ml/min/1.73m^2, *P<0.119*). The eGFR slightly improved after 12 months in the ULT group; on the other hand, eGFR didn't improve in the Non-ULT group, and comparing between groups a statistically significant difference was found (*P<0.001*) (Table 2). The mean changes of eGFR in the ULT were higher than the Non-ULT group after 12 months of observation (*P<0.001*) (Figure 2B).

BUN levels at baseline were also comparable between the ULT group and the Non-ULT group (9.04 ± 1.21 mmol/L vs. 8.99 ± 1.4 mmol/L, respectively, *P<0.783*). However, after 12 months of observation, the levels of BUN were reduced in the ULT compared to the Non-ULT group which showed no reduction, with a statistically significant difference (*P<0.001*) (Table 2). The mean changes of BUN in the ULT group were higher than the Non-ULT group with statistical difference (*P<0.001*) (Figure 2C).

Finally, the baseline levels of Scr were not significant between the ULT group and the Non-ULT group with a mean value of (215.39 ± 58.52 µmol/L vs. 209.75 ± 64.12 µmol/L, respectively, *P<0.518*). After 12 months of observation, the levels of Scr reduced in both groups. However, Scr levels were significantly lower in the ULT group compared to the Non-ULT group with a statistically significant difference (*P<0.001*) (Table 2). The mean changes were higher in the ULT group than in the Non-ULT group with a statistically significant difference (*P<0.001*) (Figure 2D).

3.3 ULTs effects on lipid profiles

The mean baseline levels of LDL-c were (2.38 ± 0.38 mmol/L vs. 2.39 ± 0.34 mmol/L, *P*<0.837) in the ULT group and the Non-ULT group respectively. From baseline to 3 months, the levels of LDL-c reduced significantly in the ULT group but showed no reduction in the Non-ULT group. The differences between the two groups were statistically significant (*P*<0.027). Each time point is listed in (Table 3). The levels of LDL-c reduced even further after 12 months of observation in the ULT group, and the mean changes were higher in the ULT compared to the Non-ULT group (*P*<0.001) (Figure 3A).

At baseline, the levels of HDL-c were comparable between the ULT and the Non-ULT groups (1.22 ± 0.16 mmol/L vs. 1.20 ± 0.14 mmol/L, respectively, *P*<0.381). The HDL-c levels of both groups improved after 3, 6, and 9 months of observation, but it was more significant in the ULT group compared to the Non-ULT group, each time point is listed in (Table 3). The levels of HDL-c continued to improve in the ULT group after 12 months of observation; on the other hand, it showed no further improvement in the Non-ULT group. The mean changes of HDL-c were higher in the ULT group compared to the Non-ULT group with statistical significance (*P*<0.001) (Figure 3B).

The levels of TC were similar at baseline in the ULT group and the Non-ULT group (4.73 ± 0.27 mmol/L vs. 4.68 ± 0.31 mmol/L, respectively, *P*<0.232). TC levels decreased from baseline to 12 months in both groups, but it was more significant in the ULT group than the Non-ULT group, each time point is listed in (Table 3). The mean changes of TC levels from baseline to 12 months in the ULT group were higher than the Non-ULT group with a statistically significant difference (*P*<0.001) (Figure 3C).

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TABLE 2 Comparison of kidney function markers according to Urate lowering therapies in the study population.

Variable	Time	ULT group	Non-ULT group	Mean difference [95%CI]	*P value*
No. Of patients		n=94	n=106		
SUA µmol/L	Baseline	498.17 ± 42.52	487.53 ± 40.30	10.64 [-0.91 to 22.19]	0.071
	3rd month	477.71 ± 43.74	480.41 ± 39.21	-2.69 [-14.26 to 8.87]	0.647
	6th month	446.78 ± 43.45	470.88 ± 39.44	-24.10 [-35.66 to -12.54]	<0.001
	9th month	421.06 ± 44.62	463.34 ± 38.07	-42.27 [-53.81 to -30.74]	<0.001
	12th month	398.55 ± 45.48	456.66 ± 38.23	-58.10 [-69.78 to -46.42]	<0.001
*eGFR ml/min/1.73 m²	Baseline	38.38 ± 7.42	36.64 ± 8.16	1.73 [-0.44 to 3.92]	0.119
	3rd month	39.14 ± 7.66	36.06 ± 8.03	3.07 [0.88 to 5.27]	0.006
	6th month	40.03 ± 7.82	35.36 ± 7.85	4.67 [2.48 to 6.86]	0.001
	9th month	40.40 ± 7.65	34.85 ± 7.78	5.54 [3.39 to 7.70]	<0.001
	12th month	40.83 ± 7.50	34.43 ± 7.68	6.39 [4.32 to 8.51]	<0.001
BUN mmol/L	Baseline	9.04 ± 1.21	8.99 ± 1.41	0.05 [-0.31 to 0.42]	0.783
	3rd month	8.49 ± 1.05	8.98 ± 1.32	-0.49 [-0.83 to -0.16]	0.004
	6th month	8.23 ± 0.99	8.93 ± 1.40	-0.70 [-1.04 to -0.35]	<0.001
	9th month	7.93 ± 0.93	8.87 ± 1.29	-0.94 [-1.25 to -0.62]	<0.001
	12th month	7.66 ± 0.82	8.91 ± 1.27	-1.25 [-1.55 to -0.94]	<0.001
Scr µmol/L	Baseline	215.39 ± 58.52	209.75 ± 64.12	5.64 [-11.55 to 22.84]	0.518
	3rd month	206.14 ± 58.16	204.36 ± 66.67	1.78 [-15.77 to 19.33]	0.842
	6th month	192.26 ± 53.69	202.90 ± 66.03	-10.64 [-27.55 to 6.27]	0.216
	9th month	186.63 ± 48.23	202.12 ± 67.00	-15.49 [-31.96 to 0.97]	0.065
	12th month	178.64 ± 41.64	203.57 ± 63.46	-24.92[-40.10 to -9.75]	<0.001

Measurement data are given as mean ± SD. The endpoint of the study was compared with that before treatment.
Student t-test was used to compare the variables, P<0.05 is considered statistically significant.
*eGFR (ml/min/1.73m²) was calculated according to the Chronic Kidney Disease Epidemiology Collaboration formula
SUA, serum uric acid; eGFR, estimated glomerular filtration rate; Scr, serum creatinine; BUN, blood urea nitrogen; Cl, 95% confidence interval

TG levels at baseline were similar in the ULT and the Non-ULT groups (2.61 ± 0.69 mmol/L vs. 2.63 ± 0.59 mmol/L, respectively, *P*<0.819). The levels of TG decreased in the ULT after 12 months of observation; however, it was not significant from baseline to 3, 6, and 9 months. It was significant in the 12 months of observation with (*P*<0.016). For each time point, refer to (Table 3). The mean changes of TG in the ULT group were higher than the Non-ULT group with statistical significance (*P<0.016*) (Figure 3D).

3.4 Subgroup analyses to investigate the effects of ULTs corresponding to sex

We divided patients into male and female groups and compared their lipid profiles based on whether they received ULTs or Non-ULTs. There were 54 (27%) male and 40 (20%) female patients in the ULT group, and 57 (28.5%) male and 49 (24.5%) female patients in the Non-ULT group.

In the male group, ULT reduced LDL-c by -0.28 mmol/L [95% CI: -0.32 to -0.14], *P<0.001*. Mean values (2.58 ± 0.25 mmol/L baseline vs. 2.30 ± 0.20 mmol/L 12 months) comparing to the Non-ULT group, for each time point comparison between ULT and Non-ULT please refer to (Table 4, Figure 4A1). Similarly, ULT reduced LDL-c levels in the female group by -0.20 mmol/L [95% CI: -0.49 to -0.21], *P<0.001*. Mean values (2.11 ± 0.36 mmol/L baseline vs. 1.91 ± 0.31 mmol/L 12 months), (Table 4, Figure 4A2).

