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FEATURES OF THE STATE OF THE CELLULAR AND HUMORAL COMPONENTS OF IMMUNE SYSTEM IN PATIENTS WITH ANKYLOSING SPONDYLOARTHRITIS AFTER COVID-19

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The article presents data from our own studies on the study of the state of the immune status in patients with ankylosing spondylitis who have undergone COVID-19. In patients, a detailed immunogram was studied, as well as scales of disease activity. According to the results of the research, a sharp suppression of the cellular link of the immune system was revealed in patients with ankylosing spondylitis who underwent COVID-19, compared with the group who did not have coronavirus infection.
Key words: immune status , COVID -19, ankylosing spondylitis.

According to the WHO, diseases of the musculoskeletal system are the leading factor in disability worldwide [5]. COVID-19, which gave rise to a pandemic in 2020, is characterized not only by lung damage, but also by the worsening of existing comorbid conditions in patients, in particular, autoimmune rheumatological diseases [2] . According to the Association of American Rheumatologists, ankylosing spondylitis occurs in 0.1-1.5% of cases among the population, it is based on an autoimmune lesion of the spine, sacroiliac joints , the disease has social significance leading to disability in young and middle-aged patients [3, 4 , 6] . The medical and social significance of the disease is associated with a high risk of developing early disability in the young population, which in turn leads to high economic costs, for this reason, today ankylosing spondylitis (AS) is a very serious problem that needs to be addressed [8, 9].

AS having an autoimmune nature is characterized by the presence of immunological changes [2, 7, 10, 12] . Given this fact, many scientists have come to the conclusion that with COVID-19 there is an impaired immune response, and the study of the immune status in AS patients who have had a coronavirus infection is of particular interest.

The purpose of the study: to study the clinical course and the state of the immune status in patients with AS who underwent COVID-19.

Materials and methods of research:

In the period from 2020-2022, 211 patients with a diagnosis of AS were examined in the 3-city clinical hospital of Tashkent and the Multidisciplinary Clinic of the Tashkent Medical Academy, of which there were 174 men , 37 women, the average duration of the disease was 8.8 ± 2.4 years. The control group consisted of 40 healthy volunteers of the appropriate middle age. The diagnosis was made according to the modified New York criteria for the diagnosis of AS. Patients were initially divided into two groups: group I - 91 patients with AS who underwent COVID-19 and group II - 120 patients with AS who did not have a

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history of coronavirus infection. The first group, in turn, was divided into two groups: group IA - 48 patients with AS who underwent COVID-19 who did not receive basic therapy, group IB - 43 patients who underwent COVID-19 and received basic therapy, and group II - 120 patients with a history of AS who have not had a history of COVID-19 infection. The mean age of patients in group I A was 42.2±13.3 years, in group IB 41.4±10.1 years and in group II 40.2±8.3 years .

All patients underwent in-depth clinical, laboratory and immunological studies. All patients underwent PCR, as well as ICLA tests for the presence of antibodies to COVID-19.

Statistical processing of the study results was carried out using Microsoft applications office Excel 2013, "Statistics" on a personal computer.

Research results:

The patients were divided into three groups: group IA - 48 patients with AS who underwent COVID-19 who did not receive basic therapy, group IB - 43 patients who underwent COVID-19 and received basic therapy, and group II - 120 patients with a history of AS who did not have a history of COVID-19 infections. The mean age of patients in group I A was 42.2±13.3 years, in group IB 41.4±10.1 years, and in group II 40.2±8.3 years.

The main complaints of patients in the three groups were such as morning stiffness, which was observed in 88.6% of patients in group IA, in 65.10% of group IB and 49.5% of patients in group II; back pain was observed in 95.1% of patients of group IA, in 75.2% of group IB and 53.01% of patients of group II; swelling of the joints (in patients with a peripheral form of the disease) in 56.1 % of patients of group IA, in 43.10% of group IB and 36.4% of patients of group II; limitation of movements in 74.3% of group IA, in 57.3% of group IB and in 40.2% of group II.

When considering disease activity, very high ASADAS and BASDAI activity (4.4±0.71 and 5.6±1.2) was found in group IA , moderately high activity in group I B (3.1±0.39 and 4.3±0 .69) and average activity in group II (2.4±0.57 and 3.7±0.75).

Comparison of the immune status of the groups revealed significant differences in the CD of molecular receptors of the immune system (Table 1.) .

Table 1.

Indicators of the cellular link of immunity in the studied groups.

