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Value Of Uric Acid In Patients With Chronic Kidney Disease In Pre-Dialysis Stage

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ABSTRACT

The study examined the relationship between uric acid levels and renal function, as well as its role as a prognostic marker of cardiovascular risk in chronic kidney disease. In a multivariate regression analysis, taking into account the adjustment of potential risk factors, the level of uric acid was a significant factor affecting the glomerular filtration rate. The results of the study showed that elevated serum uric acid levels are associated with a higher risk of renal dysfunction.

KEY WORDS: *chronic kidney disease, uric acid, hyperuricemia, prognosis*

INTRODUCTION

In recent decades, the prevalence of hyperuricemia has increased due to an aging population, the wider use of drugs that can cause hyperuricemia and obesity [5, 9,13, 14]. Hyperuricemia is associated with poor quality of life, with joint dysfunction, decreased fertility and the risk of death [6, 7, 10]. Studies show that hyperuricemia is an independent risk factor for cardiovascular morbidity and mortality in both women and men [1, 2, 11]. Given the prevalence and significance of hyperuricemia, it seems necessary to identify factors that impede the optimal treatment of hyperuricemia in both women and men in order to ensure individual therapeutic measures.

However, it has been proven that arterial hypertension leading to nephrosclerosis is exacerbated in the presence of metabolic disorders such as hyperuricemia, hyperglycemia and dyslipidemia. Even with an uncomplicated course of essential hypertension, a moderate decrease in glomerular filtration rate leads to a doubling of the risk of cardiovascular mortality, while blood pressure is in the range 130–139 / 85–89 mm Hg. associated with an increase in the risk of developing albuminuria by more than two times in comparison with patients with lower blood pressure.

A growing number of studies are exploring the possible association of uric acid levels with renal function, especially with nephrotic proteinuria, and its role as a prognostic marker of cardiovascular risk in chronic kidney disease.

The aim of our study was to study the relationship between uric acid levels and renal function, as well as its role as a prognostic marker of cardiovascular risk in chronic kidney disease.

MATERIALS AND METHODS

A prospective study included 200 patients with chronic kidney disease aged 34 to 70 years (mean age 51.6 ± 1.1 years). The study did not include patients with a duration of chronic kidney disease of less than 5 years, with a single kidney, hemodynamically significant renal vascular stenosis, and cancer. All patients underwent general clinical and instrumental research. The examination of patients included a general examination, assessment of complaints, collection of medical history data, identification of risk factors for the development and progression of chronic kidney disease. During a biochemical blood test, the following parameters were determined: urea, creatinine, residual nitrogen, bilirubin, transaminases, uric acid. Blood samples were collected on an empty stomach in the morning, after at least 10 hours of fasting. Blood samples were processed in a clinical laboratory. Serum glucose concentration was measured using a modified enzymatic hexokinase method. A study of the lipid spectrum of the blood. In order to assess the functional state of the kidneys, all patients underwent calculation of glomerular filtration rate according to the CKD-EPI formula, modification 2011. Stratification

of chronic kidney disease by the degree of decrease in glomerular filtration rate, as well as the degree of albuminuria was carried out according to the classification of KDIGO 2013 and HONP 2012.

In order to study the role of hyperuricemia as an independent risk factor for the development and progression of chronic kidney disease, we analyzed the data of 200 patients with this pathology who were hospitalized. All subjects were measured blood pressure, uric acid level and the glomerular filtration rate was calculated.

RESULTS

The results of the study showed that the average concentration of uric acid in the group of patients with chronic kidney disease C2 was 268.41 ± 15.33 μmol / L, in the group of patients with chronic kidney disease C3a - 376.63 ± 18.46 μmol / L, in the group patients with chronic kidney disease C3b - 371.82 ± 19.14, in the group of patients with chronic kidney disease C4 - 291.94 ± 12.36. Compared to men with hyperuricemia, women with hyperuricemia were older (71 vs 61 years old, p <0.001) and had a greater severity of concomitant diseases (p <0.001, such as hypertension, diabetes mellitus and obesity). Risk factors for hyperuricemia differed from women who were more likely to take diuretics (p <0.001), while men more often had dietary triggers (p <0.05).

