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Research Article

The Impact of Serum Uric Acid Level on Progression of Chronic Kidney Disease in Non-Diabetic Patients: A Retrospective Analysis

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Abstract

Objectives: Hyperuricemia is common in CKD patients. This retrospective study aimed to investigate the relationship between serum uric acid and the progression of CKD in stage 2 and 3 non-diabetic patients with CKD.

Methods: The study sample included non-diabetic patients with stage 2 and 3 CKD, aged between 30 and 90 years, who were on nephrology follow-up for more than a year at our hospital. Serum uric acid levels recorded at presentation were considered baseline uric acid levels and annual eGFR, was calculated based on MDRD whereas BUN and blood creatinine values measured during patient visits were recorded retrospectively, as annual mean values.

Results: 71 patients were included. Annual reductions in eGFR were significantly higher in male patients (3.8±4.7 ml/min/1.73 m^2) compared to female patients (1.7±2.3 ml/min/1.73 m^2) ($p<0.032$). In a multivariate linear regression analysis, the variables associated with annual reductions in eGFR measurements were baseline serum albumin level, baseline eGFR, and annual mean uric acid levels. No statistically significant differences were found between patients with hyperuricemia (n: 49) and patients without hyperuricemia (n: 22) in annual eGFR decline (2.9±4.5 vs. 2.0±2.71 ml/min/1.73 m^2, respectively; $p=0.894$) and annual eGFR decline in patients treated with allopurinol was comparable to those in patients who were not treated with allopurinol (2.2±2.4 vs. 3.2±4.3 ml/min/1.73 m^2, $p=0.323$; respectively).

Conclusion: We couldn't find any significant association between baseline serum uric acid levels and declines in eGFR. This finding reinforces the notion that hyperuricemia may arise from declining eGFR rather than accelerating CKD progression.

Keywords: allopurinol, chronic kidney disease, estimated glomerular filtration rate, uric acid

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A reduced uric acid excretion may result in hyperuricemia in chronic kidney disease (CKD). Hyperuricemia has been suggested to trigger the progression to chronic kidney failure by inducing vascular smooth muscle cell proliferation in afferent arterioles.[1-4] Several studies were recently conducted to investigate any potential association between serum uric acid levels and the progression of CKD. Available data suggest that the treatment of hyperuricemia using allopurinol may delay the progression of CKD.[5] However, there is limited evidence for the benefit of treatment of hyperuricemia in slowing down the progression of CKD. Furthermore, it is not clear whether serum uric acid level is an independent indicator of disease progression.

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In this study, we investigated any potential association between serum uric acid levels and CKD progression in non-diabetic patients with stage 2 or 3 CKD who were on follow-up in our nephrology outpatient clinics.

Methods

This study included non-diabetic men and women who were on nephrology outpatient follow-up for stage 2 (estimated glomerular filtration rate(eGFR) 60-89 ml/min/1.73 m^2) or stage 3 (eGFR 30-59 ml/min/1.73 m^2) CKD at the Pendik Teaching Hospital of Marmara University. Patients were required not to have an eGFR decline greater than 15 ml/min/1.73 m^2 during the last year and were aged from >30 to <90 years. Data on serum uric acid levels at presentation were obtained retrospectively from patient files and recorded as baseline uric acid levels. Patient's height and body weight, age, body mass index (BMI), blood pressure, 24-hour urinary protein, albuminuria, blood urea nitrogen (BUN), creatinine, sodium, potassium, calcium, phosphorus, estimated glomerular filtration rate (eGFR) (calculated based on "Modification of Diet in Renal Disease" (MDRD) formula), parathormone, hemoglobin, ferritin, hemoglobinA1c (HBA1c) levels at presentation were also recorded. Furthermore, current or history of smoking, hypertension, diabetes, hyperlipidemia, (Low-density lipoprotein>100 mg/dl), coronary artery disease (CAD) (including medical treatment, history of stent placement, prior coronary artery bypass), retinopathy (if present) were recorded. Other data retrieved from patient files included the use of erythropoietin (EPO) and phosphate-binding agents, allopurinol, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), losartan, calcium channel blockers, thiazide diuretics and furosemide at the presentation. Annual mean blood pressure denoted the mean of blood pressure readings obtained during outpatient visits in one year. Annual mean serum uric acid level denoted the mean of serum uric acid levels measured during outpatient visits in one year. eGFR was calculated based on BUN and creatinine values (measured with a one-year interval) using the MDRD formula:

$$Glomerular\ Filtration\ Rate = 186 \times SerumCr^{-1.154} \times age^{-0.203} \times gender\ coefficient \times race\ coefficient$$

