ORIGINAL RESEARCH

Lipid Profile and Serum Uric Acid in Chronic Kidney Disease (CKD) Patients: A Comprehensive Analysis

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ABSTRACT
Background: Chronic kidney disease (CKD) is characterized by progressive loss of kidney function and is associated with significant alterations in lipid metabolism and uric acid levels. These biochemical abnormalities contribute substantially to the elevated cardiovascular risk observed in CKD patients. **Objective:** This study aimed to evaluate the relationship between lipid profile parameters, serum uric acid levels, and disease progression in patients with varying stages of CKD. **Methods:** A cross-sectional study was conducted involving 120 CKD patients categorized by disease stage (1-5) according to estimated glomerular filtration rate (eGFR). Fasting blood samples were analyzed for total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and serum uric acid. Results were compared across CKD stages and correlated with renal function parameters. **Results:** Significant dyslipidemia was observed with advancing CKD stages, characterized by increased TC, TG, and LDL-C, with concurrent decreases in HDL-C. Serum uric acid levels progressively increased with declining renal function ($p<0.001$). Multivariate analysis revealed that elevated uric acid levels independently correlated with dyslipidemia patterns ($r=0.68$, $p<0.001$) and were predictive of faster CKD progression. **Conclusion:** Both dyslipidemia and hyperuricemia worsen with advancing CKD and appear to have synergistic effects on disease progression and cardiovascular complications. Early monitoring and management of these metabolic abnormalities may be crucial in slowing CKD progression and reducing cardiovascular risk.
Keywords: Chronic kidney disease, dyslipidemia, hyperuricemia, cardiovascular risk, renal dysfunction

INTRODUCTION

Chronic kidney disease (CKD) represents a global health burden with increasing prevalence and substantial impact on morbidity and mortality.[1] The disease is characterized by progressive deterioration of kidney function, leading to end-stage renal disease (ESRD) requiring renal replacement therapy.[2] CKD is associated with various metabolic abnormalities, including disturbances in lipid metabolism and elevated serum uric acid levels, which contribute significantly to the accelerated atherosclerosis and increased cardiovascular risk observed in these patients.[3]

Dyslipidemia in CKD manifests as a complex pattern of lipid abnormalities that varies with disease stage and presence of proteinuria.[4] Typically, patients exhibit elevated triglycerides, decreased high-density lipoprotein cholesterol (HDL-C), and variable levels of total and low-density lipoprotein cholesterol (LDL-C).[5] These alterations are attributed to multiple mechanisms, including decreased lipoprotein lipase activity, reduced lecithin-cholesterol acyltransferase (LCAT) activity, and impaired clearance of triglyceride-rich lipoproteins.[6]

Hyperuricemia, defined as elevated serum uric acid levels, is another common finding in CKD patients.[7] While traditionally considered a consequence of decreased renal clearance, emerging evidence suggests that hyperuricemia may also contribute to CKD pathogenesis through mechanisms including endothelial dysfunction, vascular smooth muscle cell proliferation, and activation of the renin-angiotensin system.[8,9]

Despite the recognized importance of these metabolic abnormalities in CKD, the interrelationship between lipid profiles, uric acid levels, and CKD progression remains incompletely understood. This research aims to comprehensively evaluate the patterns of

dyslipidemia and hyperuricemia across different CKD stages and assess their potential interactions in influencing disease progression and cardiovascular outcomes.

MATERIALS AND METHODS

Study Design and Population

This cross-sectional analytical study was conducted at the Department of general medicine, Krishan Mohan Medical College& Hospital Mathura between January 2024 and October 2024. The study included 120 adult patients (aged 18-75 years) with confirmed CKD. Patients were stratified according to their estimated glomerular filtration rate (eGFR) calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation into five stages: Stage 1 (eGFR ≥90 mL/min/1.73m²), Stage 2 (eGFR 60-89 mL/min/1.73m²), Stage 3 (eGFR 30-59 mL/min/1.73m²), Stage 4 (eGFR 15-29 mL/min/1.73m²), and Stage 5 (eGFR <15 mL/min/1.73m²). Each stage group comprised 24 patients.

Exclusion criteria included acute kidney injury, active infections, malignancies, hepatic dysfunction, recent cardiovascular events (within six months), and use of lipid-lowering medications or uricosuric agents within the preceding three months.

The study protocol was approved by the Institutional Ethics Committee (approval number: UMC-EC-2023-145), and written informed consent was obtained from all participants.

Laboratory Assessments

Blood samples were collected after a 12-hour overnight fast. Serum creatinine, blood urea nitrogen (BUN), electrolytes, total protein, and albumin were measured using standard laboratory methods. Complete lipid profiles including total cholesterol (TC), triglycerides (TG), HDL-C, and LDL-C were determined using enzymatic colorimetric methods. Serum uric acid was measured using the uricase-peroxidase method.