In the male group, ULT reduced TC by -0.47 mmol/L [95% CI: -0.22 to -0.01], *P<0.032*. Mean values (4.86 ± 0.17 mmol/L baseline vs. 4.39 ± 0.29 mmol/L 12 months) comparing to the Non-ULT group (Table 4, Figure 4B1). Similarly, ULT reduced TC levels in the female group by -0.64 mmol/L [95% CI: -0.72 to -0.30], *P<0.001*. Mean values (4.54 ± 0.28mmol/L baseline vs. 3.90 ± 0.46mmol/L 12 months) comparing to the Non-ULT group, (Table 4, Figure 4B2).

In the male group, ULT reduced TG by -0.22 mmol/L [95% CI: -0.44 to -0.04], *P<0.102*. Mean values (2.71 ± 0.70 mmol/L baseline vs. 2.49 ± 0.69 mmol/L 12 months), although there was a slight reduction in the TG in the male group it showed no statistical significance compared to the Non-ULT group, (Table 4, Figure 4C1). On the other hand, ULT reduced TG levels in the female group by -0.15 mmol/L [95% CI: -0.45 to -0.01], *P<0.052*. Mean values (2.49 ± 0.65 mmol/L baseline vs. 2.34 ± 0.55 mmol/L 12 months) comparing to the Non-ULT group, (Table 4, Figure 4C2).

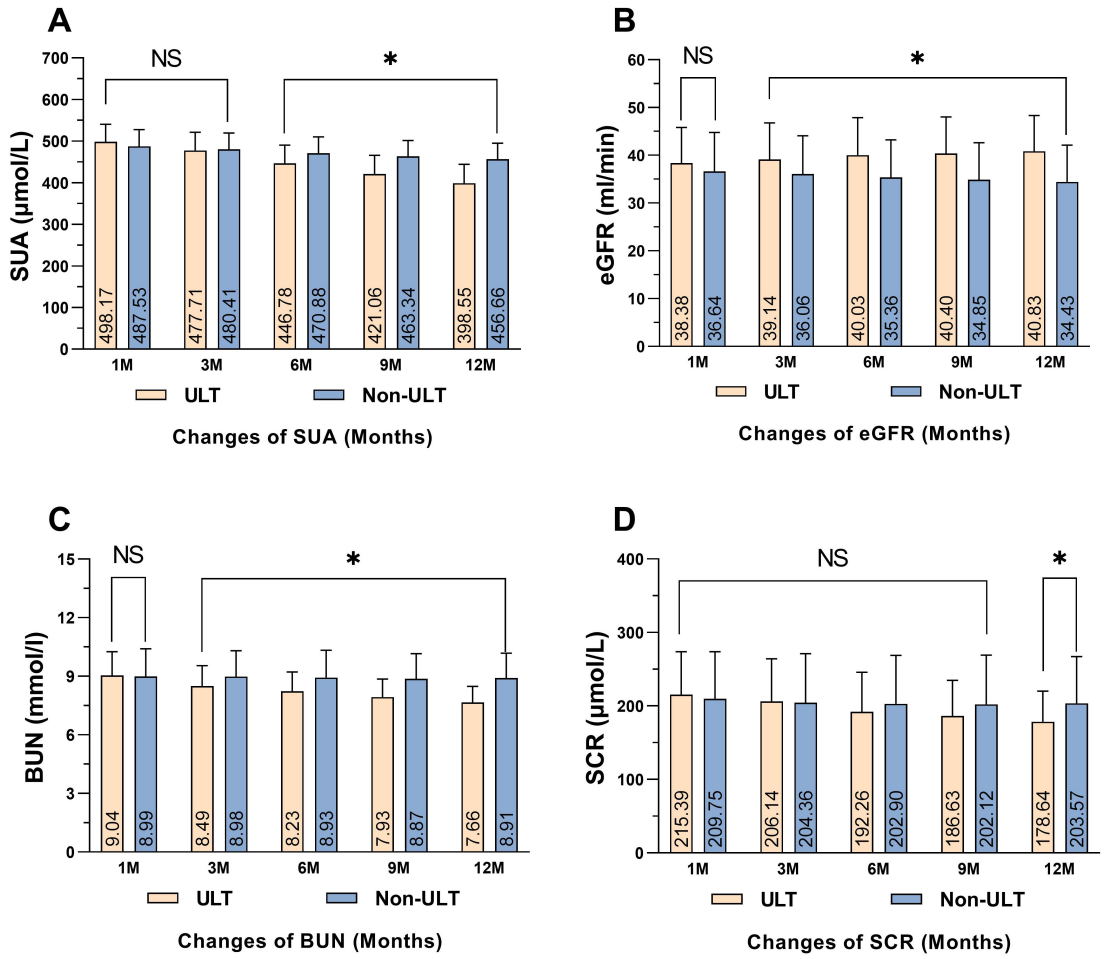

FIGURE 2
Mean comparisons of renal function biomarkers in the study population. **(A)** Comparison of SUA, **(B)** Comparison of eGFR, **(C)** Comparison of BUN, **(D)** Comparison of SCR. **P<0.05* statistical significant between both groups. SUA, serum uric acid; eGFR, estimated glomerular filtration rate; SCR, serum creatinine; BUN, blood urea nitrogen, NS, Not significant.

In the male group, ULT increased HDL-c by +0.23 mmol/L [95% CI: 0.07 to 0.18], *P<0.001*. Mean values (1.11 ± 0.11 mmol/L baseline vs. 1.34 ± 0.10 mmol/L 12 months) comparing to the Non-ULT group, (Table 4, Figure 4D1). Similarly, ULT increased HDL-c levels in the female group by +0.13 mmol/L [95% CI: 0.18 to 0.29], *P<0.001*. Mean values (1.36 ± 0.10 mmol/L baseline vs. 1.49 ± 0.12 mmol/L 12 months) comparing to the Non-ULT group, (Table 4, Figure 4D2).

In summary, males had better LDL-c reduction and HDL-c elevation compared to females, which demonstrates sex-specific differences in lipid profile responses to ULT.

3.5 Changes in SUA correlations with LDL-c and HDL-c following treatment

We conducted a spearman correlation analysis in the ULT before and after treatment between SUA and LDL-c/HDL-c to. The results showed a significant correlation between these variables.

The association of SUA with LDL-c/HDL-c was evident in the ULT group before and after treatment based on analysis. Before treatment, SUA was associated with LDL-c (R=0.2745, R^2=0.0753, 95% CI: [0.0760–0.4520], *P=0.0074*) up to 7.5% variability of LDL-c (Table 5, Figure 5A). Following treatment of 12 months, the association was higher (R=0.2942, R^2=0.2639, 95% CI: [0.0974–0.4689], *P<0.0040*) which accounted for 26.4% variability in LDL-c (Table 5, Figure 5A1).

On the other hand, there was an extremely negative correlation between SUA pre-treatment and HDL-c (R=-0.6674, R^2=0.4455, 95% CI: [-0.7664 to -0.5375], *P<0.0001*), which accounted for 44.6% variance of HDL-c (Table 5, Figure 5B). There was still a negative correlation after 12 months of ULT which remained statistically significant (R=-0.3935, R^2=0.1548, 95% CI: [-0.5521 to -0.2074], *P<0.0001*) (Table 5, Figure 5B1).

These findings validate that ULTs can modulate the interaction between SUA and lipid metabolism differentially with significant implications for cardiovascular risk treatment.

TABLE 3 Comparison of lipid profiles according to Urate-lowering therapy in the study population.

