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Original article

An Analysis of Laboratory Parameters of Chronic Kidney Failure in Elderly Patients

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SUMMARY

Aim: The chief aim of this study was monitoring of laboratory parameters of chronic kidney failure in elderly patients.
Methods: All samples were taken and processed by standard methods and according to the principles of good laboratory practice. Data were collected in an organized and systematic manner in the form of a questionnaire with respect to ethical principles and as such were analyzed by statistical tests and analyses (Student's t-test, Analysis of variance-ANOVA, Pearson's and Spearman's correlation coefficients). The limit of statistical significance was set at $p < 0.05$.
Results: Mean values of creatinine clearance and proteinuria for the total study population were: 41.30 ± 21.43 mL/min, 1.5 ± 2.3 g/L/24 h, respectively. Hematological parameters did not significantly differ from normal values. The highest frequency of comorbidities was observed in subjects aged ≥ 80 years with an average of 2.03 comorbidities per subject. Serum creatinine and urea values as well as creatinine clearance are good indicators of disease progression.
Conclusion: The results of the presented research suggest that old age is a predisposing risk factor for the development of chronic kidney disease, and that in combination with comorbidities (hypertension and/or diabetes), it contributes to poor prognosis or disease progression.

Keywords: **older age, chronic kidney disease, GFR, proteinuria**

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INTRODUCTION

The increase in the number of elderly people in the general population or aging of the population has long been recognized as a phenomenon that is taking on global proportions and has multiple consequences for society (1). Aging is a natural and universal process that is often described by the acronym-CUPUR (cumulative, universal, progressive, internal, destructive process) (2). This period of life is characterized by anatomical and physiological changes that give predispositions for the development of certain diseases that have a significantly higher frequency in the elderly than in other age groups (3). These diseases certainly include chronic kidney disease for which age is a predisposing risk factor (4). According to the KDIGO guidelines (kidney disease improving global outcomes), chronic kidney disease is defined as damage to the kidney or reduction of its function for a minimum of three months, regardless of the cause, and has consequences for health. Also, according to these guidelines, grading of the disease is done depending on the value of glomerular filtration and albuminuria (5). Research shows that the most common underlying diseases are hypertensive and diabetic nephropathy in patients in developed and developing countries. Other diseases are considerably less common (glomerulonephritis, pyelonephritis, obstructive diseases, tumors, endemic nephropathy, etc.). In addition, hypertension and diabetes are the most common comorbidities of chronic kidney disease, therefore, it is difficult to distinguish whether they are initiating or progressive risk factors (6 - 8). There are several approaches in the diagnosis of this disease, but laboratory tests are considered optimal and include a wide range of tests, the most important of which are: glomerular filtration (creatinine clearance or estimated eGFR), proteinuria and/or albuminuria, urea, creatinine, urine sediment analysis (6, 9, 10). Given that the basis of this disease is a deterioration of the nephron, which is irreversible, timely diagnosis and recognition of progression play a key role in the treatment of chronic kidney disease (7, 4, 11).

METHODS

The study was designed as a retrospective observational study. A total of 100 elderly respondents (≥ 60 years) were included, who were divided into three groups according to age: 60 - 69 years, 70 - 79 years, ≥ 80 years. The study used the personal and anamnestic data of the subjects (sex, age, primary/secondary kidney disease, comorbidities) and the results of laboratory tests (creatinine clearance, daily proteinuria, diuresis, glycosuria, sediment finding, complete blood count, non-protein nitrogenous compounds and blood). Blood and urine were used as samples for laboratory tests. All samples were taken and processed by standard methods and according to the principles of good laboratory practice. Data were collected in an organized and systematic manner in the form of a questionnaire with respect to ethical principles and as such were analyzed by statistical tests and analyzes (Student's t- test, Analysis of variance-ANOVA, Pearson's and Spearman's correlation coefficients). The limit of statistical significance was set at $p < 0.05$.

RESULTS

The research included 100 respondents, 63 men and 37 women. The ratio of men to women was 1.7. The average age in the total population of respondents was 74.94 years. Respondents were divided according to age into three groups: early older age 60 - 69 years (n = 34), middle-aged 70 - 79 years (n = 37), deep age ≥ 80 years (n = 29). There were more men than women in each age group.

The prevalence of chronic kidney disease was higher in women than in men, but the probability of disease progression was higher in men, and most subjects were hospitalized for worsening of the disease, i.e. impairment of renal function (12, 13). In the total examined population, secondary diseases had the highest frequency: hypertension and diabetes (Figure 1).

