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A MODERN VIEW OF THE CYLINIC COURSE OF RHEUMATOID ARTHRITIS IN CORONAVIRUS INFECTION

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Abstract: Rheumatoid arthritis (RA) is a rheumatological disease accompanied by joint syndrome, functionally characterized by erosive damage and destruction of joints. The disease occurs predominantly in young and middle-aged individuals and leads to early disability of patients, which in turn determines the social significance and relevance of the problem. COVID-19 infection has caused new features of the course of RA, which determines the medical and social relevance of studying the problem.
Key words: rheumatoid arthritis, COVID-19 infection, muscle and joint damage, immune-inflammatory rheumatic diseases.

Relevance: COVID-19 is a global health emergency. The relevance of this problem in immunoinflammatory rheumatic diseases is due to the initial presence of immunosuppression, damage to internal organs, various comorbid pathologies that occur more often than in the population, genetic and other factors that can increase the risk of SARS-CoV-2 infection and its severe course.

In rheumatic diseases, the risk of developing infections is higher than in the general population [1]. After the outbreak of the COVID-19 pandemic, a large amount of data has appeared on the diversity of post-COVID symptoms, including the presence of muscle-joint syndrome [2]. The development of the COVID-19 pandemic has drawn the attention of the medical community to fundamentally new clinical and fundamental problems of the immunopathology of human diseases [3]. Among the current problems of rheumatology, the possibility of developing a wide range of long-term consequences of COVID-19, the so-called post-COVID syndrome, is being considered [4]. To date, there are a large number of studies devoted to the impact of COVID-19 on the course of autoimmune rheumatic diseases and the importance of vaccination for the prevention of this dangerous viral infection [5]. There are currently approximately 20 million people worldwide suffering from rheumatoid arthritis (RA) who have been infected with SARS-CoV-2 at least once since the start of the pandemic in 2020. In an operational cohort clinical study of the consequences and outcomes of COVID-19, conducted by K.M. D'Silva et al. in a number of regions of the United States with the highest epidemiological rates of this infection in patients with immune-inflammatory rheumatic diseases [6]. There are many descriptions in the literature of cases of rheumatoid arthritis (RA) onset after SARS-CoV-2. The question arises: is this a coincidence, or could COVID-19 (coronavirus disease 2019) be a trigger factor for rheumatoid arthritis? [7]. Rheumatoid arthritis (RA) is characterized by a dominant clinical picture of chronic inflammation of the synovial membrane of the joints, accompanied by progressive destruction of cartilage and bone tissue, in the pathogenesis of which autoimmune mechanisms play a significant role [8]. Among the current problems of rheumatology, the possibility of developing a wide range of long-term consequences of COVID-19, the so-called post-COVID syndrome (PCS) is being considered [9]. It is known that in patients with IRR, the frequency of infectious complications is increased due to both

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secondary immunodeficiency and increased activity of this group of diseases, as well as the use of antirheumatic drugs that have an immunosuppressive effect [10]. The pandemic of the new coronavirus infection has drawn attention to new clinical problems of immunopathology, as it can act as a trigger for autoimmune processes due to dysregulation of immunity [11]. According to a number of studies, SARS-CoV-2 infection can affect the clinical course of rheumatoid arthritis, cause exacerbations, increase the inflammatory process and change the immunological profile of patients. SARS-CoV-2 causes activation of autoimmune mechanisms due to excessive production of proinflammatory cytokines, such as interleukin-6 (IL-6) and interleukin-17 (IL-17), which play a key role in the pathogenesis of RA. It is important to study the clinical and immunological characteristics of RA patients with post-COVID status syndrome [1,12].

Objective: To assess the clinical course of rheumatic diseases in patients who have had a new coronavirus infection.

Materials and methods of the study: The clinical study was conducted in 2020-2022 at the departments of rheumatology and cardiorheumatology of the multidisciplinary clinic of the Tashkent Medical Academy. During the inpatient treatment, targeted examination and prospective observation of patients were conducted. The study involved 120 patients with rheumatoid arthritis, including 60 patients with rheumatoid arthritis who had recovered from COVID-19, 60 patients with true rheumatoid arthritis, and 30 healthy individuals. The patients were divided into 2 groups depending on the purpose and objectives of the study. The results of subjective, objective and instrumental examination of each patient were recorded in an individual registration card based on the following criteria. Patients underwent joint radiography and VAS examination to assess the functional activity of the disease in accordance with EULAR recommendations. For each patient, the HAQ and RICHI questionnaires were completed, exclusion criteria were defined, and patients in whom the diagnosis of RA was rejected according to the EULAR/ACR criteria were identified. Patients were divided into 2 groups depending on whether they had COVID-19 or not, and a comparative assessment between them was carried out by studying the following indicators: The disease activity, joint syndrome and functional indicators, extra-articular signs, X-ray examination of joints, assessment of markers of the acute phase of inflammation, rheumatoid factor, anti-CCP test, TGFB-1 protein level and cytokines were determined. Clinical, biochemical parameters of blood and urine tests were performed in a standardized manner. The diagnosis of the autoantibody panel was quantitatively determined by the Waaler-Rose method using the OLYMPUS automatic analyzer (Japan). To detect ACCP, the ORGENTEC Anti-CCPELISA diagnostic test system (Moscow) was used, based on enzyme immunoassay. The cytokine level was measured by enzyme immunoassay using a chemiluminescent biochip system with an automatic analyzer Evidence (Great Britain). In a prospective study, 60 patients with rheumatoid arthritis who had recovered from COVID-19 were divided into 2 groups depending on the type of treatment they received. The first group of patients with RA (n=30) received methotrexate 15–20 mg once a week (basic therapy), vitamin D, anticoagulants, glucocorticosteroids and nonsteroidal anti-inflammatory drugs. The second group (n=30) received the same basic treatment - the genetically engineered biological drug (GEBD) interleukin-6 inhibitor tocilizumab (TB) at a dose of 8 mg/kg as subcutaneous injections every 4 weeks. The clinical efficacy of treatment was monitored for 3 months.