Variables	Time	ULT group	Non-ULT group	Mean difference [95%CI]	*P value*
No. Of patients		n=94	n=106		
LDL -c mmol/L	Baseline	2.38 ± 0.38	2.39 ± 0.34	-0.01 [-0.11 to 0.09]	0.837
	3rd month	2.30 ± 0.34	2.42 ± 0.33	-0.11 [-0.21 to -0.01]	0.027
	6th month	2.24 ± 0.36	2.41 ± 0.32	-0.17 [-0.26 to -0.07]	<0.001
	9th month	2.20 ± 0.33	2.41 ± 0.32	-0.20 [-0.29 to -0.11]	<0.001
	12th month	2.14 ± 0.32	2.42 ± 0.32	-0.27 [-0.36 to -0.18]	<0.001
HDL-c mmol/L	Baseline	1.22 ± 0.16	1.20 ± 0.14	0.01 [-0.02 to 0.06]	0.381
	3rd month	1.31 ± 0.17	1.23 ± 0.14	0.07 [0.03 to 0.11]	<0.001
	6th month	1.35 ± 0.14	1.24 ± 0.14	0.11 [0.07 to 0.15]	<0.001
	9th month	1.39 ± 0.13	1.24 ± 0.14	0.15 [0.11 to 0.19]	<0.001
	12th month	1.41 ± 0.13	1.23 ± 0.15	0.17 [0.13 to 0.21]	<0.001
TC mmol/L	Baseline	4.73 ± 0.27	4.68 ± 0.31	0.05 [-0.03 to 0.13]	0.232
	3rd month	4.60 ± 0.34	4.64 ± 0.33	-0.04 [-0.13 to 0.05]	0.359
	6th month	4.46 ± 0.40	4.57 ± 0.37	-0.10 [-0.21 to 0.00]	0.064
	9th month	4.34 ± 0.41	4.53 ± 0.39	-0.18 [-0.30 to -0.07]	<0.001
	12th month	4.18 ± 0.44	4.47 ± 0.39	-0.28 [-0.40 to -0.16]	<0.001
TG mmol/L	Baseline	2.61 ± 0.69	2.63 ± 0.59	-0.02 [-0.19 to 0.15]	0.819
	3rd month	2.57 ± 0.64	2.64 ± 0.61	-0.06 [-0.24 to 0.10]	0.449
	6th month	2.53 ± 0.63	2.65 ± 0.57	-0.12 [-0.28 to 0.04]	0.153
	9th month	2.49 ± 0.63	2.64 ± 0.57	-0.15 [-0.32 to 0.01]	0.065
	12th month	2.43 ± 0.62	2.63 ± 0.58	-0.20 [-0.37 to -0.03]	0.016

Measurement data are given as mean ± SD. The endpoint of the study was compared with that before treatment.
Student t-test was used to compare the variables, P<0.05 is considered statistically significant.
TG, triglyceride; TC, total cholesterol; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; Cl, 95% confidence interval.

3.6 Renal function decline according to eGFR in the study population

A survival analysis test was utilized to measure renal function decline according to changes of eGFR rate in the study population between the ULT group and the Non-ULT group during the 12 months observation. Patients without renal function reduction were defined as 0 and with renal function reduction as 1. n, case. The results after 12 months showed (HR=0.4732, 95% CI [0.335 to 0.666], *P=0.0001*). This means the risk of renal function decline was lower in the ULT compare to the Non-ULT groups, as shown in (Figure 6).

4 Discussion

ULT use was associated with improved lipid profiles (reduced LDL-c, elevated HDL-c) and correlated with better renal outcomes in CKD patients. These observations align with the known renoprotective potential of ULTs like allopurinol and febuxostat in HUA management.

The main aims of ULTs are to treat HUA, and have received significant attention mainly for their potential benefits on renal function in the CKD population. ULTs act to lower SUA concentrations, such drugs including allopurinol and febuxostat. By decreasing SUA levels, ULTs can attenuate the adverse effects of high SUA levels, thus leading to a lesser decline in eGFR and slowing down of CKD progression (35). The results of our study prove that ULTs may significantly establish a better renal function among the CKD population; SUA levels in the ULT group were significantly decreased from baseline to 12 months, compared with the Non-ULT group, a finding that corroborates with earlier reports. Specifically, SUA reductions in our ULT group paralleled attenuated CKD progression; consistent with Goicoechea et al (46). RCT showing 50% lower ESKD risk with allopurinol. This highlights the renoprotective effects of ULTs in the CKD population. Similarly, Lin et al (47). meta-analysis corroborated febuxostat's renoprotective effects. Notably, the magnitude of renal benefit may depend on baseline factors such as CKD severity and ULT dosing protocols.

ULT use was associated with improved eGFR trajectories in our cohort, with the ULT group showing increased eGFR from 38.38 ±

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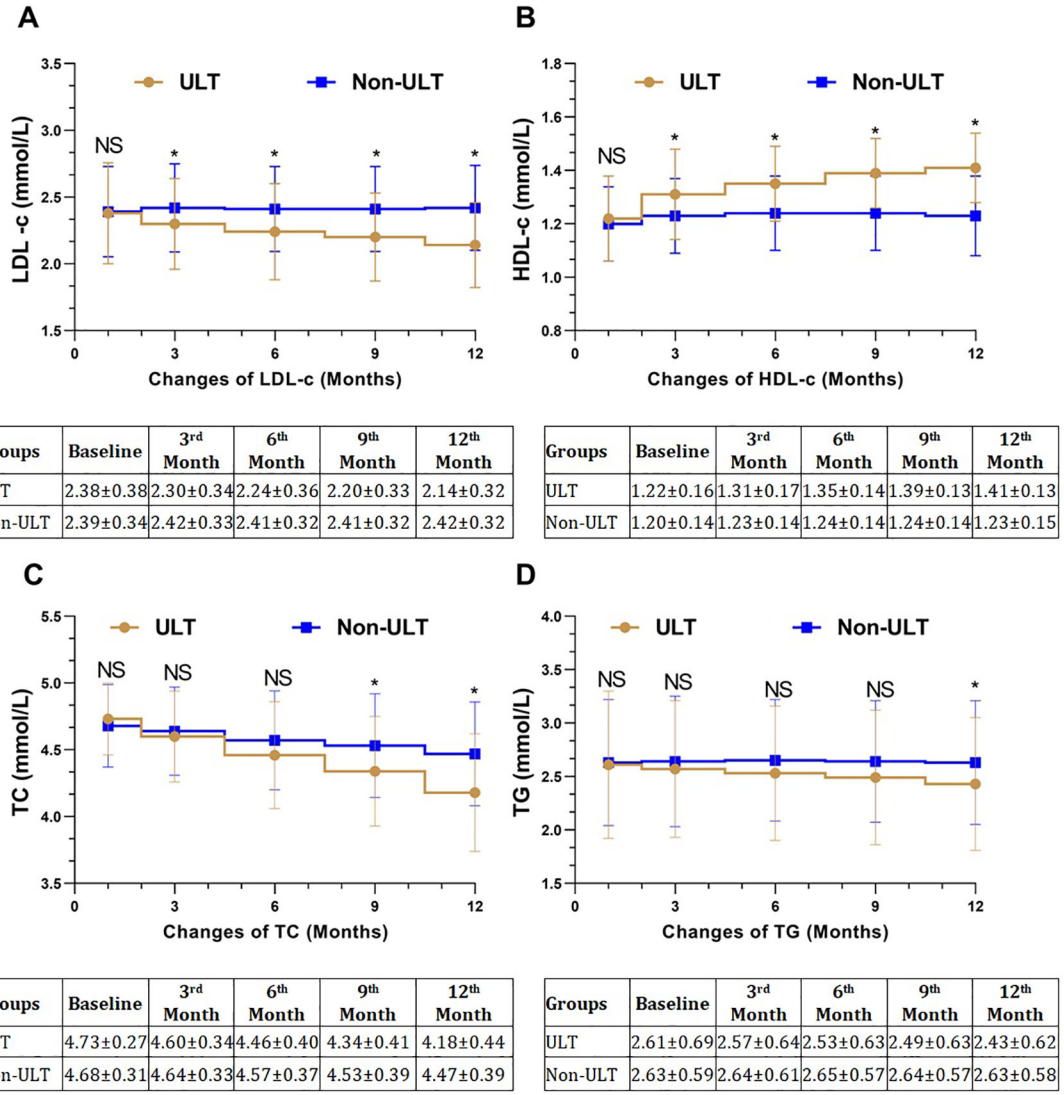

Groups	Baseline	3rd Month	6th Month	9th Month	12th Month
ULT	2.38±0.38	2.30±0.34	2.24±0.36	2.20±0.33	2.14±0.32
Non-ULT	2.39±0.34	2.42±0.33	2.41±0.32	2.41±0.32	2.42±0.32

Groups	Baseline	3rd Month	6th Month	9th Month	12th Month
ULT	1.22±0.16	1.31±0.17	1.35±0.14	1.39±0.13	1.41±0.13
Non-ULT	1.20±0.14	1.23±0.14	1.24±0.14	1.24±0.14	1.23±0.15

Groups	Baseline	3rd Month	6th Month	9th Month	12th Month
ULT	4.73±0.27	4.60±0.34	4.46±0.40	4.34±0.41	4.18±0.44
Non-ULT	4.68±0.31	4.64±0.33	4.57±0.37	4.53±0.39	4.47±0.39

Groups	Baseline	3rd Month	6th Month	9th Month	12th Month
ULT	2.61±0.69	2.57±0.64	2.53±0.63	2.49±0.63	2.43±0.62
Non-ULT	2.63±0.59	2.64±0.61	2.65±0.57	2.64±0.57	2.63±0.58

FIGURE 3
Mean changes of lipid markers in the study population. **(A)** Changes of LDL-c, **(B)** Changes of HDL-c, **(C)** Changes in TC, **(D)** Changes in TG. **P<0.05* statistical significant between both groups. LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; TG, triglyceride; TC, total cholesterol, NS, Not significant.