The results of clinical-biochemical and hematological tests were also used in the research and are summarized in Table 1. The values of the mentioned laboratory parameters were analyzed according to age groups and in relation to gender. There were statistically significant differences in the value of creatinine clearance between age groups (Figure 2). The values of glomerular filtration-GFR (clearance test or estimated GFR-eGFR) and serum creatinine are still considered optimal laboratory parameters for the progression of chronic kidney disease (14).

In contrast, serum urea levels did not show statistically significant differences between age groups (Figure 3). The values of hematological pa-

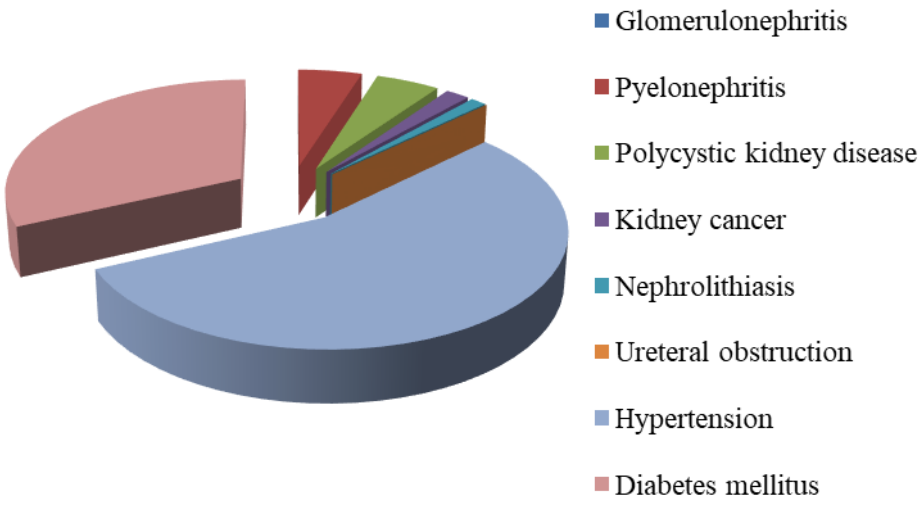

Figure 1. *The incidence of underlying kidney disease*

Table 1. *Laboratory parameters in the total study population*

Parameter (unit of measure)	Mean value	Standard error	Standard deviation	Minimum value	Maximum value
Serum creatinine (μmol/L)	209.3	12.6	125.7	73	683
Urea (mmol/L)	13.7	0.6	6.2	5.8	34.8
Uric acid (μmol/L)	444.8	11.1	111.7	251	945
Glucose (mmol/L)	6.9	0.2	2.2	4.1	16.2
Creatinine clearance (mL/min)	41.3	2.1	21.4	5	104
Protein in 24 h urine (g/L)	1.5	0.2	2.3	0.01	12.5
Diuresis (mL/24 h)	1696.1	67.5	675.2	600	3950
Erythrocytes (10^{12}/L)	4.3	0.07	0.6	2.6	6.3
Hemoglobin (g/L)	128.3	2.06	20.6	82	181
Hematocrit (%)	39.8	0.6	6.6	25.9	64,9
MCV (fL)	91.1	0.5	5.01	75.7	104
MCH (pg)	29.7	0.1	1.8	23	34.6
MCHC (g/L)	323.4	1.9	19.0	180	366
Leukocytes (10^9/L)	7.8	0.1	1.7	3.8	12.4
Platelets (10^9/L)	212.6	6.1	61.2	101	387

