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CONTENT

PRINCIPLES OF EARLY DIAGNOSIS OF KIDNEY DAMAGE IN PATIENTS OF RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDILOARTHRITIS

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Abstract. Systemic rheumatic diseases rheumatoid arthritis and ankylosing spondylitis are common and cause serious medical and economic problems. Chronic kidney disease occurring at any stage serves as a direct risk factor for cardiovascular complications. Detection of urinary syndrome, as well as changes in renal function are the main criteria for kidney damage. Thus, the detection of signs of kidney damage in the early stages can correct the timely treatment and thus influence the outcome of the underlying disease. Therefore, in the selected patients in the study, the indicators of renal impairment - urinary syndrome and GFR were studied. The study examined the characteristics of kidney damage in 60 patients with rheumatoid arthritis and 20 with ankylosing spondyloarthritis patients. Changes in renal function in these groups were analyzed depending on the age groups of the patients, the stage of disease activity, the duration of the disease, and the medications taken.

Keywords: rheumatoid arthritis, ankylosing spondyloarthritis, urine syndrome, chronic kidney disease, glomerular filtration rate, kidney damage.

INTRODUCTION. Improving the effectiveness of prevention and treatment of chronic non-communicable diseases is considered by the World Health Organization as a priority project of the XXI century aimed at improving the quality of life of the world's population (WHO, 2011). Diseases that cause deformity and deformation of the musculoskeletal system due to inflammatory and dystrophic, exudative-proliferative processes in the wrist joints are a topical issue for rheumatoid arthritis (RA) and ankylosing spondylitis (AS). [1,8]

RA is one of the most common autoimmune diseases, with an incidence of 0.5–2% in the adult population (5% in women over 60 years of age) and seronegative spondyloarthritis ranging from 0.15 to 4%, and is currently associated with the use of modern drugs. despite the fact that the disease is growing. In 50% of patients who come to the first examination by a rheumatologist, they present with a limited condition of the movement joints. In 60-90% of patients with a 20-year duration of the disease, there is a loss of ability to work, and in 3/1 of cases there is a complete disability. Rheumatoid arthritis and ankylosing spondylitis are socially significant rheumatic inflammatory diseases due to their high incidence, onset of age, chronic progression, long-term persistence, as well as the use of expensive drugs.

But here the outcome of the disease depends not only on the damage to the musculoskeletal system, but also on other internal organs (non-skeletal signs, STB) - damage to the eyes, heart, intestines, skin and kidneys [2,7]. According to a study by scientists, in about 42% of AS patients, nonverbal symptoms are observed, and kidney damage is a factor of negative consequences and causes disability in patients. According to various authors, kidney damage in RA accounts for 35 - 73% of patients. Within 5 years, half of these patients lose their ability to work, and 70% develop renal complications. Uremia causes the death of every fourth RA patient. [3,10]

Rheumatoid arthritis is a systemic inflammatory disease characterized by erosive destructive damage of the joints in the form of polyratritis, manifested by various extraarticular changes. The prevalence of RA is 0.7% in the global community. Every year, 0.02% of the population is infected with RA. [4]

Ankylosing spondylitis is also one of the most discussed issues by the therapeutic community. Over the past decade, the principles of monitoring and treatment of patients with these diseases have been revised, and new classifications, new genetic and immunological dependencies have been identified. In 2016, an international recommendation by the ASAS-EULAR group of experts outlined the characteristics of ankylosing spondylitis in patients with ankylosing

spondylitis, disease activity when associated with comorbidities, and management of the general condition of patients. Particular attention is paid here to satellite-related comorbidities. According to E. Strobel, various renal symptoms (erythrocyturia, leukocyturia, protinuria, increased serum creatinine), which are quite common in AS, are not always detectable and occur in up to 35%. [5,9]

In this case, the occurrence of symptoms as a primary symptom or complication of the disease, as well as a comorbid disease, it is difficult to clearly distinguish and classify these cases. According to A. Jacobson and co-authors, the risk of developing nephrolithiasis in AS patients is twice as high as in the general population [10]. As a risk factor, the author points to male gender, inflammatory bowel disease, and impaired intestinal absorption.

Many scientific studies on AS and kidney damage are similar. A selective study was conducted among 8–15% of AS patients, depending on changes in the urine analysis of patients. According to the research of B.Samia and co-authors, the epidemiological, clinical, therapeutic, prognostic features and predisposing factors in the development of nephropathy in AS patients were evaluated [3, 10].