7.42 to 40.83 ± 7.50 mL/min/1.73m² over 12 months, while the non-ULT group declined from 36.64 ± 8.16 to 34.43 ± 7.68 mL/min/1.73m². This eGFR benefit may relate to earlier intervention timing, consistent with Kim et al (48). findings in stage 3 CKD patients with HUA. Notably, while Kim's study demonstrated significant CKD delay specifically in stage 3, our results extend these observations to broader CKD stages 3/4, suggesting ULT's renal benefits may be more pronounced in earlier stages where residual nephron function permits greater therapeutic response. Mechanistically, SUA reduction may attenuate tubular injury and oxidative stress, key drivers of eGFR decline, particularly before the progression of kidney function decline.

Scr and BUN decreased from baseline to 12 months in the ULT group compared to the Non-ULT group, suggesting potential renal function improvements. These changes may reflect reduced oxidative stress and improved renal hemodynamics, which could provide anti-inflammatory effects as proposed in mechanistic studies of urate-lowering therapies. While our observational data demonstrate associations between ULT use and attenuated renal function decline, we acknowledge conflicting evidence from other studies: The FEATHER trial (Febuxostat versus Placebo Randomized Controlled Trial Regarding Reduced Kidney Function in Patients with Hyperuricemia Complicated by Chronic Kidney Disease Stage 3) revealed no significant improvement in halting renal function decline after ULT use (49), potentially due to their cohort's more advanced baseline CKD severity (predominantly stage 3b-4 versus our stage 3/4) and fixed-dose protocols. Similarly, Sunil et al (26). documented no CKD progression benefit with allopurinol in stages 3–4 CKD, possibly attributable to later intervention timing (mean baseline eGFR 28 mL/min/1.73m² versus 37 mL/min/1.73m² in our cohort) or geographical/ethnic factors influencing treatment response.

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TABLE 4 Subgroup analysis of lipid profiles according to sex in the study population.

Variables	Baseline	3rd month	6th month	9th month	12th month
Male patients					
LDL-c					
ULT	2.58 ± 0.25	2.50 ± 0.23	[1]2.43 ± 0.22	[2]2.38 ± 0.21	[2]2.30 ± 0.20
Non-ULT	2.53 ± 0.28	2.55 ± 0.27	[1]2.54 ± 0.25	[2]2.53 ± 0.25	[2]2.54 ± 0.25
TC					
ULT	4.86 ± 0.17	4.77 ± 0.25	4.66 ± 0.28	4.55 ± 0.27	[1]4.39 ± 0.29
Non-ULT	4.75 ± 0.23	4.72 ± 0.25	4.63 ± 0.27	4.59 ± 0.29	[1]4.51 ± 0.27
TG					
ULT	2.71 ± 0.70	2.67 ± 0.69	2.59 ± 0.67	2.54 ± 0.68	2.49 ± 0.66
Non-ULT	2.67 ± 0.61	2.65 ± 0.60	2.74 ± 0.55	2.71 ± 0.58	2.69 ± 0.62
HDL-c					
ULT	1.11 ± 0.11	[1]1.27 ± 0.10	[2]1.27 ± 0.10	[2]1.32 ± 0.10	[2]1.34 ± 0.10
Non-ULT	1.13 ± 0.11	[1]1.19 ± 0.14	[2]1.19 ± 0.14	[2]1.21 ± 0.14	[2]1.22 ± 0.16
Female patients					
LDL-c					
ULT	2.11 ± 0.36	[1]2.04 ± 0.36	[2]1.99 ± 0.36	[2]1.97 ± 0.33	[2]1.91 ± 0.31
Non-ULT	2.24 ± 0.35	[1]2.26 ± 0.34	[2]2.27 ± 0.34	[2]2.27 ± 0.34	[2]2.27 ± 0.34
TC					
ULT	4.54 ± 0.28	[1]4.37 ± 0.31	[2]4.19 ± 0.38	[2]4.05 ± 0.49	[2]3.90 ± 0.46
Non-ULT	4.59 ± 0.37	[1]4.56 ± 0.38	[2]4.49 ± 0.46	[2]4.45 ± 0.47	[2]4.42 ± 0.50
TG					
ULT	2.49 ± 0.65	2.44 ± 0.54	2.44 ± 0.56	2.41 ± 0.56	[1]2.34 ± 0.55
Non-ULT	2.59 ± 0.56	2.64 ± 0.63	2.54 ± 0.57	2.56 ± 0.54	[1]2.56 ± 0.53
HDL-c					
ULT	1.36 ± 0.10	[2]1.44 ± 0.11	[2]1.46 ± 0.11	[2]1.47 ± 0.11	[2]1.49 ± 0.12
Non-ULT	1.28 ± 0.12	[2]1.30 ± 0.13	[2]1.29 ± 0.12	[2]1.27 ± 0.13	[2]1.25 ± 0.13

Measurement data are given as mean ± standard deviation. The study's endpoint was compared with the baseline.
TG, triglyceride; TC, total cholesterol; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol;
[1]Significant differences between the groups ($P<0.05$).
[2]Significant differences between the groups ($P<0.001$).
Male patients; ULT (n=54), Non-ULT (n=57).
Female patients; ULT (n=40), Non-ULT (n=49).

Conversely, Sircar et al (50). randomized trial showed slowed renal function decline with febuxostat in stage 3/4 CKD patients, aligning with our findings and suggesting protocol-specific variables like ULTs dosing intensity may explain outcome variations. While these studies present conflicting conclusions regarding ULT's renoprotective efficacy, accumulating evidence supports potential benefits particularly when initiated early in moderate CKD, with favorable outcomes more likely when residual renal function permits therapeutic response before irreversible progression of kidney function decline.

Patients with CKD frequently exhibit dyslipidemia, characterized by elevated LDL-c and TG alongside reduced HDL-c levels (51). While dyslipidemia is an established cardiovascular risk factor in the general population, its implications in CKD more complex due to altered lipid metabolism and heightened inflammation. Our findings indicate ULT use was associated with potential kidney function improvements and correlated with significant lipid profile modifications. Specifically, LDL-c levels decreased significantly in the ULT group versus non-ULT after 12 months (Table 3), while TG and TC reductions and HDL-c elevations were observed exclusively in ULT participants. These patterns suggest that managing HUA with ULTs may help control dyslipidemia in CKD patients, potentially reducing statin dependence. We hypothesize that SUA reduction may indirectly modulate lipid metabolism, possibly through antioxidant