Albumin and proteinuria values measured at a one-year interval were also recorded. The use of ACE inhibitors, ARBs, and losartan during the follow-up period was assessed and recorded. Patients remained in the study until they were lost to follow-up, they needed to undergo dialysis or until death. Exclusion criteria included nephrotic-range proteinuria, a diagnosis of glomerulonephritis, macroscopic hematuria/microscopic hematuria detected in urinary sediment, diabetic nephropathy, malignancy, severe renal artery stenosis, chronic inflammatory diseases, gout, rapidly progressive renal dysfunction (an annual eGFR decline rate greater than 15 ml/min/1.73 m^2), active and chronic infections, hepatitis and a positive HIV serology result, chronic liver disease, hospitalizations for cardiovascular events, immunosuppressive therapy, and congestive heart failure. The study was approved by Marmara University Medical Faculty Ethical Committee (09.2013.0137).

Statistical analyses were performed using SPSS software version 22.0, and appropriate significance levels ($p<0.05$) were used to determine statistical significance. Descriptive statistics were used to summarize the demographic characteristics and laboratory data of the study population. Multivariate linear regression analysis was conducted to identify independent predictors of annual decline in eGFR. Regression coefficients, p-values, and 95% confidence intervals were estimated for each predictor variable included in the model. Comparisons between different groups (e.g., males vs. females, patients with hyperuricemia vs. normouricemia, patients with different rates of eGFR decline) were performed using appropriate statistical tests such as independent t-tests or Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables. Cox regression analysis, was used to assess the association between specific variables (e.g., serum uric acid levels, baseline eGFR) and the risk of experiencing an eGFR decline greater than 3 ml/min ml/min/1.73 m^2 per year.

Results

Demographic characteristics and laboratory data of 71 study patients are summarized in Table 1. The mean age of patients was 60.6±12.9 years and 40.8% (n=29) of all patients were female. The mean BMI, systolic blood pressure and diastolic blood pressure readings at baseline were 29.4±6.7, 139.8±23.7, and 81.3±11.7, respectively. Baseline laboratory measurements were as follows (mean±SD): BUN, 26.6±9 mg/dl; creatinine 1.52±0.34 mg/dl, GFR 45.2±11.2 ml/min/1.73 m^2; uric acid 7.25±1.98; proteinuria 534.2±203.7 mg/24 h. Comorbidities included hypertension (61 patients), hyperlipidemia (60 patients), and coronary artery disease (14 patients). 53 patients were on ACE inhibitors and/or ARBs. 8 patients were on losartan. 40 patients had CKD associated with hypertension or CKD of unknown etiology whereas the underlying etiology of CKD was a urological disorder in 30 patients and 1 patient had chronic interstitial nephritis.

The mean follow-up duration was 17.3±10.1 months (range:12-52 months) and the annual mean eGFR decline was 2,9±3 (0-14) ml/min/1.73 m^2. The mean systolic blood pressure and the mean diastolic blood pressure were

Table 1. Demographic characteristics and laboratory data

Parameter	
Age (mean±SD), years	60.6±12.9
Female sex, n (%)	29 (40.8)
BMI (mean±SD) (kg/m^2)	29.4±6.7
Smoking status (n)	
Never smoker	34
Past smoker	32
Active smoker	5
Duration of follow-up (months)	17.3±10.1
Hypertension at baseline [n (%)]	61 (85.9)
Hyperlipidemia at baseline [n (%)]	60 (84.5)
CAD at baseline [n (%)]	14 (19.7)
Systolic Blood Pressure (mean±SD) (mm/Hg)	139.8±23.7
Diastolic Blood Pressure (mean±SD) (mm/Hg)	81.3±11.7
BUN (mean±SD) (mg/dl)	26.6±9
Creatinine (mean±SD) (mg/dl)	1.52±0.34
Sodium (mean±SD) (mEq/L)	140.9±3.6
Potassium (mean±SD) (mEq/L)	4.67±0.54
Calcium (mean±SD) (mg/dl)	9.57±0.60
Phosphorus (mean±SD) (mg/dl)	3.36±0.63
Parathormone (mean±SD) (pg/ml)	91.6±83.8
Ferritin (mean±SD) (mg/dl)	143±185.1
Proteinuria (mean±SD) (mg/day)	203.7±534.2
Uric acid (mean±SD) (mg/dl)	7.25±1.98
Hemoglobin (mean±SD) (gr/dl)	13.2±1.74
Albumin (mean±SD) (gr/dl)	4.45±0.43
GFR (mean±SD) (ml/min/1,73m^2)	45.7±11.2
CKD etiology (n)	
Hypertension or unknown etiology	40
Urological disorders	30
Chronic interstitial nephritis	1
Current medications	
ACE inhibitors	19
ARBs	31
ACE inhibitor + ARB	3
Losartan	8
Allopurinol	20
Diuretics	44
Furosemide	8
Thiazide	43