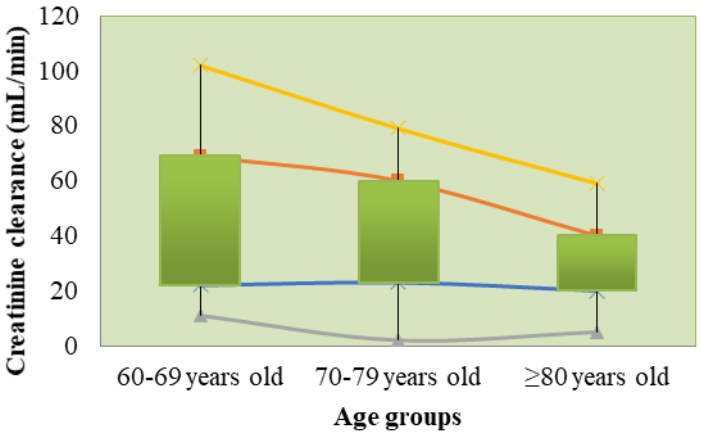

Figure 2. *Differences in creatinine clearance*

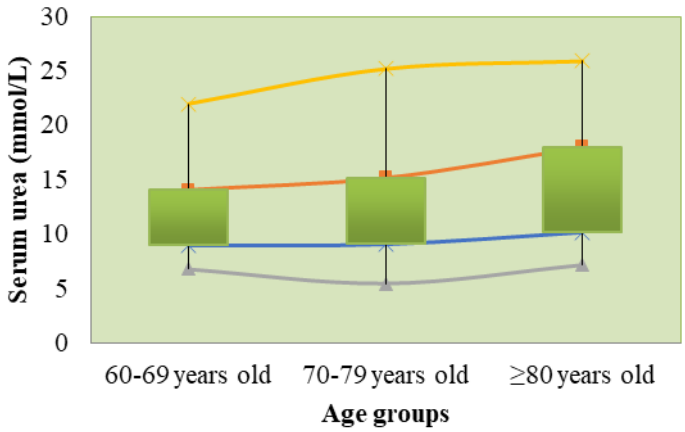

Figure 3. *Differences in urea levels between age groups*

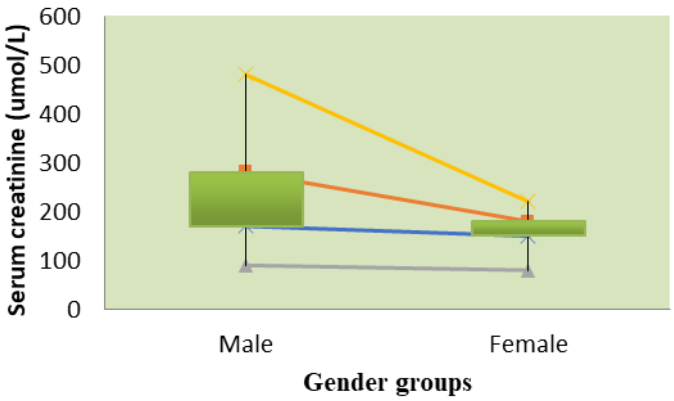

Figure 4. *Differences in creatinine levels between gender groups*

rameters were mainly within the reference values both in the total study population and by age groups of subjects. In relation to gender, statistically significant differences were found for the parameters of serum creatinine (p = 0.009) (Figure 4), urea (p = 0.023) and MCV (p = 0.028).

DISCUSSION

The results of the frequency of hypertension and diabetes in our study agree with the data from the literature (12). When it comes to comorbidities, the following comorbidities were found in the total population: myocardial infarction (n = 13), ictus cerebrovascularis (n = 12), diabetes mellitus (type 1 n = 0, type 2 n = 28, type 2b n = 24), hypertension (n = 90), anemia (n = 22), mineral-bone disease (n = 6). The most common comorbidities are hypertension and diabetes (12). The highest frequency of comorbidities was in subjects of the third age group (≥ 80 years) and averaged 2.03 per subject. The frequency of comorbidities correlates with the age of the patients and with the prognosis of the disease (15). According to the CKD (chronic kidney disease) classification of the degree of damage, all subjects were classified on the basis of GFR values; the frequency of individual degrees of damage in the total examined population was: degree I (n = 2), degree II (n = 20), II/III, degree IIIa (n = 21), degree IIIb (n = 17), degree IV (n = 25), degree V (n = 9). It was found that the lowest average degree of impairment was in the first age group (60 - 69 years) and was $\acute{X}$ = 4.00; in the middle age group (70 - 79 years) it was $\acute{X}$ = 4.38, and in the third age group (≥ 80 years) it was $\acute{X}$ = 4.97.

In relation to gender, the most frequent degree of impairment was higher in men (degree IV, n = 18) than in women (degree IIIa, n = 11), which is in accordance with the data from the literature (12, 15). Statistical values for urine proteins differed significantly between the first and second (p = 0.045) and the first and third age group (p = 0.016). Proteinuria is an indicator of disease progression with the assumption of correct interpretation of urine protein findings. The normal finding of proteinuria in patients with advanced disease should be interpreted in the context of nephrosclerosis, which is why this finding is seemingly paradoxical (16). Serum creatinine and urea levels depend primarily on muscle mass and diet, respectively, as laboratory parameters are traditionally used in the assessment of renal function.