The analysis showed that the average uric acid level in patients with chronic kidney disease in men exceeds the norm by 16% (489.3 μmol / L), and in women - by 12% (394.1 μmol / L) (Table 1).

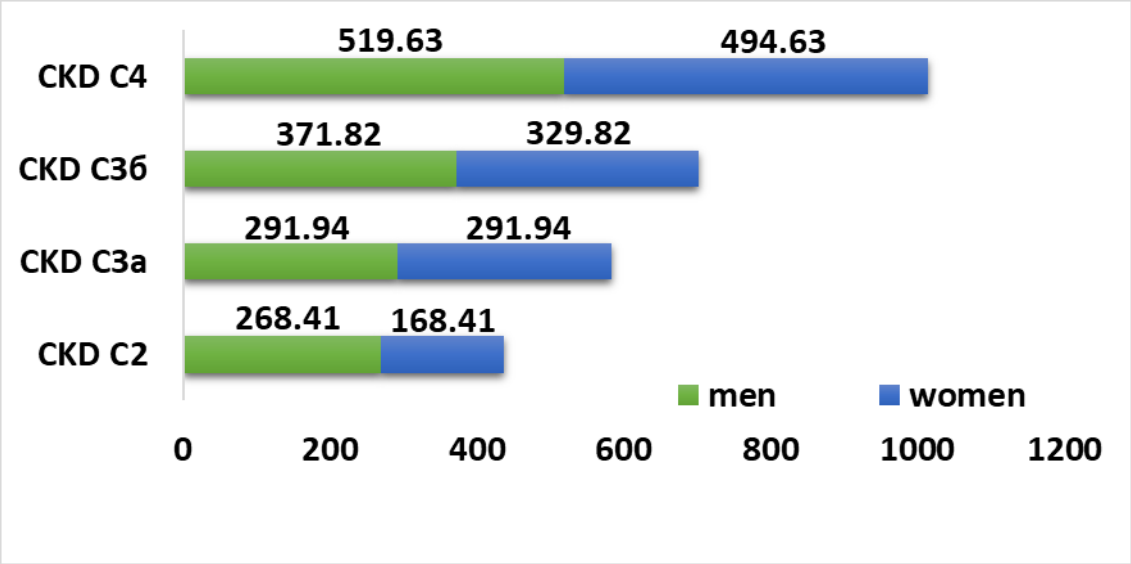
Table 1. Biochemical parameters in the studied groups of patients with pre-dialysis stages of chronic kidney disease

Indicator	CKD C2 n=114	CKD C3a n=48	CKD C3б n=28	CKD C4 n=10
MK, μmol / L, men, 202.3-416.5 μmol / L	268,41±15,33	291,94±12,36$^{\Delta,\circ,\square}$	371,82±19,14*	519,63±18,46*
MK, μmol / l, women Norm 142.8-339.2	168,41±15,33	291,94±12,36$^{\Delta,\circ,\square}$	329,82±19,14*	494,63±18,46*
Глюкоза крови, ммоль/л	4,72±0,25	5,54±0,19*$^{,\Delta}$	4,74±0,18$^{\Delta,\#}$	4,89±0,17$^{\Delta,}$
GFR, ml / min	75,60±7,31	52,81±7,49	37,95±7,13$^{*,\Delta,\#,+}$	25,80±6,80*
XC total, mmol / l	5,26±0,261	6,09±0,213*	5,29±0,221$^{\Delta,\#}$	5,53±0,228$^{\Delta}$
TG, mmol / l	1,43±0,30	2,66±0,115*	2,88±0,121 $^{\Delta,\#}$	3,49±0,118 $^{\Delta}$

Note: * - P <0.05 compared with the control, Δ - P <0.05 compared with the outcome, ° - P <0.05 compared with 1g., P <0.05 compared with the third group.