141.3±21.2 mmHg and 80.7±12.1 mmHg, respectively. Annual kidney function test results are summarized in Table 2.

Factors associated with annual eGFR decline:

A correlation analysis was conducted to detect potential correlations between annual eGFR decline and BMI, CKD etiology, smoking status, systolic blood pressure (SBP), diastolic blood pressure (DBP), BUN, creatinine, sodium (Na), potassium (K), baseline GFR, baseline serum uric acid level, the mean annual serum uric acid and proteinuria. Only male sex, annual mean serum uric acid, baseline eGFR, and albumin levels were found to correlate with annual eGFR decline (Table 3).

No statistically significant correlations were found between annual eGFR decline and smoking status at baseline, CKD etiology, the presence of CAD, treatment with ACE inhibitors and/or ARB, losartan, diuretics, and allopurinol. However, annual eGFR decline was significantly greater in males (3.8±4.7 ml/min/1.73 m^2) than in females (1.7±2.3 ml/min/1.73 m^2) (p=0.032). In a multivariate linear regression analysis only baseline serum albumin, baseline eGFR, and the annual mean uric acid correlated with the mean annual eGFR decline (Table 4).

In parallel with these findings, the annual mean uric acid value was significantly greater in 28 patients with an annual eGFR decline greater than 3 ml/min/1.73 m^2 (rapidly progressive CKD) (7.6±1.6 mg/dl) compared to the annual mean uric acid value in 43 patients who had an annual eGFR decline less than 3 ml/min/1.73 m^2 (6.6±1.6 mg/dl) (p=0.012) (Table 5). However, baseline uric acid values were similar in both groups. The mean baseline uric acid values in patients with rapidly progressive CKD and slowly progressive CKD were 7.4±2.1 mg/dl and 7.0±1.8 mg/dl, respectively (p=0.419). A Cox regression analysis revealed a significant correlation between an eGFR decline greater than 3 ml/min/1.73 m^2 per year and the annual mean uric acid value (exp B:1.066, P=0.022 95% CI=1.009-1.125) (Table 6).

No statistically significant difference was found between 49 patients with uricemia (defined as serum uric acid levels greater than 7 mg/dl in males and 6 mg/dl in females) at the baseline and 22 patients without uricemia in the mean annual eGFR decline (2.9±4.5 ml/min vs. 2.0±2.71 ml/min, p=0.894) (Table 7). No significant associations were found between hyperuricemia and sex, CKD etiology, smoking status, hypertension, hyperlipidemia, or CAD.

20 Patients continued to receive allopurinol during the follow-up. Baseline serum uric acid levels were significantly higher in patients who were on allopurinol (8.6±2.1 mg/dl) compared to those who were not on allopurinol (6.7±1.7 mg/dl) (p=0.0001) and baseline eGFR was significantly lower in patients who were on allopurinol (40.8±9.6 ml/min/1.73 m^2) compared to those who were not (46.8±11.3 ml/min/1.73 m^2) (p=0.038) whereas the mean annual eGFR decline in patients who were on allopurinol did not differ significantly from that in patients who were not on allopurinol (2.2±2.4 ml/min/1.73 m^2 vs. 3.2±4.3 ml/min/1.73 m^2, respectively, p=0.323).