As the male sex on average has higher muscle mass and different eating habits compared to women, the differences in the concentration of the mentioned parameters are interpreted in the context of physiological differences between the sexes (17, 18). Most subjects had a normal urine sediment finding, only one subject had a renal cell finding in the sediment, 79% had a negative bacterial finding, ten subjects had a cylinder finding in the sediment (granular n = 9, hyaline n = 1). Also, the finding of erythrocytes and leukocytes in the sediment was abnormal in a small number of subjects (n = 21, n = 24, respectively). The finding of urine sediment is of great importance in assessing the severity of renal damage in relation to biochemical tests that show abnormal values when the disease has already progressed, while renal biopsy is an invasive procedure. A urine sediment finding is often called a "liquid renal biopsy" (19).

Statistical significance of differences between age groups was examined by Analysis of variance (ANOVA), statistically significant differences were found for creatinine clearance parameters (F = 3.993; p = 0.022) and protein in 24h urine (F = 4.173; p = 0.018). Low protein values in 24-hour urine in elderly subjects are the result of nephrosclerosis, which is more common in the elderly, and a sharp decline in proteinuria in elderly patients is considered a poor prognostic sign (16, 20).

Examination of the Pearson's and Spearman's correlation coefficients revealed a significant negative correlation between creatinine clearance and the degree of impairment of renal function-CKD (-0.983; p < 0.001) and between age and creatinine clearance (-0.229; p = 0.022). As expected, a strong negative correlation was found between serum creatinine and creatinine clearance (-0.692; p < 0.001), but also urea and creatinine clearance (-0.641; p < 0.001). Serum creatinine correlated with urea value (0.788; p < 0.001).

The erythrocyte value correlated with the level of serum creatinine (-0.400; p < 0.001) and urea (-0.515; p < 0.001). Correlations of hematological parameters were also determined: erythrocytes-hematocrit (0.851; p < 0.001), hemoglobin-MCHC (0.827; p < 0.001), MCV-MCH (0.529; p < 0.001). The hematocrit value correlated with urea levels (-0.466; p < 0.001). Anemia associated with chronic kidney disease is mostly normocytic and normochromic,

caused by a deficiency of erythropoietin that is synthesized in the kidneys. Anemia is one of the leading comorbidities of chronic kidney disease, so tests of hematological parameters are indispensable in monitoring the disease and for the purpose of determining the type of anemia and the choice of therapy (20).

CONCLUSION

The results of the presented research suggest that old age is a predisposing risk factor for the development of chronic kidney disease, and that in combination with comorbidities (hypertension and/or diabetes), it contributes to poor prognosis or disease progression.

The research had several limitations. In addition to the limitations on the number of subjects and the impossibility of comparison with the values of the parameters of the healthy population of older subjects (lack of reference values), the study was designed as an observational one. Future research should lead to the optimization of the laboratory-diagnostic approach and to the creation of a unique framework to conduct screening for the elderly population.

Conflicts of interest

There are no conflicts of interest.

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Analiza laboratorijskih parametara hronične bubrežne insuficijencije kod starijih bolesnika

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SAŽETAK

Cilj. Osnovni cilj ovog istraživanja bio je praćenje laboratorijskih parametara hronične bubrežne insuficijencije kod starijih bolesnika.
Metode. Svi uzorci uzeti su i obrađeni standardnim metodama i u skladu sa principima dobre laboratorijske prakse. Podaci su prikupljeni organizovano i sistematski u vidu upitnika, u skladu sa etičkim principima i kao takvi ispitivani statističkim testovima i analizama (Studentov t test, analiza varijanse – ANOVA, Pirsonov i Spirmanov koeficijent korelacije). Granica statističke značajnosti je $p < 0,05$.
Rezultati. Srednje vrijednosti klirensa kreatinina i proteinurije za ukupnu ispitivanu populaciju bile su: 41,30 mL/min ± 21,43 mL/min, 1,5 g/L/24 h ± 2,3 g/L/24 h, respektivno. Hematološki parametri nisu pokazali znatne razlike u odnosu na normalne vrijednosti. Učestalost hipertenzije i dijabetesa kod ispitanika odgovara podacima iz literature. Najveća učestalost komorbiditeta uočena je kod ispitanika sa ≥ 80 godina, sa prosijekom od 2,03 komorbiditeta po ispitaniku. Vrijednosti serumskog kreatinina i uree, kao i klirensa kreatinina, dobar su pokazatelj progresije bolesti.
Zaključak. Rezultati prikazanog istraživanja upućuju na to da je starost predisponirajući faktor rizika za nastanak hronične bolesti bubrega, te da u kombinaciji sa komorbiditetima (hipertenzija i/ili dijabetes) doprinosi lošoj prognozi ili progresiji bolesti.

Ključne reči: **starije životno doba, hronična bubrežna bolest, GFR, proteinurija**