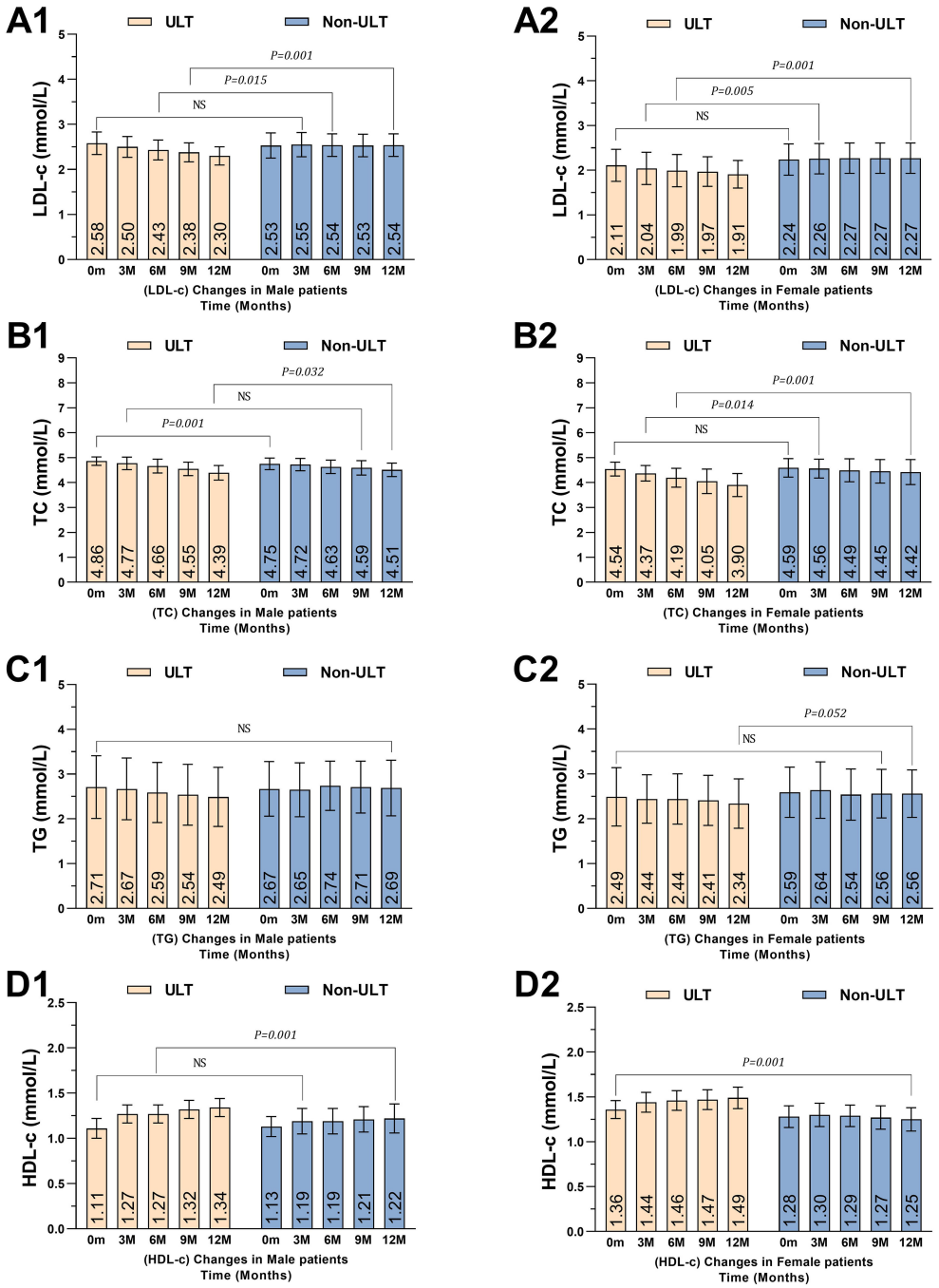

FIGURE 4
Mean changes of lipid profile levels over time according to gender. **(A1)** LDL-c in males, **(A2)** LDL-c females, **(B1)** TC in males, **(B2)** TC in females, **(C1)** TG in males, **(C2)** TG in females, **(D1)** HDL-c in males, **(D2)** HDL-c in females. *P<0.05* means statistically significant. TG, triglyceride; TC, total cholesterol; LDL-c, low-density lipoprotein cholesterol; HDL-c, high- density lipoprotein cholesterol. Male patients; ULT (n=54), Non-ULT (n=57) Female patients; ULT (n=40), Non-ULT (n=49).

pathways proposed in mechanistic studies. The observed LDL-c reductions and HDL-c elevations could relate to attenuated oxidative stress, which disrupts lipid homeostasis in CKD. However, conflicting evidence exists regarding ULT's lipid effects across populations, potentially due to genetic polymorphisms in urate transporters or ethnic variations in lipid responses. Large randomized trials needed to confirm these associations and evaluate ULT's role in dyslipidemia management for CKD-hyperuricemic patients, particularly given statins' diminished efficacy in advanced CKD.

The precise mechanisms regulating lipid metabolism in kidney disease remain incompletely characterized, though emerging research suggests podocyte-specific pathways (e.g. JAML-SIRT1-SREBP1 signaling) modulate lipid accumulation and renal injury. While lipid-lowering interventions in CKD remain debated, statins

TABLE 5 Correlation analysis of serum uric acid with LDL-c and HDL-c pre and post treatment in the ULT group.

Variable	Pre-treatment			*P value*	Post-treatment			*P value*
	R	R^2	95% CI		R	R^2	95% CI	
LDL-c	0.2745	0.0753	0.0760 to 0.4520	0.0074	0.2942	0.2639	0.0974 to 0.4689	<0.0040
HDL-c	-0.6674	0.4455	-0.7664 to -0.5375	<0.0001	-0.3935	0.1548	-0.5521 to -0.2074	<0.0001

Spearman correlation analysis was utilized to confirm the association. *P*<0.05 was deemed statistically significant.
HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; CI, 95% confidence interval.

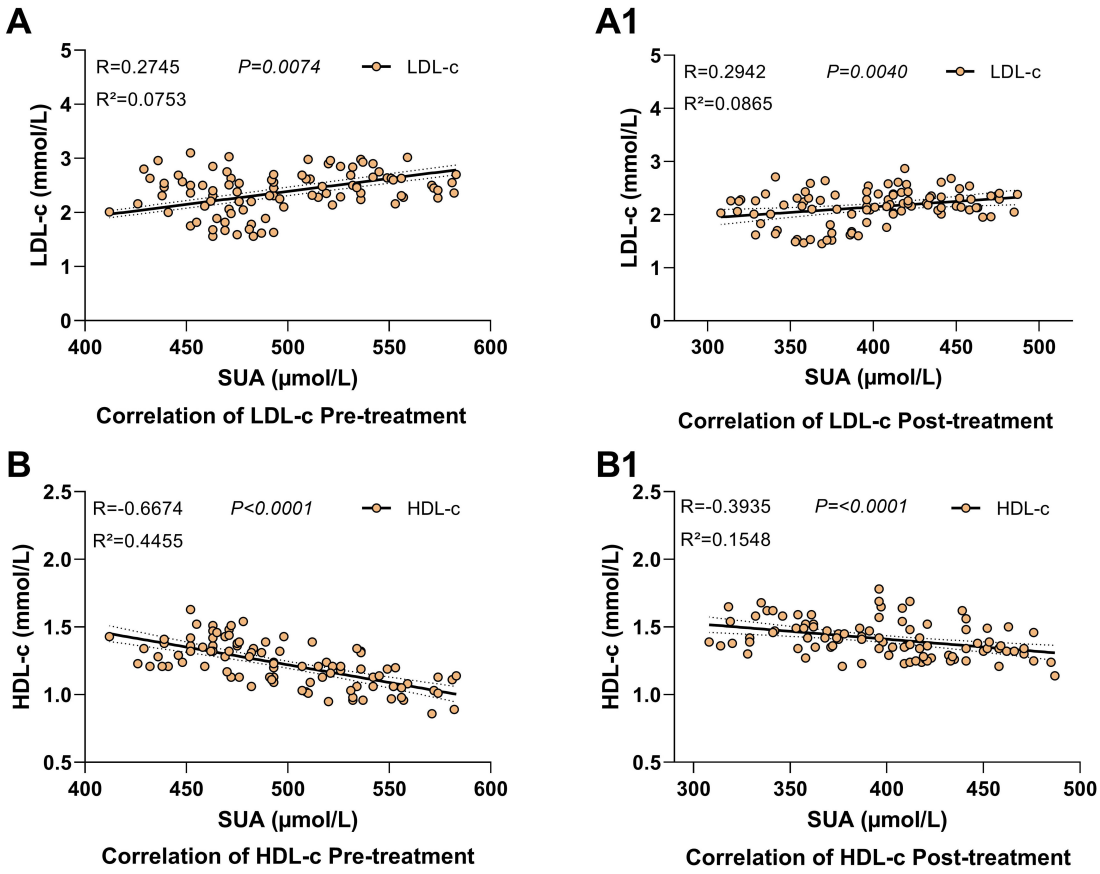

FIGURE 5
Scatter plots correlation between serum uric acid and lipid profiles Pre- and Post-Treatment in the ULT group. **(A, B)** Pre-treatment correlations, **(A1, B1)** Post-treatment correlations. P<0.05 was considered statistical significant. LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; SUA, serum uric acid.