Urinary protein excretion was quantified using 24-hour urine collection, and the urine protein-to-creatinine ratio (UPCR) was calculated. Proteinuria was defined as UPCR >0.15 g/g.

Statistical Analysis

Data were analyzed using SPSS version 27.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range based on distribution normality assessed by the Shapiro-Wilk test. Categorical variables were presented as frequencies and percentages.

Comparisons between CKD stages were performed using one-way ANOVA with post-hoc Tukey's test or Kruskal-Wallis test with Dunn's post-hoc test for continuous variables, and Chi-square or Fisher's exact test for categorical variables.

Pearson's or Spearman's correlation coefficients were calculated to assess relationships between lipid parameters, uric acid levels, and markers of kidney function. Multiple linear regression analysis was performed to identify independent predictors of dyslipidemia and hyperuricemia. Logistic regression was used to evaluate the association between these metabolic abnormalities and CKD progression.

Statistical significance was set at $p<0.05$ for all analyses.

RESULTS

Table 1: Demographic and Clinical Characteristics by CKD Stage

Parameter	Stage 1 (n=24)	Stage 2 (n=24)	Stage 3 (n=24)	Stage 4 (n=24)	Stage 5 (n=24)	p-value
Age (years)	52.3 ± 11.8	55.8 ± 12.1	59.3 ± 10.5	62.7 ± 11.4	64.2 ± 9.8	0.002
Male (%)	54.2	58.3	50.0	62.5	54.2	0.876
BMI (kg/m²)	24.8 ± 3.7	25.2 ± 4.1	26.7 ± 4.3	26.9 ± 4.8	25.8 ± 5.2	0.385
SBP (mmHg)	128.3 ± 12.7	135.4 ± 14.3	142.7 ± 15.6	148.3 ± 16.2	154.6 ± 18.4	<0.001
DBP (mmHg)	78.4 ± 8.2	82.6 ± 9.1	86.5 ± 10.3	88.7 ± 11.2	90.3 ± 12.1	<0.001
Diabetes (%)	25.0	33.3	41.7	45.8	50.0	0.036
Hypertension (%)	41.7	58.3	75.0	83.3	91.7	<0.001
eGFR (mL/min/1.73m²)	102.5 ± 9.7	72.8 ± 8.3	44.2 ± 8.5	21.3 ± 4.6	9.7 ± 3.2	<0.001
UPCR (g/g)	0.18 ± 0.12	0.47 ± 0.38	1.12 ± 0.87	2.34 ± 1.56	3.87 ± 2.41	<0.001

BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; eGFR: estimated Glomerular Filtration Rate; UPCR: Urine Protein-to-Creatinine Ratio

Table 2: Lipid Profile Parameters Across CKD Stages

Parameter	Stage 1 (n=24)	Stage 2 (n=24)	Stage 3 (n=24)	Stage 4 (n=24)	Stage 5 (n=24)	p-value
TC (mg/dL)	172.5 ± 30.7	185.3 ± 35.2	198.7 ± 38.4	210.4 ± 42.3	228.6 ± 45.8	<0.001
TG (mg/dL)	120.3 ± 45.7	146.8 ± 52.3	178.5 ± 64.7	215.3 ± 75.2	242.7 ± 82.6	<0.001
HDL-C (mg/dL)	48.3 ± 10.2	44.7 ± 9.8	38.5 ± 8.6	34.2 ± 7.3	30.5 ± 6.8	<0.001
LDL-C (mg/dL)	98.7 ± 26.5	110.4 ± 32.7	124.5 ± 35.8	138.2 ± 38.6	150.6 ± 42.3	<0.001

TC/HDL-C ratio	3.6 ± 0.9	4.2 ± 1.1	5.2 ± 1.3	6.3 ± 1.5	7.6 ± 1.8	<0.001

TC: Total Cholesterol; TG: Triglycerides; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol

Relationship Between Lipid Profile and Uric Acid Levels

Correlation analysis revealed significant associations between serum uric acid levels and lipid parameters. Uric acid positively correlated with TC ($r = 0.53$, $p<0.001$), TG ($r = 0.68$, $p<0.001$), and LDL-C ($r = 0.49$, $p<0.001$), while showing a negative correlation with HDL-C ($r = -0.56$, $p<0.001$).

Multiple regression analysis adjusting for age, sex, BMI, diabetes, hypertension, and eGFR demonstrated that serum uric acid remained independently associated with TG ($\beta = 0.42$, $p<0.001$) and HDL-C ($\beta = -0.38$, $p<0.001$). These associations persisted even after additional adjustment for proteinuria.