Retrospectively, 212 AS patients were examined, and signs of kidney damage were identified in 32 of them. In 22 patients - microscopic hematuria, 23 - proteinuria, 11 - nephrotic syndrome, 24 - decreased renal function. Secondary amyloidosis was detected in 13 patients (6.1%) and in 17 people with a terminal stage of CKD with a duration of 29.8 ± 46. Factors contributing to the development of smoking, high inflammatory character, stage 3-4 sacroileitis, complete ankylosis of the spine, nephropathy in patients with AS with and without renal impairment.

When the importance of the majority of chronic diseases (cardiovascular, allergic, neurological, oncological, hematological, chronic lung diseases, diabetes mellitus) is studied, the ability to work is reduced, the patient's general condition worsens, the number of visits to the general practitioner increases in 1 year. were found to be Rheumatic diseases occur at any age, and in recent years there has been an increase in the number of cases of this disease. Expenditure on rheumatic diseases in the health sector is also having a negative impact on the state economy [6,8].

The aim of the study: To develop an algorithm for the assessment and early diagnosis of kidney damage in patients with RA and AS.

MATERIALS AND METHODS. The study was held at the Bukhara Regional Multidisciplinary Medical Center Department of Rheumatology RA and AS patients underwent clinical, instrumental, laboratory analyzes in all inpatients treated in 2019 and 2020, and 60 RA and 20 AS patients who came with them were randomly selected. The diagnosis of RA and AS was made on the basis of diagnostic criteria based on the 2010 classification of the American Society of Rheumatologists. Exception criteria were primary kidney disease, arterial hypertension stage II-III, diabetes mellitus.

Patients were evaluated for the course of the underlying disease, comorbidities, as well as medical history and pharmacotherapy they were receiving. Clinical blood analysis, urine analysis (Nechiporenko test and daily protein loss analysis according to the instructions), renal ultrasound examination was performed. Renal function was assessed according to GFR (Modification of Diet in Renal Disease Study (MDRD) formula), blood urea and creatinine levels.

RESULTS AND DISCUSSION. RA and AS are the most common systemic rheumatic diseases and cause serious medical and economic problems. Chronic kidney disease occurring at any stage serves as a direct risk factor for cardiovascular complications. Detection of urinary syndrome, as well as changes in renal function are the main criteria for kidney damage. Thus, the detection of signs of kidney damage in the early stages can correct the timely treatment and thus influence the outcome of the underlying disease. Therefore, in the selected patients in the study, the indicators of renal impairment - urinary syndrome and GFR were studied.

The total 60 RA patients was divided in two group, the first group without kidney damage 34 patients and with kidney damage 26 patients. Of the 34 patients without RA damage from RA

patients, 22 were female, 12 were male, and 26 patients with renal impairment, including 18 female and 8 male patients. The mean age was 52 ± 2.4.

Urine syndrome in patients with RA and AS proteinuria -13 % (10), erythrocyturia 16% (13), leukocyturia 14 % (11), proteinuria and erythrocyturia 6,5 %, proteinuria and leukocyturia 8 %, leukocyturia and erythrocyturia 6%, proteinuria , erythrocyturia and leukocyturia accounted for 2%.

When these results were compared with the control group, urinary syndrome was 32% in patients with RA and AS, while the wash rate was 5% in the control group, r = 0.001.

Correspondingly, hematuria was found in one in four patients with RA and AS alone or with other pathological changes, and a combination of leukocyturia and proteinuria was found to be relatively rare.

When renal function was examined, 56% of patients had normal GFR (> 90 ml / min / 1.73 m2), 28% had a slight decrease in GFR (60–89 ml / min / 1.73 m2), and 15% had a moderate decrease in GFR (30–59 ml / min / 1.73 m2) were observed. In the control group, normal GFR (> 90 ml / min / 1.73 m2) was detected in 82% of cases. In 18% of cases, a slight decrease in GFR (60–89 ml / min / 1.73 m2) was detected. It was not detected in the control group with GFR below 60 ml / min / 1.73 m^2.

Thus, with a decrease in renal function, RA and AS were detected in 40% of patients and in 18% in the control group, and when the relative level was compared, a difference was found between these groups. (r = 0.05)

In the next stage, the incidence of changes in the indicators of urinary syndrome according to the characteristics of the satellite disease and the course of the main disease was studied.

When comparing the age indicators of RA and AS patients with urinary syndrome, the highest change was found in patients aged 31–40 years.