represent the most extensively utilized approach. Their efficacy in reducing proteinuria and slowing CKD progression is well-documented in early-stage disease (52), though benefits attenuate in advanced CKD and become non-significant in ESKD. To date, no clinical trials have specifically evaluated ULTs for preventing lipid abnormalities in HUA with CKD, though mechanistic studies suggest SUA reduction may improve lipid homeostasis through antioxidant effects and endothelial function modulation. Our findings thus provide foundational evidence for ULT's lipid-modifying associations and highlight the need for multicenter RCTs to determine whether ULTs could serve as an adjunctive therapy rather than a replacement for lipid management in HUA with CKD. This aligns with Saini et al (53). observation that dyslipidemia progression correlates with CKD severity, emphasizing the importance of early intervention in populations like our stage 3/4 cohort where residual renal function may optimize therapeutic response.

Overall, our results indicate that ULT use was associated with improved lipid profiles specifically reductions in LDL-c and elevations in HDL-c in patients with HUA and CKD. These beneficial changes may relate to attenuated oxidative stress and inflammation, both recognized disruptors of lipid metabolism in renal disease. While ULTs primarily indicated for HUA and gout management, our findings suggest potential ancillary benefits for

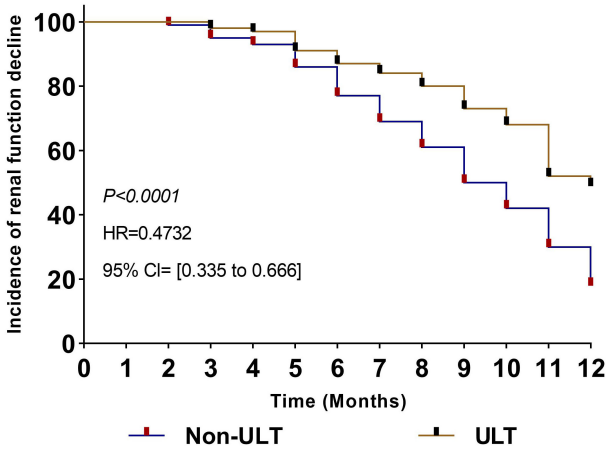

FIGURE 6
Hazard ratio of renal function decline according to changes in estimated glomerular filtration rate. Patients without renal function reduction are defined as 0 and renal function reduction as 1. n, case. HR, hazard ratio; HUA, hyperuricemia; CI, 95% confidence interval; ULT, urate-lowering therapy.

dyslipidemia control in CKD, potentially mitigating cardiovascular risks where statin efficacy diminishes in advanced CKD stages. These findings suggest that ULTs may alleviate dyslipidemia in CKD patients and inflammation, which is known to exacerbate lipid abnormalities (54). Notably, these lipid improvements exhibited sex-specific patterns: males showed greater HDL-c elevation (+0.23 mmol/L vs. +0.13 mmol/L in females), aligning with identified sex-specific HDL-c protective thresholds (males: ≥0.93 mmol/L). This might be an indicator that hormonal influence on lipid metabolism creates this difference or sex differences in baseline HDL-c levels (55). In addition, the persistent decrease of LDL-c in ULT females (−0.20 mmol/L) versus a steady state in Non-ULT females suggests ULT could have an apparent cardioprotective effect in this subgroup. Larger randomized trials standardizing ULT dosing and accounting for metabolic heterogeneity needed to validate these associations and evaluate ULT's role in dyslipidemia management for CKD-hyperuricemic patients.

The limited TG response to ULTs in both sexes aligns with prior inconsistent findings, potentially reflecting sex-specific lipid metabolism pathways: testosterone promotes lipolysis while estrogen inhibits adipose triglyceride lipase, explaining differential regulation, ULTs were inconsistent and seemed to depend on diet or genetic factors (56). Proposed mechanisms for ULT's lipid effects include reduced xanthine oxidase activity and improved endothelial function. Our results suggest ULT's association with sex-specific dyslipidemia modulation in CKD-hyperuricemia (LDL-c reduction in males, HDL-c elevation in females). These findings support sex-tailored management and highlight the need for longitudinal studies exploring hormonal mechanisms, particularly androgen/estrogen receptor signaling in lipid processing. Federica et al (57). revealed that women and races underrepresented in clinical trials testing ULTs drugs. In our study, women constituted 44.5% of the enrolled participants in the CKD-HUA population (n=89/200), reflecting a lower enrolment rate than men. Our enrolment of 89 female participants' represents a meaningful advancement toward equitable inclusion. Our sample size, though not so large, is sufficient to justify the sex-stratified findings, particularly when viewed considering the legacy of disparity and methodological rigor applied in subgroup analyses. Future trials should build on these insights to further close enrolment gaps and ensure translational relevance across diverse populations.

In our study, we observed an association between SUA and lipid profile both before and after treatment with ULTs. Increasing SUA levels have been shown to be highly correlated with any sort of dyslipidemia like increased LDL-c as well as decreased HDL-c. This corresponds with studies that indicate SUA has the capacity to increase oxidative stress and inflammation inhibiting lipid metabolism and enhancing atherogenic profiles (58). Furthermore, the anti-inflammatory effect of ULT may normalize HDL-c function and help increase reverse cholesterol transport. Notably, Male patients had a greater extent of improvements in lipids after ULTs which may be in part due to possible effects of hormones on SUA elimination and lipid metabolism.

While this investigation provides insight and evidence on the impact of ULTs on lipid profiles, certain limitations do need to be stated. First, the study is observational instead of a randomized controlled trial which could independently affect metabolic outcomes, and limit our ability to conclusively explore the effects of ULTs on sex and baseline characteristics and unmeasured variables. In our cohort study adjusting for demographics and laboratory parameters (eGFR, SUA, and lipid profiles), we acknowledge unmeasured confounders such as dietary purines, and genetic variants may still exist. Furthermore, we performed sensitivity analyses excluding patients with gout (which is a major modifier of SUA) and stratified analyses by metabolic syndrome status to assess robustness. Besides, the sample size (n=200), though adequate to detect moderate effect sizes, may lack the power to identify smaller yet clinically meaningful differences in lipid parameters or subgroup-specific effects. Furthermore, the study is from one city which limits the generalizability to broader populations, particularly those with demographic or clinical characteristics differing from our cohort. These limitations underscore the need for a cautious interpretation of associations and highlight the value of future prospective studies or randomized controlled trials that are necessary to validate these findings.

5 Conclusion

This observational cohort study demonstrated that ULT use was associated with improved lipid profiles, specifically lower LDL-c, TG and TC levels, and higher HDL-c levels in CKD stages 3/4 patients with hyperuricemia. Changes in the lipid profile appeared to be sex-dependent as there were greater reductions in LDL-c and increases in HDL-c in males than in females. Furthermore, ULT exposure also appeared to be associated with slower progression of CKD. Collectively, these findings highlight ULT's potential role in managing dyslipidemia and renal decline in non-dialysis CKD and should be validated in randomized trials.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by scientific research ethics committees of all participating hospitals, the Faculty of Nephrology, Xuzhou Medical University, with project ethics numbers (XYFY2024-KL642-01) and Department of Nephrology, Fengxian People's Hospital (LLSC-2025-001) and Department of Nephrology, the Second Affiliated Hospital of Xuzhou Medical University ([2025] 030501). This study is part of a broader research project titled 'Assessment of lipid profiles correlation with serum uric acid in non-dialysis dependent chronic kidney disease patients and the effects of urate-lowering therapy on lipids'. All procedures adhere to the ethical standards outlined in the approved protocol. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

YW: Conceptualization, Data curation, Formal Analysis, Methodology, Software, Writing – original draft, Writing – review & editing. HY: Data curation, Formal Analysis, Investigation, Supervision, Writing – review & editing. JL: Data curation, Formal Analysis, Investigation, Supervision, Writing – review & editing. SA: Writing – review & editing. MB: Writing – review & editing. KS: Writing – review & editing. SF: Writing – review & editing. SL: Investigation, Supervision, Writing – review & editing. DW: Investigation, Supervision, Writing – review & editing. XZ: Investigation, Supervision, Writing – review & editing. DS: Funding acquisition, Investigation, Project administration, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be constructed as a potential conflict of interest.