Table 2. Annual kidney function test results

Parameter	Baseline	Year 1	Year 2	Year 3	Year 4
BUN (mg/dl) (mean±SD)	26.6±9	25.4±9.9	23.9±7.2	27.7±11.3	39.3±22.2
CREATININE (mg/dl) (mean±SD)	1.52±0.34	1.55±0.39	1.56±0.42	1.69±0.43	1.77±0.54
GFR (ml/min/1.73 m^2) (mean±SD)	45.7±11.2	45.7±12.8	45.2±14.9	45.0±12.2	38.8±13.6

Table 3. Pearson's Correlation Analyses for annual eGFR decline

Variation	Pearson's coefficient	p
Age	0.136	0.258
BMI (kg/m^2)	-0.027	0.823
SBP (mmHg)- Year 1	-0.131	0.279
DBP (mmHg)- Year 1	-0.124	0.308
BUN (mg/dl) - Baseline	0.039	0.749
Creatinine (mg/dl)- Baseline	-0.103	0.391
Sodium (mEq/l)	-0.050	0.680
Potassium (mEq/l)	0.103	0.395
Calcium (mg/dl)	0.152	0.210
Uric Acid (mg/dl) - Baseline	-0.134	0.264
Uric Acid (mg/dl) - Year 1	0.238	0.046
eGFR (ml/min/1.73 m^2)- Baseline	-0.241	0.044
Albumin (g/dl)- Baseline	-0.395	0.001
Proteinuria (mg/day) Baseline	0.175	0.168

Table 4. Factors Associated with Annual eGFR Decline in a Multivariate Analysis

Parameter	Beta	p	95% CI
Serum Albumin (g/dl)	-0.408	0.0001	(-5.849) -(-1.825)
GFR (ml/min/1.73 m^2) -Baseline	0.326	0.004	0.043-0.217
Uric Acid (mg/dl) - Year 1	0.267	0.017	0.136-1.329
Sex			
Female	0.100	0.439	(-1.294) -(-2.946)

Discussion

In this study, patients with higher mean serum uric acid levels showed a faster decline in the mean eGFR during the first year compared to those with lower serum uric acid levels. Similarly, significantly higher mean serum uric acid levels were detected in CKD with a rapid decline (>3 ml/ min/1.73 m^2) in eGFR during the first year. However, no association was found between baseline uric acid levels and the rate of kidney disease progression. Controversial results have been reported from studies investigating if serum uric acid level is an independent risk factor for the progression of chronic kidney disease. Kuo et al. investigated a potential relationship between hyperuricemia and the decline in kidney function in 63,785 patients during 12 years of follow-up.[6] This study included patients who had at least two uric acid measurements during 1 year of follow-up and a creatinine clearance higher than 60 ml/ min/1.73 m^2. In this study, a multivariate analysis showed a significant association between serum uric acid levels and eGFR after adjusting for age, sex, BUN, cholesterol, and fasting blood glucose level (every 1 mg/dl increase in serum uric level was associated with a decrease of 1 ml/min/1.73 m^2 in eGFR) and annual eGFR decline was found to be significantly greater in the hyperuricemia group compared to normouricemia group (two times higher in the hyperuricemia group — 2.5 ml/ min/1.73 m^2 — p< 0.001). In the hyperuricemia group, 22.6% of patients (n=2684) progressed to stage 3 or higher CKD whereas this rate was 10.2% in the normouricemia group (n=5280) at the end of the follow-up period. However, the rate of eGFR decline and the risk for the rapid e-GFR decline were found to be lower in the highest uric acid level group compared to the second-highest uric acid level group. Furthermore, baseline eGFR levels were significantly higher in the hyperuricemia group compared to the normouricemia group. Considering these two findings from the study, associations between hyperuricemia and increased rate of eGFR decline or CKD progression appear controversial. A study design similar to that of epidemiological studies may present a barrier to detecting a potential causal relationship between uric acid levels and eGFR in this study.[6] As with our study, several studies have failed to demonstrate an association between uric acid levels and CDK progression. A potential association between uric acid levels and CDK progression was investigated in 840 patients with stage 3 or 4 diseases in the "Modification of Diet in Renal Disease (MDRD)" study.[7] The uric acid level was not found to be an independent risk factor for CDK progression in this study at the end of 10 years of follow-up. A potential explanation for these conflicting results may be the reduced uric acid clearance that results in increased uric acid, even in the early stages of CKD.[8] In other words, uric acid levels may be a sensitive indicator of kidney dysfunction and the use of GFR instead of eGFR might exclude a possible association in the MDRD study.[7] Another shared feature between our study and this study was the exclusion of patients with diabetic nephropathy.