In different age groups of patients, it was possible to trace the relationship between the level of uric acid in blood serum and the stage of chronic kidney disease: in the group of young men p> 0.05 (p = 0.06), k = 0.5; in the middle-aged group - p <0.01 (p = 0.01), k = 0.9; in the elderly group, p <0.01 (p = 0.01), k = 0.9. In the groups of middle-aged and elderly patients, a stronger correlation was found between the level of uric acid and the stages of CKD. In the same groups, a higher average level of uric acid was noted (Fig. 1).

Fig. 1. The average level of uric acid in patients with chronic kidney disease (µmol / L)



Among the studied patients, patients with C4 stage chronic kidney disease recorded the highest average level of uric acid, namely: 519 µmol / L in men and 454.8 µmol / L in women. The study found that with the progression of chronic kidney disease, the average level of uric acid increases.

In addition, a strong correlation was found between the level of uric acid and albuminuria r = 0.7, p <0.05. When dividing patients depending on the presence / absence of arterial hypertension, the strongest correlation between the level of uric acid and CKD was revealed: r = 0.9, p <0.01. In turn, in the group of patients with no hypertension, this correlation is also traced, but less significant: r = 0.7, p <0.05.

Then, the examined individuals were divided into four groups in accordance with the quartile of the initial concentration of uric acid; in all the groups examined, the glomerular filtration rate was compared. A relationship was found between the level of uric acid and systolic blood pressure (Q1 - 110.9, Q2 - 110.1, Q3 - 112.8, Q4 - 116.1 mmHg, respectively), as well as between the concentration of uric acid and glomerular filtration rates (P <0.01). In a multivariate regression analysis, taking into account the adjustment of potential risk factors, including age, gender, body mass index, systolic blood pressure and lipids, uric acid level was found to be a significant factor affecting the glomerular filtration rate (β = -0.335, P <0, 01). The results of the study showed that elevated serum uric acid levels are associated with a lower estimated glomerular filtration rate.

Thus, the profiles of women and men with hyperuricemia were markedly different, which indicates the need to take into account gender differences. The relationship between the level of uric acid and the lipid spectrum in the blood was established in patients with asymptomatic hyperuricemia in various stages of chronic kidney disease.

DISCUSSION

The level of uric acid was evaluated, the dependence of the level of hyperuricemia on the age of patients, the stage of the disease, the presence of arterial hypertension was studied. The most significant hyperuricemia was detected in patients with stage C4 chronic kidney disease. Thus, hyperuricemia can be used as an additional marker of the progression of chronic kidney disease along with albuminuria.

Shiori Nagano et al. (2017) demonstrated a relationship between serum uric acid concentration and arterial stiffness and kidney function in people with normal blood pressure. It is known that an increase in serum uric acid correlates with an increased risk of not only gout, but also cardiovascular disease.

Currently, the most important role in the development of renal pathology is played by metabolic disorders often found in civilized countries: type 2 diabetes mellitus, obesity, hyperuricemia, as well as hypertension, often existing in association with other symptoms, which is referred to as "Metabolic syndrome."

Obviously, metabolic disorders, along with essential arterial hypertension, are key determinants of the gradual deterioration of kidney function in the general population. Noteworthy is the commonality of risk factors for chronic kidney disease and cardiovascular diseases, as well as the commonality of key pathogenesis of diseases of the cardiovascular system and renal lesions caused by metabolic disorders, among which endothelial dysfunctions play a special role, markers of which, in particular, al ¬ buminuria, always reflect the high probability of corresponding complications. Attention to these risk factors is important because the associated forms of kidney damage and chronic kidney disease are modifiable.

At the same time, kidney damage (active nephritis, nephrotic syndrome, renal failure) lead to severe disorders of various types of metabolism - purine, lipid, phosphorus-calcium. The adverse effects of metabolic disturbances in relation to the kidneys are realized both through the direct toxic effect of metabolites on the renal structures, and indirectly through renal hemodynamic disorders. Metabolic disorders not only cause and accelerate the development of nephrosclerosis, but also lead to cardiovascular complications, worsening the overall prognosis.