Results: IBM SPSS 26.0 and Microsoft Excel 2013 were used for statistical analysis of the results. The main group consisted of 60 patients with rheumatoid arthritis who had COVID-

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19, of which 76% were women, 14% were men, the average age was 45±6.2 years. The control group consisted of 60 patients with rheumatoid arthritis who had not had COVID-19, of which 79% were women, 11% were men, the average age was 38±5.2 years. A group of 30 healthy volunteers who had no acute or chronic diseases over the past 6 months was selected. Of these, 70% were women, 30% wer 2 years.

Targeted surveillance:

Patients with RA

Main group
RA+ COVID-19 survivors
n=60

Control group
Patients with true RA
n=60

Prospective study of RA + Covid 19:

1 group of 30
Methotrexate
7.5–25 mg + Secuquinimab
Vit D
Anticoagulants

2 group of 30 people
Methotrexate 7.5-25 mg+
Vit D
Anticoagulants

The average age of the observed patients was 39.5 ± 11.4 years. The distribution of patients by age groups is presented in Table 1.

Table-1
Distribution of patients by age:

Groups	18-19 years old		20-29 years old		30-39 years old		40-49 years old		50-59 years old		60-69 years old	
	абс	%	Абс	%	абс	%	абс	%	Абс	%	абс	%
1st group (n=60)	5	8.3	10	16.7	15	25.0	12	20.0	10	16.7	8	13.3
2-group (n=60)	4	6.7	12	20.0	14	23.3	13	21.7	9	15.0	8	13.3
Total	9	7.5	22	18.3	29	24.2	25	20.8	19	15.8	16	13.3

Most patients in the first group were aged 40–49 years, while most patients in the second group were aged 30–39 years. Most patients in our study — 114 (95%) — were of working age.

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When analyzing patients by disease duration, the following results were obtained (Table 2)

Table 2
Distribution of patients by duration of disease:

Groups	up to 5 years		5-10 years		11-15 years		16-20 years		21-25 years		More than 25 years	
	абс	%	Абс	%	абс	%	абс	%	Абс	%	абс	%
1st group (n=60)	16	25.0	19	33.3	10	16.7	8	13.3	5	8.3	2	3.3
2-group (n=60)	9	16.7	19	30.0	12	20.0	9	15.0	7	11.7	4	6.7
Total	25	20.8	38	31.7	22	18.3	17	14.2	12	10.0	6	5.0

In most of the observed patients, the disease duration was 5–10 years. The average disease duration was 12.3±0.6 years. The level of treatment effectiveness assessment according to the HAQ index: The difference between the minimal clinically significant changes in the HAQ index before and after treatment was 0.22.

Discussion of results: All patients were diagnosed with rheumatoid arthritis based on the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) diagnostic criteria. The diagnosis was based on the classification criteria adopted by the American College of Rheumatology and the European League Against Rheumatism (ACR/EULAR, 2010). Disease severity: Patients with RA and COVID-19 were found to have a higher risk of disease exacerbation, increased levels of C-reactive protein (CRP), D-dimer, and other inflammatory markers.

Conclusions: Assessment of the risk of developing PCS is necessary for adequate distribution of the burden on the healthcare system, as well as for developing a strategy aimed at prevention, timely diagnosis and treatment of this syndrome in patients with rheumatic diseases [5,13]. Since the beginning of the COVID-19 pandemic, a large amount of information has been accumulated regarding the frequency, clinical features and outcomes of this disease in patients with rheumatological profile, as well as its impact on the course of rheumatoid arthritis and other rheumatoid arthritis. Currently, data are accumulating on the negative impact of therapy with a number of representatives of the class of genetically engineered biological drugs (GEBD) on the course of COVID-19. These facts determine the relevance of studying the factors of severe course and unfavorable outcome in patients suffering from immune-inflammatory rheumatic diseases (IIRD) undergoing treatment with GEBD of immunity [7,12]. Undoubtedly, attention should be paid to PCS, the assessment of the risk of its development is necessary for adequate distribution of the burden on the healthcare system, as well as for developing a strategy aimed at its prevention [6,12]. Thus, studying the clinical and

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immunological features of RA in patients with COVID-19 is crucial for developing individual treatment approaches, improving prognosis and enhancing the quality of life of patients.

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