Table №1

Age of patients	**<30, n = 7**	**31–40, n = 26**	**41–50, n = 15**	**51–60, n = 4**	**>60, n = 8**	**P < 0,05**
Urinary syndrome incidence rate,%	28 % (2 out of 7 patients)	54 % (14 out of 26 patients)	40 % (6 out of 15 patients)	25 % (one out of 4 patients)	37 % (3 out of 8 patients)	p1-2, p3-2, p4-2, p5-2, p1-5, p1-5, p2-5, p3-5, p4-5*

Note: If the difference between the groups has reached the level of statistical reliability (r = 0.05), the value of r is displayed.

It was found that RA and AS were more active at a younger age, which was the reason for the corresponding age in the selected patients. That is, RA stage 3 occurs in patients aged 31–40 years. In addition, the toxic effects of long-term drug therapy over time are certainly not absent.

When the symptoms of kidney damage in each disease were studied, the following results were obtained.

Table № 2

Levels of disease activity in patients of different ages

RA disease activity	<30, n = 7	31–40, n = 26	41–50, n = 15	51–60, n = 4	>60, n = 8	P < 0,05
I stage		1% (4 out of 60)	0,02 % (one out of 60)	0,02% (one out of 60)	0,02% (2 out of 60)	
II stage		10,0% (6 out of 60)	1 % (4 out of 60)	0,02 % (one out of 60)	0,02 % (2 out of 60)	
III stage	12 % (7 out of 60)	27 % (16 out of 60)	17 % (10 out of 60)	1 % (3 out of 60)	1 % (4 out of 60)	p1-2, p2-3, p2-4

The average incidence of ankylosing spondylitis in patients with ankylosing spondylitis is 26.04 ± 6.8, and the average disease duration is 5.0 ± 4.60. An average of 60% of AS patients received YQDV and basal medications during treatment. Overall, axial joint and peripheral joint involvement in 54% of cases were found to be involved in the process. HLA B27 positive result was detected in 95% of the selected AS patients.

Kidney damage was detected in a total of 20 patients (45.7%). Hematuria (15%) was detected in 3 of these patients, proteinuria in 10 patients (10%), and decreased GFR in 2 patients. The results showed that renal changes such as hematuria were detected in the majority of AS patients.

When comparing clinical blood analysis and renal changes in patients with AS, erythrocyte sedimentation rate and C reactive protein levels were higher in the group in which renal changes were detected. (20% and 15%; 43.6 ± 30.23 mm / s and 38.07 ± 26.02 mm / h; 32.12 ± 30.51 mg / L vs 27.27 ± 28.73 mg / L, respectively). These figures were statistically significant (P <0.05). It was also found that the rates of AS patients with renal impairment were higher than those of patients without renal impairment due to their age, age at first onset of the disease, age at first correct diagnosis, and duration of disease. (Table № 3)

Table № 3

№	Indications	Kidney damage		P
		Yes	Not	
	Demographic characteristics			
1.	Gender, male (%)	15 (75 %)	5 (25)	< 0,05
2.	Age (years)	35.20 ±6,5	30,44 ±5,8	0,05
3.	The age at which the disease was first diagnosed was (year)	26,65 ±8,6	25,76±7,6	0,22
4.	The year of diagnosis	32,78±9,8	31,66±8,7	0,06
	Clinic features			
5.	NSAID, n (%)	8 (30 %)	12 (70 %)	0,72
6.	Basic drugs, n (%)	6 (28 %)	14 (72 %)	0,53
.	Disease duration (years)	5,4 ±4,8	4,2±6,4	0,22
.	Peripheral arthritis, n (%)	5 (25 %)	15 (75 %)	0,05
	Biochemical parameters			
0.	HLA –B27 positive, n (%)	19 (95 %)	1 (5 %)	0,50
1.	ESR (mm/h)	46,86 ±20,56	42,68 ±22,68	< 0,05
2.	SRP (mg/L)	29,56 ±6,8	23,46 ±8,5	< 0,05
3.	Albumin (g/L)	42,23 ±8,6	45 ± 6,8	< 0,05

Among AS patients, 42% (71 patients) with chronic kidney disease (CKD) were reported. Hematuria was detected in 70% (49) and nephrotic syndrome in 20% (14) of these patients with renal impairment. Renal impairment was observed in 28 (40%) patients.

When comparing female and male patients with CKD, proteinuria was more pronounced in hematuria than in male patients, and the rate of renal hemorrhage was also found to be lower. Changes in renal function were also 6.2 and 2.7%, respectively. In addition, CKD male patients were found to be younger, had higher body weight, more frequent hypertension, and higher uric acid levels during AS activity than female patients. HLA-B27 was more positive in men. AS duration, ECG, and SRP values did not show a significant difference between male and female patients.