Choncol et al. retrospectively searched the Cardiovascular Health Study database to find out if uric acid levels correlated with CDK progression in patients aged 65 years and

Table 5. Comparisons between the group of patients with a eGFR decline > 3 ml/min/1.73 m^2 and the group of patients with a eGFR decline ≤3 ml/min/1.73 m^2

Variable	eGFR decline ≤3 ml/min n=43	eGFR decline >3 ml/min	p
Age	59.1±13.9	63.1±11.2	0.208
BMI (kg/m^2)	29.3±7.3	29.5±5.8	0.889
SBP (mmHg)- Year 1	139.9±21.1	143.6±21.8	0.48
DBP (mmHg)- Year 1	80.9±12.7	80.7±11.5	0.949
BUN (mg/dl) - Baseline	26.2±9.2	27.3±9.1	0.621
Follow-up duration (months)	17.8±9.9	16.4±10.4	0.095
Creatinine (mg/dl)- Baseline	1.6±0.3	1.5±0.3	0.351
Sodium (mEq/l)	140.9±3.6	140.8±3.8	0.82
Potassium (mEq/l)	4.6±0.6	4.8±0.5	0.175
Calcium (mg/dl)	9.5±0.6	9.7±0.6	0.258
Phosphorus (mg/dl)	3.4±0.5	3.4±0.8	0.954
Parathormone (pg/ml)	79.3±58.6	110.4±110.7	0.168
Hemoglobin (g/dl)	13.3±1.7	13.1±1.8	0.756
Ferritin (ng/ml)	118.3±150.2	177.5±225.1	0.306
Uric Acid (mg/dl) - Baseline	7.4±2.1	7.0±1.8	0.419
Uric Acid (mg/dl) - Year 1	6.6±1.6	7.6±1.6	0.012
GFR (ml/min/1.73 m^2)- Baseline	43.4±11.6	47.9±10.2	0.094
Mean annual GFR decline (ml/min/1.73 m^2)	0.4±0.8	6.8±4.0	0.0001
Albumin (g/dl)- Baseline	4.5±0.4	4.4±0.5	0.248
Proteinuria (mg/day) Baseline	214.5±186.1	462.8±244.4	0.074

Table 6. Correlations with an eGFR decline >ml/min/1.73 m^2 based on a COX regression analysis

Parameter	exp B	p	95% CI per ExpB
Sex	0.901	0.883	0.225 - 3.587
Uric Acid (mg/dl) - Year 1	1.066	0.022	1.009 - 1.125
Proteinuria (mg/day) Baseline	1.003	0.058	1.000 - 1.005
eGFR (ml/min/1.73 m^2) -Baseline	1.474	0.985	2.205 - 0.059

over.[9] A linear and strong correlation was detected between baseline uric acid levels and kidney dysfunction (eGFR < 60 ml/ min/1.73 m^2). However, no significant correlation was found between uric acid levels and kidney disease progression when eGFR was calculated using the Cockcroft-Gault(C-G) equation whereas a weak correlation was reported when eGFR was calculated using the MDRD formula. The strong correlation detected between kidney dysfunction and uric acid levels in this study supports the effect of kidney function on serum uric acid levels rather than a direct effect of serum uric acid levels on kidney functioning.

Sturm et al. investigated whether the level of uric acid might be a risk factor for disease progression in nondiabetic patients with CDH.[10] 227 patients aged from 18 to 65 years were included in this prospective study and followed up for 7 years. The endpoint of the study was defined as the doubling of serum creatinine or the need for initiating renal replacement therapy. Those who met the study's endpoint were older patients with higher serum creatinine levels, lower baseline eGFR, and higher serum uric acid levels (7.00+/-1.62 vs. 6.63+/-1.59 mg/dl, p=0.14).[10] The use of uric acid lowering agents was significantly more prevalent in this patient group, although a Cox regression analysis failed to show that uric acid was an independent risk factor for disease progression (p<0.12, p<0.57). A significant association was found between uric acid levels and disease progression in an analysis performed after excluding patients on uric acid lowering medications (p<0.02) but subsequent analysis eliminated such association after the adjustments for GFR and proteinuria.