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References

1. Obermayr RP, Temml C, Gutjahr G, Knechtelsdorfer M, Oberbauer R, Klauser-Braun R. Elevated uric acid increases the risk for kidney disease. *J Am Soc Nephrol.* (2008) 19:2407–13. doi: 10.1681/ASN.2008010080

2. Soomro A, Khajehei M, Li R, O'Neil K, Zhang D, Gao B, et al. A therapeutic target for CKD: activin A facilitates TGFβ1 profibrotic signaling. *Cell Mol Biol Lett.* (2023) 28:10. doi: 10.1186/s11658-023-00424-1

3. Fiorentino TV, Sesti F, Succurro E, Pedace E, Andreozzi F, Sciacqua A, et al. Higher serum levels of uric acid are associated with a reduced insulin clearance in non-diabetic individuals. *Acta Diabetol*. (2018) 55:835–42. doi: 10.1007/s00592-018-1153-8

4. Waheed Y, Yang F, Sun D. Role of asymptomatic hyperuricemia in the progression of chronic kidney disease and cardiovascular disease. *Korean J Intern Med*. (2021) 36:1281–93. doi: 10.3904/kjim.2020.340

5. Waheed YA, Liu J, Almayahe S, Sun D. The role of hyperuricemia in the progression of end-stage kidney disease and its molecular prospective in inflammation and cardiovascular diseases: A general review. *Ther Apher Dial*. (2025). doi: 10.1111/1744-9987.70000

6. Jakše B, Jakše B, Pajek M, Pajek J. Uric acid and plant-based nutrition. *Nutrients*. (2019) 11:1736. doi: 10.3390/nu11081736

7. Chinese society of endocrinology. Guidelines for the diagnosis and management of hyperuricemia and gout in China (2019). *Chin J Endocrinol Metab*. (2020) 2020:1–13. doi: 10.3760/cma.j.issn.1000-6699.2020.01.001

8. Liu R, Han C, Wu D, Xia X, Gu J, Guan H, et al. Prevalence of hyperuricemia and gout in mainland China from 2000 to 2014: A systematic review and meta-analysis. *BioMed Res Int*. (2015) 2015:762820. doi: 10.1155/2015/762820

9. Lv YL, Liu YM, Dong KX, Ma XB, Qian L. Association of serum uric acid with all-cause and cardiovascular mortality in cardiovascular disease patients. *Sci Rep*. (2024) 14:26675. doi: 10.1038/s41598-024-76970-1

10. Pan J, Yang Q, Peng J, Li A, Liu Y, Yi B. A cohort study on the correlation between serum uric acid trajectory and the progression of renal function in patients with Type 2 diabetes mellitus. *Zhong nan da xue xue bao. Yi xue ban = J Cent South University. Med Sci*. (2023) 48:725–32. doi: 10.11817/j.issn.1672-7347.2023.220539

11. Tseng CH. Correlation of uric acid and urinary albumin excretion rate in patients with type 2 diabetes mellitus in Taiwan. *Kidney Int*. (2005) 68:796–801. doi: 10.1111/j.1523-1755.2005.00459.x

12. Moorhead JF, Chan MK, El-Nahas M, Varghese Z. Lipid nephrotoxicity in chronic progressive glomerular and tubulo-interstitial disease. *Lancet*. (1982) 2:1309–11. doi: 10.1016/s0140-6736(82)91513-6

13. Vaziri ND, Moradi H. Mechanisms of dyslipidemia of chronic renal failure. *Hemodial Int*. (2006) 10:1–7. doi: 10.1111/j.1542-4758.2006.01168.x

14. Kalantar-Zadeh K, Block G, Humphreys MH, Kopple JD. Reverse epidemiology of cardiovascular risk factors in maintenance dialysis patients. *Kidney Int*. (2003) 63:793–808. doi: 10.1046/j.1523-1755.2003.00803.x

15. Kadatane SP, Satariano M, Massey M, Mongan K, Raina R. The role of inflammation in CKD. *Cells*. (2023) 12:1581. doi: 10.3390/cells12121581

16. Endemann DH, Schiffrin EL. Endothelial dysfunction. *J Am Soc Nephrol*. (2004) 15:1983–92. doi: 10.1097/01.ASN.0000132474.50966.DA

17. Ritz E, Wanner C. Lipid changes and statins in chronic renal insufficiency. *J Am Soc Nephrol*. (2006) 17:S226–30. doi: 10.1681/ASN.2006080919

18. Kasiske B, Cosio FG, Beto J, Bolton K, Chavers BM, Grimm R Jr, et al. Clinical practice guidelines for managing dyslipidemias in kidney transplant patients: a report from the Managing Dyslipidemias in Chronic Kidney Disease Work Group of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative. *Am J Transplant*. (2004) 4 Suppl 7:13–53. doi: 10.1111/j.1600-6135.2004.0355.x

19. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. (2004) 351:1296–305. doi: 10.1056/NEJMoa041031

20. Shibagaki Y, Ohno I, Hosoya T, Kimura K. Safety, efficacy and renal effect of febuxostat in patients with moderate-to-severe kidney dysfunction. *Hypertens Res*. (2014) 37:919–25. doi: 10.1038/hr.2014.107

21. Peng YL, Tain YL, Lee CT, Yang YH, Huang YB, Wen YH, et al. Comparison of uric acid reduction and renal outcomes of febuxostat vs allopurinol in patients with chronic kidney disease. *Sci Rep*. (2020) 10:10734. doi: 10.1038/s41598-020-67026-1

22. Liu CW, Chang WC, Lee CC, Shau WY, Hsu FS, Wang ML, et al. The net clinical benefits of febuxostat versus allopurinol in patients with gout or asymptomatic hyperuricemia - A systematic review and meta-analysis. *Nutr Metab Cardiovasc Dis*. (2019) 29:1011–22. doi: 10.1016/j.numecd.2019.06.016

23. Liu X, Wang H, Ma R, Shao L, Zhang W, Jiang W, et al. The urate-lowering efficacy and safety of febuxostat versus allopurinol in Chinese patients with asymptomatic hyperuricemia and with chronic kidney disease stages 3-5. *Clin Exp Nephrol*. (2019) 23:362–70. doi: 10.1007/s10157-018-1652-5

24. Chou HW, Chiu HT, Tsai CW, Ting IW, Yeh HC, Huang HC, et al. Comparative effectiveness of allopurinol, febuxostat and benzbromarone on renal function in chronic kidney disease patients with hyperuricemia: a 13-year inception cohort study. *Nephrol Dial Transplant*. (2018) 33:1620–7. doi: 10.1093/ndt/gfx313

25. Golmohammadi S, Almasi A, Manouchehri M, Omrani HR, Zandkarimi MR. Allopurinol against progression of chronic kidney disease. *Iran J Kidney Dis*. (2017) 11:286–93.