Index	Group I A	Group IB	Group II	Control Group
CD3+, %	31.7±9.3	34.4±6.6	54.3±5.7	59.8±2.5
CD3+, µl	490.8±48.1 *&	605.1±45.7 #	712.4±54.4	$ 1231.7±89.3
CD4+, %	20.4±1.9*	23.8±3.1	31.2±2.2	36.7±3.1
CD4+, µl	278.6±46.1*	311.5±36.8 #	496.4±35.5	$ 687.4±65.2
CD8+, %	17.1±1.6	19.9±2.2	23.7±2.4	26.4±2.1
CD8+, µl	264±22.4 *&	302±35.3 #	448±33.2	$ 521.8±58.2

CD16+, %	23.2±2.7	21.1±1.6	19.5±1.8	16.2±1.5
CD20+, %	19.5±2.01	20.3±3.1	21.2±2.4	23.1±2.8
CD 20+ , µl	290.7±35.6*	320.1±24.5 #	380.4±40.8	$ 350.9±38.3
CD3 8+ , %	35.1±3.1	31.4±3.9*	27.9±2.7	21.4±1.9
CD95+, %	28.5±2.7	25.1±2.05	23.1±1.9	18.7±1.4
IRI (CD4/CD8)	1.1±0.8	1.2±0.9	1.5±0.5	1.8±0.7

Note: significant difference in indicators - * - between I A and II groups; # - between I B and II groups; & - between I A and I B groups; $ - between I A and the control group; @ -between I B and the control group.

When studying the cellular link of immunity, a significant decrease in CD3 was revealed in groups I A (31.7 ± 9.3%, 490.8 ± 48.1 µl) and IB (34.4 ± 6.6%, 605.1 ± 45 .7 µl) compared with group II (54.3±5.7%, 712.4±54.4 µl), as well as with healthy individuals (59.8±2.5%, 1231.7±89.3 µl) ($p < 0.05$). CD4 was also ($p < 0.05$) reduced in the groups IA and IB (20.4±1.9%, 2 78.6±46.1 µl and 23.8±3.1% 311.5±36.8, respectively) compared with group II (31.2 ±2.2 %, 496.4±35.5 µl) and control group 36.7±3.1%, 687.4±65.2 µl). In the study, the number of CD8 showed a significant decrease in group I A (17.1±1.6%, 264.1±22.4 µl), in group I B (19.9±2.2%, 302.7±22.4 µl) compared with group II (23.7±2.4%, 448.5±33.2 µl) and control group (26.4±2.1%, 521.8±58.2 µl). When considering CD16, an increase in their number was found in group I A (23.2±2.7 %), IB (21.1±1.6 %), II (19.5 ±1.8%) groups compared with ($p < 0.05$) with the control group (16.2±1.5 %), while the CD20 level remained within the normal range in all groups (19.5±2.01%, 290.7±35.6 µl in IA , 20 , 3 ± 3.1 %, 320, 1±24.5 µl in IB , 21.2 ± 2.4 % , 380.4 ±40.8 in group II). CD38 and CD95 levels also differed and were elevated ($p < 0.05$) in IA group (35.1±3.1 and 28.5±2.7, respectively) and in IB group (3 1 , 4 ± 3.9 and 2 5 , 1 ± 2. 05 , respectively) , compared with group II (27.9 ± 2.7% and 23.1 ± 1.9%, respectively) and the control group (21.4±1.9% and 18.7±1.4, respectively). And the CD4/CD8 immunoregulation index (IRI) was lowered in groups I A (1.1±0.8) and IB (1.2±0.9), compared with group II (1.5±0.5) and control group (1.8 ±0.7) ($p < 0.05$) .

The study of the humoral link of the immune system (Table 2) showed an increase in IgG in all studied groups (17.49±1.25 g/l, 15.2± 2.45 g/l and 14.58±0.99 g/l, respectively) compared with the control group (10.7±0.73). IgM was elevated in group I A (4.67±1.82 g/l) and was within normal limits in group II (2.23±0.76 g/l) and control groups (2.1±0.7 g/l) ($p < 0.05$) . IgA was elevated in group I A and amounted to 5.2±1.5 g/l ($p <0.05$) , with normal values in group II (3.01±1.2 g/l). Circulating immune complexes (CIC) associated with IgM were within the normal range (15.1±1.7 a.u. and 12.3±1.02 a.u., respectively) in both groups, and the CIC associated with IgG were slightly increased in the first group (41.1± 3.5 c.u.), with normal values in group II ($p < 0.05$) .