In summary, in the literature, there are controversial publications on whether uric acid levels present a risk factor for disease progression. Although several observational studies reported that serum uric acid levels might play a role in disease progression,[6,11-13] other observational studies have failed to demonstrate a cause-and-effect relationship.[9,10,14] Considering publications claiming that uric acid might be an independent risk factor for kidney disease progression,[1,12,13] one may suggest that multiple measurements taken over a predefined period could better reflect disease progression compared to a single uric acid measurement, as the result of a single measurement may be affected by simultaneous dietary protein intake or any factor that may

Table 7. Comparisons between patients with serum uric acid levels > 7 mg/dl (males) or >6 mg/dl (females) and patients with serum uric acid levels ≤ 7 mg/dl (males) or ≤6 mg/dl (females)

Parameter	Patients Baseline uric acid levels >6/7 mg/dl (n=49)	Patients Baseline uric acid levels ≤6/7 mg/dl (n=22)	p
Age	62.6±11.7	56.3±14.6	0.055
BMI (kg/m^2)	29.9±7.6	28.2±3.8	0.307
SBP (mmHg)	141.4±22.4	141.1±19.1	0.957
DBP (mmHg)	81.1±13.1	80.0±10.0	0.434
BUN (mg/dl) - Baseline	26.3±10.0	23.5±9.9	0.919
Follow-up duration (months)	17.1±9.8	17.6±10.9	0.850
Creatinine (mg/dl)- Baseline	1.5±0.3	1.5±0.4	0.648
Sodium (mEq/l)	140.0±3.9	141.3±3.5	0.177
Potassium (mEq/l)	4.7±0.5	4.7±0.7	0.891
Calcium (mg/dl)	9.6±0.6	9.5±0.7	0.400
Phosphorus (mg/dl)	3.4±0.7	3.3±0.5	0.444
Parathormone (pg/ml)	88.5±90.6	99.9±64.1	0.645
Hemoglobin (g/dl)	13.1±1.6	13.5±2.0	0.454
Ferritin (ng/ml)	127.5±149.3	172.0±241.8	0.460
eGFR (ml/min)- Baseline	43.5±10.5	49.0±12.2	0.058
Albumin (g/dl)	4.5±0.4	4.4±0.4	0.494
Proteinuria (mg/day)	320±217.2	261±215.5	0.695
Mean annual eGFR decline (ml/min)	2.9±4.5	2.0±2.71	0.894

cause temporary changes in eGFR. Negative correlations were found between baseline uric acid levels and baseline eGFR (Pearson's correlation coefficient=-0.2811, p=0.018) as well as between uric acid levels at Year 1 and eGFR at Year 1 (Pearson's correlation coefficient=-0.261, p=0.028) whereas no significant correlation was found between baseline uric acid levels and eGFR at Year 1 (Pearson's correlation coefficient=-0.123, p=0.305) in additional correlation analyses that we performed to address this question. These data provide support to the assumption that increases in uric acid levels mainly result from the decline in eGFR. Associations were found between higher uric acid levels and old age, male sex, smoking, higher BMI, increased hypertension prevalence, diabetes, antihypertensive medication, and particularly, the use of diuretics, in the same study conducted by Chonchol et al.[9]

As with prior studies, we detected a significant association between male sex and rapid progression of kidney disease.[15] In this study, we have demonstrated a significant association between lower baseline eGFR and eGFR decline per year in a multivariate analysis. Similarly, in a meta-analysis conducted by Hallan et al., lower baseline eGFR was found to be a risk factor for ESRD and mortality, independently from other variables.[16]

In our study, another variable that negatively correlated with eGFR decline was serum albumin level. Similarly, Chen et al. investigated possible associations between the renal outcome in CKD and left atrial diameter or serum albumin level, in a study with 395 participants.[17] Participants were divided into four groups based on median LAD ("left atrial diameter") index and serum albumin levels. A significant association was found between albumin levels and the LAD index (β= -0.108, p=0.024). 74 patients were started on dialysis during the follow-up. Multivariate analysis revealed that renal function rapidly deteriorated and initiation of dialysis was more common in the group of patients with higher LAD index and lower serum albumin levels.

One of the limitations of our study was the retrospective design and small study sample (n=71). Furthermore, the use of eGFR instead of GFR in staging chronic kidney disease or measuring renal functioning might affect the results of our study.