26. Badve SV, Pascoe EM, Tiku A, Boudville N, Brown FG, Cass A, et al. Effects of allopurinol on the progression of chronic kidney disease. *N Engl J Med*. (2020) 382:2504–13. doi: 10.1056/NEJMoa1915833

27. Hsu YO, Wu IW, Chang SH, Lee CC, Tsai CY, Lin CY, et al. Comparative renoprotective effect of febuxostat and allopurinol in predialysis stage 5 chronic kidney disease patients: A nationwide database analysis. *Clin Pharmacol Ther*. (2020) 107:1159–69. doi: 10.1002/cpt.1697

28. Dennison EM, Rubin KH, Schwarz P, Harvey NC, Bone KW, Cooper C, et al. Is allopurinol use associated with an excess risk of osteoporotic fracture? A National PreScription Registry study. *Arch Osteoporos*. (2015) 10:36. doi: 10.1007/s11657-015-0241-4

29. Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. *N Engl J Med*. (2008) 359:1811–21. doi: 10.1056/NEJMra0800885

30. Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C, Mu W, et al. Hyperuricemia induces endothelial dysfunction. *Kidney Int*. (2005) 67:1739–42. doi: 10.1111/j.1523-1755.2005.00273.x

31. Minami M, Ishiyama A, Takagi M, Omata M, Atarashi K. Effects of allopurinol, a xanthineoxidase inhibitor, on renal injury in hypercholesterolemia-induced hypertensive rats. *BloodPressure*. (2005) 14:120–5. doi: 10.1080/08037050510008878

32. Castro VMF, Melo AC, Belo VS, Chaves VE. Effect of allopurinol and uric acid normalization on serum lipids hyperuricemic subjects: A systematic review with meta-analysis. *Clin Biochem*. (2017) 50:1289–97. doi: 10.1016/j.clinbiochem.2017.07.013

33. Saito Y, Tanaka A, Yoshida H, Nakashima H, Ban N, Matsuhisa M, et al. Effects of xanthine oxidase inhibition by febuxostat on lipid profiles of patients with hyperuricemia: insights from randomized PRIZE study. *Nutrients*. (2024) 16:2324. doi: 10.3390/nu16142324

34. Zhang M, Zhu X, Wu J, Huang Z, Zhao Z, Zhang X, et al. Prevalence of hyperuricemia among chinese adults: findings from two nationally representative cross-sectional surveys in 2015–16 and 2018-19. *Front Immunol*. (2022) 12:791983. doi: 10.3389/fimmu.2021.791983

35. Waheed YA, Yang F, Liu J, Almayahe S, Selvam KKM, Wang D, et al. Efficacy of febuxostat on hyperuricemia and estimated glomerular filtration rate in patients with non-dialysis stage 3/4 chronic kidney disease and assessment of cardiac function: a 12-month interventional study. *Front Nephrol*. (2025) 5:1526182. doi: 10.3389/fneph.2025.1526182

36. Matsui M, Kosugi T, Tansho K, Kitamura S, Nishimoto M, Okamoto K, et al. Effects of SGLT2 Inhibitors on Lower eGFR Decline in Non-Diabetic CKD Patients without Proteinuria. *Kidney*. (2025) 360. doi: 10.34067/KID.0000000886

37. Cobo G, Hecking M, Port FK, Exner I, Lindholm B, Stenvinkel P, et al. Sex and gender differences in chronic kidney disease: progression to end-stage renal disease and haemodialysis. *Clin Sci (London England: 1979)*. (2016) 130:1147–63. doi: 10.1042/CS20160047

38. Fang J, Alderman MH. Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971-1992. National Health and Nutrition Examination Survey. *JAMA*. (2000) 283:2404–10. doi: 10.1001/jama.283.18.2404

39. Kuwabara M. Hyperuricemia, cardiovascular disease, and hypertension. *Pulse (Basel)*. (2016) 3:242–52. doi: 10.1159/000443769

40. Inker LA, Schmid CH, Tighiouart H, Eckfeldt JH, Feldman HI, Greene T, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med*. (2012) 367:20–9. doi: 10.1056/NEJMoa1114248

41. Bloomgarden Z, Ning G. Journal of diabetes: ushering in volume 10. *J Diabetes*. (2018) 10:4–5. doi: 10.1111/1753-0407.12609

42. Ostchega Y, Hughes JP, Zhang G, Nwankwo T, Graber J, Nguyen DT. Differences in hypertension prevalence and hypertension control by urbanization among adults in the United States, 2013-2018. *Am J Hypertens*. (2022) 35:31–41. doi: 10.1093/ajh/hpab067

43. Machin D, Campbell MJ, Tan SB, Tan SH. *Sample size tables for clinical studies. 3rd ed*. Wiley-Blackwell (2009). doi: 10.1002/9781444300710

44. Rychik J, Ayres N, Cuneo B, Gotteiner N, Hornberger L, Spevak PJ, et al. American Society of Echocardiography guidelines and standards for performance of the fetal echocardiogram. *J Am Soc Echocardiogr*. (2004) 17:803–10. doi: 10.1016/j.echo.2004.04.011

45. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr*. (2005) 18:1440–63. doi: 10.1016/j.echo.2005.10.005

46. Goicoechea M, Garcia de Vinuesa S, Verdalles U, Verde E, Macias N, Santos A, et al. Allopurinol and progression of CKD and cardiovascular events: long-term follow-up of a randomized clinical trial. *Am J Kidney Dis*. (2015) 65:543–9. doi: 10.1053/j.ajkd.2014.11.016

47. Lin TC, Hung LY, Chen YC, Lo WC, Lin CH, Tam KW, et al. Effects of febuxostat on renal function in patients with chronic kidney disease: A systematic review and meta-analysis. *Med (Baltimore)*. (2019) 98:e16311. doi: 10.1097/MD.0000000000016311

48. Kim Y, Shin S, Kim K, Choi S, Lee K. Effect of urate lowering therapy on renal disease progression in hyperuricemic patients with chronic kidney disease. *J Rheumatol*. (2015) 42:2143–8. doi: 10.3899/jrheum.150067

49. Kimura K, Hosoya T, Uchida S, Inaba M, Makino H, Maruyama S, et al. Febuxostat therapy for patients with stage 3 CKD and asymptomatic hyperuricemia: A randomized trial. *Am J Kidney Dis*. (2018) 72:798–810. doi: 10.1053/j.ajkd.2018.06.028

50. Sircar D, Chatterjee S, Waikhom R, Golay V, Raychaudhury A, Chatterjee S, et al. Efficacy of febuxostat for slowing the GFR decline in patients with CKD and asymptomatic hyperuricemia: A 6-month, double-blind, randomized, placebo-controlled trial. *Am J Kidney Dis*. (2015) 66:945–50. doi: 10.1053/j.ajkd.2015.05.017

51. Muhammed Sanoop AV, Shifa K, Vipindas K. Comparative Study of Lipid Profile in Patients with Chronic Kidney Disease on Haemodialysis / Conservative Management with Control Population. *Am J Biochem*. (2019) 9(2):17–20. doi: 10.5923/j.ajb.20190902.01

52. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med*. (2003) 139:137–47. doi: 10.7326/0003-4819-139-2-200307150-00013

53. Saini M, Vamne A, Kumar V, Chandel MS. The study of pattern of lipid profile in chronic kidney disease patients on conservative management and hemodialysis: A comparative study. *Cureus*. (2022) 14:e21506. doi: 10.7759/cureus.21506

54. Kanbay M, Yilmaz MI, Sonmez A, Solak Y, Saglam M, Cakir E, et al. Serum uric acid independently predicts cardiovascular events in advanced nephropathy. *Am J Nephrol*. (2012) 36:324–31. doi: 10.1159/000342390

55. Wang X, Magkos F, Mittendorfer B. Sex differences in lipid and lipoprotein metabolism: it's not just about sex hormones. *J Clin Endocrinol Metab*. (2011) 96:885–93. doi: 10.1210/jc.2010-2061

56. Katsiki N, Doumas M, Mikhailidis DP. Lipids, statins, and heart failure: an update. *Curr Pharm Des*. (2016) 22:4796–806. doi: 10.2174/1381612822666160701073452

57. Fogacci F, Borghi C, Di Micoli A, Degli Esposti D, Cicero AFG. Inequalities in enrolment of women and racial minorities in trials testing uric acid lowering drugs. *Nutr Metab Cardiovasc Dis*. (2021) 31:3305–13. doi: 10.1016/j.numecd.2021.09.011

58. Li W, Wang Y, Ouyang S, Li M, Liu R, Zhang Y, et al. Association between serum uric acid level and carotid atherosclerosis and metabolic syndrome in patients with type 2 diabetes mellitus. *Front Endocrinol*. (2022) 13:890305. doi: 10.3389/fendo.2022.890305