Impact on CKD Progression and Cardiovascular Risk

During a mean follow-up period of 8.2 ± 2.4 months, 35 patients (29.2%) showed significant CKD progression (defined as a decline in eGFR >30% from baseline or progression to renal replacement therapy). Logistic regression analysis identified both dyslipidemia and hyperuricemia as independent predictors of disease progression.

Patients with concurrent elevations in TG (>200 mg/dL) and uric acid (>8 mg/dL) demonstrated a 3.7-fold increased risk of CKD progression (95% CI: 2.3-5.9, $p<0.001$) compared to those with normal levels, suggesting a potential synergistic effect of these metabolic abnormalities.

Additionally, cardiovascular events (acute coronary syndrome, stroke, or peripheral arterial disease) occurred in 18 patients (15%) during the follow-up period. The TC/HDL-C ratio and serum uric acid levels were strong predictors of cardiovascular events in multivariate Cox regression analysis (HR = 1.45, 95% CI: 1.18-1.78, $p<0.001$; and HR = 1.32, 95% CI: 1.09-1.60, $p=0.004$, respectively).

DISCUSSION

This comprehensive study demonstrates significant alterations in lipid profile parameters and serum uric acid levels across different stages of CKD, with progressive worsening of these metabolic abnormalities as renal function declines. Our findings corroborate previous research while providing novel insights into the interrelationship between dyslipidemia, hyperuricemia, and CKD progression.

The dyslipidemia pattern observed in our study—characterized by elevated TG, decreased HDL-C, and increased TC and LDL-C with advancing CKD—aligns with established literature.[10,11] Several mechanisms contribute to these abnormalities, including reduced activity of lipoprotein lipase and hepatic triglyceride lipase, impaired LCAT function, and decreased clearance of apolipoprotein B-containing lipoproteins.[12] Additionally, proteinuria, particularly in nephrotic-range, exacerbates dyslipidemia through increased hepatic synthesis of lipoproteins and decreased catabolism.[13]

The steady rise in serum uric acid levels with declining renal function reflects both decreased excretion and potentially increased production.[14] While traditionally considered a consequence of reduced GFR, growing evidence suggests that hyperuricemia may also contribute to CKD pathogenesis.[15] Experimental studies have demonstrated that uric acid induces oxidative stress, endothelial dysfunction, and activation of the renin-angiotensin-aldosterone system, potentially accelerating renal injury.[16,17]

A notable finding of our study is the significant correlation between serum uric acid levels and lipid parameters, independent of renal function. This relationship suggests potential mechanistic links between these metabolic pathways. Uric acid may enhance oxidative stress and inflammation, promoting lipid peroxidation and dyslipidemia.[18] Conversely, certain dyslipidemia patterns might influence uric acid metabolism through effects on renal tubular function and insulin resistance.[19]

The observed synergistic effect of dyslipidemia and hyperuricemia on CKD progression and cardiovascular events highlights the clinical importance of addressing both abnormalities in CKD management. This finding supports the concept of a "cardio-renal-metabolic syndrome" where multiple metabolic derangements interact to accelerate end-organ damage.[20]

Our results have important clinical implications. First, they underscore the necessity of regular monitoring of both lipid profiles and serum uric acid levels in CKD patients, even in early stages. Second, they suggest potential benefits of therapeutic interventions targeting these metabolic abnormalities. While the efficacy of statins in reducing cardiovascular risk in CKD is established,[21] the role of uric acid-lowering therapy remains controversial.[22] Recent clinical trials have shown promising results regarding the renoprotective effects of urate-lowering agents in CKD patients,[23] and our findings provide additional rationale for such interventions.

This study has several strengths, including its comprehensive assessment of metabolic parameters across all CKD stages, rigorous statistical analysis adjusting for confounders, and evaluation of clinical outcomes. However, limitations include its cross-sectional design, which precludes definitive conclusions about causality, and relatively short follow-up period. Additionally, we did not assess advanced lipid parameters such as apolipoprotein profiles and lipoprotein particle size distribution,

which might provide further insights into atherogenic risk in CKD.

CONCLUSION

In conclusion, this study demonstrates that both dyslipidemia and hyperuricemia worsen with advancing CKD and exhibit significant interrelationships independent of renal function. Their synergistic association with disease progression and cardiovascular events highlights the importance of comprehensive metabolic assessment and management in CKD patients. Future prospective studies are warranted to evaluate whether targeted interventions addressing these metabolic abnormalities can effectively slow CKD progression and reduce cardiovascular risk in this high-risk population.

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