When risk factors for chronic kidney disease were studied, hyperuricemia syndrome and hypertension, high total cholesterol and triglyceride levels, decreased albumin levels, increased ECG, and renal dysfunction were identified in male AS patients.

When renal function was examined, 56% of patients had normal GFR (> 90 ml / min / 1.73 m2), 28% had a slight decrease in GFR (60–89 ml / min / 1.73 m2), and 15% had a moderate decrease in GFR. (30–59 ml / min / 1.73 m2) were observed. In the control group, normal GFR (> 90 ml / min / 1.73 m2) was detected in 82% of cases. In 18% of cases, a slight decrease in GFR (60–89 ml / min / 1.73 m2) was detected. It was not detected in the control group with GFR below 60 ml / min / 1.73 m2.

Thus, AS was detected in 40% of patients with decreased renal function and 18% in the control group, and when comparing the relative levels, it was found that there was a difference between these groups. (r = 0.05)

The mean age of the patients was 43,6 ± 12.4, and the duration of AS disease was 10,2 ± 8.6. The HLA-B27 assay was 92%. The proportions of hyperuricemia syndrome and hypertension were analyzed in 20% (34 patients) and 18% (31 patients), respectively. The mean disease duration was 5.0 ± 4.60. An average of 60% of AS patients received NSAIDs and basal medications during treatment.

The incidence of kidney damage in patients with AS is hematuria, proteinuria, decreased renal function from 10% to 35%. To provide more accurate information on the risk factors for kidney damage in patients, the groups were divided into 3 according to their clinical characteristics. Patients according to demographic characteristics, clinical and biochemical indicators, sex, age, age at which the disease was first diagnosed (years), year of diagnosis (years), NSAIDS, basic drugs, disease duration (years), peripheral arthritis, HLA-B27 positive, ECG (mm / s), SRP (mg / L), albumin (g / L) readings were compared with patients with renal impairment and no renal impairment. A multivariate logistic regression analysis was performed based on one factor intergroup differences data. Statistical differences were identified in patient sex, diagnosed age, ECG, SRP, and albumin.

When comparing clinical blood analysis and renal changes in patients with AS, erythrocyte sedimentation rate and C reactive protein levels were higher in the group in which renal changes were detected. (20% and 15%; 43.6 ± 30.23 mm / s and 38.07 ± 26.02 mm / h; 32.12 ± 30.51 mg / L vs 27.27 ± 28.73 mg / L, respectively). These figures were statistically significant (P <0.05). It was also found that the indicators of AS patients with renal impairment were higher than those of patients without renal impairment due to their age, the age at which the disease first appeared, the age at which the disease was first correctly diagnosed, and the duration of the disease.

CONCLUSIONS. Based on the research, early detection of signs of kidney damage in patients with rheumatoid arthritis and ankylosing spondylitis was studied, risk factors leading to the development of the disease in the population, a risk index mathematical module was created to identify risk groups, and an algorithm for early detection and prevention of kidney disease was developed.

Rheumatoid arthritis and ankylosing spondylitis are socially significant rheumatic inflammatory diseases due to their high incidence, onset of age, chronic progression, long-term persistence, as well as the use of expensive drugs. Chronic lesions among RA and AS rheumatic diseases are characterized by high prevalence in the population, long periods of asymptomatic, high morbidity and mortality rates, leading to a sudden decrease in patient quality of life.

Early detection of kidney damage in rheumatoid arthritis and ankylosing spondylitis can help prevent the expected adverse complications and consequences. As a result, chronic kidney disease and chronic renal failure are prevented, leading to an improvement in disability and fitness.

1. Determination of urine syndrome for RA and AS patients can be a simple and sensitive marker of early kidney damage, including drug-induced pathology of kidney.

2. Renal damage in patients with ankylosing spondylitis was more pronounced in men than in women, hyperuricemia was more pronounced in both sexes, hypertension, and low albumin levels were more common in male patients.

3. Risk factors for renal complications were established: age, high activity and duration of RA and AS disease.

4. In patients with RA and AS, the development of kidney damage and the severity of its manifestations are determined by the duration and activity of the underlying disease, and by age.

Practical recommendations.

1. Given the above reasons and the high incidence of renal impairment in patients with RA and AS, it is advisable to introduce active detection of signs of subclinical renal impairment.

2. Given that the symptoms of chronic kidney disease are directly proportional to the duration of AS disease, indicators of renal subclinical damage should be checked 5 years after the diagnosis of RA and AS.

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