Hyperuricemia occurs with high frequency in patients with arterial hypertension, diabetes mellitus and obesity. Apparently, there is a genetic community between these disorders. In addition, a wide role in the development of disorders of purine metabolism is played by the widespread use of diuretics, primarily thiazides. There is a close correlation between hyperuricemia and chronic kidney disease: an increase in uric acid levels may be a consequence of decreased kidney function, on the other hand, hyperuricemia can lead to chronic kidney diseases (chronic interstitial nephritis, stone formation) and acute kidney damage (urate crisis).

The adverse effect of hyperuricemia on systemic blood pressure, renal hemodynamics, and endothelial condition was demonstrated. The damaging effect of elevated uric acid levels is apparently associated with the initiation of endothelial dysfunction and chronic systemic inflammation, a slowdown in oxidative metabolism, platelet adhesion, impaired blood rheology and aggregation [3, 12, 15].

Moreover, data from epidemiological studies on the role of hyperuricemia as a possible independent risk factor for cardiovascular complications and terminal renal failure are insufficient. According to a number of studies, the concentration of uric acid in serum significantly correlates with the severity of abdominal obesity and triglyceridemia, and in patients with arterial hypertension and hyperuricemia, left ventricular hypertrophy is more common [5, 9].

It is important to emphasize that many factors associated with renal dysfunction are simultaneously traditional risk factors for cardiovascular diseases such as arterial hypertension, diabetes mellitus, male gender, age, dyslipidemia, obesity, metabolic syndrome, and smoking.

At the same time, the results of numerous studies indicate that the so-called non-traditional risk factors for the progression of cardiovascular diseases are most likely due to progressive renal dysfunction. These include oxidative stress, anemia [8], chronic inflammation, hyperhomocysteinemia, increased synthesis of asymmetric dimethylarginine, activation of the renin-angiotensin-aldosterone system, stress, hyperuricemia, natriuretic factors, etc. (Yesayan

A.M., 2002, Mukhin et al. ., 2004, Smirnov et al., 2005, Saito A. et al., 2010). Among them, an important role is played by hyperuricemia.

A reliable correlation was found between the level of uric acid and albuminuria as a proven factor in the progression of chronic kidney disease: $p < 0.05$ ($p = 0.02$), $k = 0.8$.

Based on the results obtained, it can be hypothesized that hyperuricemia can be used as an independent marker for the progression of chronic kidney disease along with albumuria.

Thus, in chronic kidney disease, an increase in the level of uric acid was revealed, which is more significant in the group of patients with C4 stage. The strongest correlation between the level of uric acid and the age of patients was detected in patients of middle and elderly age groups. A stronger correlation was found between the level of uric acid and the stage of chronic kidney disease in the group of patients with arterial hypertension compared with the group of patients with normal blood pressure.

Data on the presence of a strong correlation between uric acid levels and albuminuria as a proven factor in the progression of chronic kidney disease suggest that hyperuricemia can be used as an independent marker of the progression of chronic kidney disease along with albuminuria.

Thus, it is reasonable to determine the concentration of uric acid in patients with advanced stages of chronic kidney disease due to the fact that hyperuricemia exacerbates the long-term regular use of diuretics in significant doses. Moreover, the intensity of uric acid formation is a marker of the severity of systemic oxidative (free radical) tissue damage, and its high level in the blood is a predictor of a poor prognosis of patients with chronic kidney disease. Therefore, it is necessary to determine the level of uric acid in patients with chronic kidney disease in order to determine the prognosis.

CONCLUSION

In a multivariate regression analysis, taking into account the adjustment of potential risk factors, including age, gender, body mass index, systolic blood pressure and lipids, the level of uric acid was a significant factor affecting the glomerular filtration rate. The results of the study showed that elevated serum uric acid levels are associated with a higher risk of renal dysfunction.

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