In conclusion, uric acid was not found to be an independent risk factor for disease progression in patients with stage 2 or 3 chronic kidney disease in this study and this finding suggests that hyperuricemia may result from the deterioration of kidney function rather than being a determinant of disease progression. The effects of uric acid levels on chronic kidney disease may potentially vary based on the etiology or stage of the kidney disease. Therefore, prospective studies designed considering all these factors that may have an impact on serum uric acid levels might better reflect a cause-and-effect relationship between uric acid levels and kidney disease.

Disclosures

Ethics Committee Approval: The study was approved by Marmara University Medical Faculty Ethical Committee (09.2013.0137).

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References

1. Ohno I, Hosoya T, Gomi H, Ichida K, Okabe H, Hikita M. Serum uric acid and renal prognosis in patients with IgA nephropathy. Nephron 2001;87(4):333–9.
2. Iseki K, Ikemiya Y, Inoue T, Iseki C, Kinjo K, Takishita S. Significance of hyperuricemia as a risk factor for developing ESRD in a screened cohort. Am J Kidney Dis 2004;44(4):642–50.
3. Sánchez-Lozada LG, Tapia E, Santamaría J, Avila-Casado C, Soto V, Nepomuceno T, et al. Mild hyperuricemia induces vasoconstriction and maintains glomerular hypertension in normal and remnant kidney rats. Kidney Int 2005;67(1):237–47.
4. Bellomo G, Venanzi S, Verdura C, Saronio P, Esposito A, Timio M. Association of uric acid with change in kidney function in healthy normotensive individuals. Am J Kidney Dis 2010;56(2):264–72.
5. Goicoechea M, de Vinuesa SG, Verdalles U, Ruiz-Caro C, Ampuero J, Rincón A, et al. Effect of allopurinol in chronic kidney disease progression and cardiovascular risk. Clin J Am Soc Nephrol 2010;5(8):1388–93.
6. Kuo CF, Luo SF, See LC, Ko YS, Chen YM, Hwang JS, et al. Hyperuricaemia and accelerated reduction in renal function. Scand J Rheumatol 2011;40(2):116–21.
7. Madero M, Sarnak MJ, Wang X, Greene T, Beck GJ, Kusek JW, et al. Uric acid and long-term outcomes in CKD. Am J Kidney Dis 2009;53(5):796–803.
8. Johnson RJ, Kang DH, Feig D, Kivlighn S, Kanellis J, Watanabe S, et al. Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? Hypertension 2003;41(6):1183–90.
9. Chonchol M, Shlipak MG, Katz R, Sarnak MJ, Newman AB, Siscovick DS, et al. Relationship of uric acid with progression of kidney disease. Am J Kidney Dis 2007;50(2):239–47.
10. Sturm G, Kollerits B, Neyer U, Ritz E, Kronenberg F; MMKD Study Group. Uric acid as a risk factor for progression of nondiabetic chronic kidney disease? The Mild to Moderate Kidney Disease (MMKD) Study. Exp Gerontol 2008;43(4):347–52.
11. Syrjänen J, Mustonen J, Pasternack A. Hypertriglyceridaemia and hyperuricemia are risk factors for progression of IgA nephropathy. Nephrol Dial Transplant 2000;15(1):34–42.
12. Ficociello LH, Rosolowsky ET, Niewczas MA, Maselli NJ, Weinberg JM, Aschengrau A, et al. High-normal serum uric acid increases risk of early progressive renal function loss in type 1 diabetes: Results of a 6-year follow-up. Diabetes Care 2010;33(6):1337–43.
13. Bo S, Cavallo-Perin P, Gentile L, Repetti E, Pagano G. Hypouricemia and hyperuricemia in type 2 diabetes: Two different phenotypes. Eur J Clin Invest 2001;31(4):318–21.
14. Madero M, Sarnak MJ, Wang X, Greene T, Beck GJ, Kusek JW, et al. Uric acid and long-term outcomes in CKD. Am J Kidney Dis 2009;53(5):796–803.
15. Levin A, Djurdjev O, Beaulieu M, Er L. Variability and risk factors for kidney disease progression and death following attainment of stage 4 CKD in a referred cohort. Am J Kidney Dis 2008;52(4):661–71.
16. Hallan SI, Matsushita K, Sang Y, Mahmoodi BK, Black C, Ishani A, et al; Chronic Kidney Disease Prognosis Consortium. Age and association of kidney measures with mortality and end-stage renal disease. JAMA 2012;308(22):2349–60.