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Table 2.
Indicators of humoral immunity in the studied groups

Index	Group I A	Group IB	Group II	Control Group
IgG, g/l	$ 17.49±1.25	1 5 , 2 ± 2.45	14.58±0.99	10.7±0.73
IgA, g/l	5.2±1.5	4.5±1.8	3.01±1.2	2.8±0.95
IgM, g/l	$ 4.67±1.82	3.4±1.42	2.23±0.76	2.1±0.7
CEC Ig G, g/l	41.1±5.6*	28.6±2.2 #	21.8±3.2	$ 18.6±2.4
CEC Ig M, g/l	15.1±1.7	12.9±1.7	12.3±1.02	$ 10.5±1.3

Note: significant difference in indicators * - between I A and II groups; # - between I B and II groups; & - between I A and I B groups; $ - between I A and the control group; @ -between I B and control group

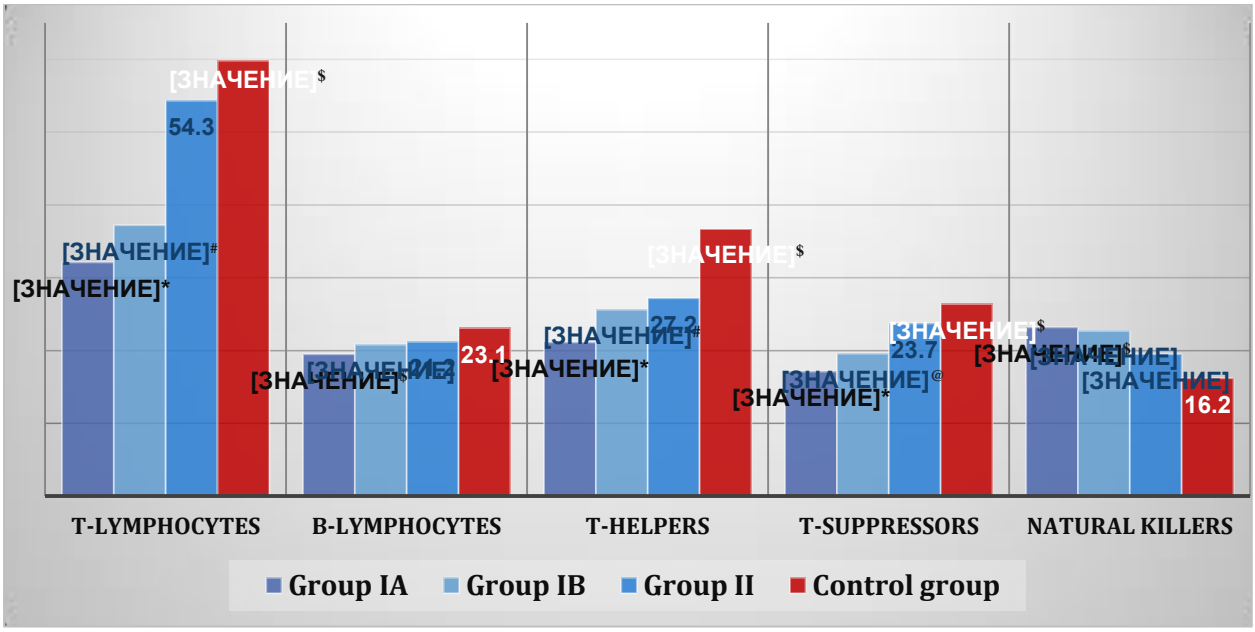

Fig. 1. Indicators of the immune status in the studied groups.

Note: significant difference in indicators th * - between I A and II groups; # - between I B and II groups; & - between I A and I B groups; $ - between I A and the control group; @ - between I B and control group

As can be seen from Fig. 1, in groups IA , IB and group II , both the total pool of T lymphocytes and their subpopulations - T helpers and T-suppressors were significantly reduced compared to the control group. At the same time, B-lymphocytes were within the normal range in all groups. Natural killers were significantly increased in group I A compared with group II ($p < 0.05$) .

The results of the immunological study showed significant changes in the immune status of patients, which were due to both the underlying pathology (AS) and the competing coronavirus infection.

Discussion:

The results of our study showed significant changes in the immune status of patients, which were due to both the underlying pathology (AS) and the coronavirus infection.

A pronounced inhibition of T-cell immunity was revealed, which is manifested by a decrease in the total number of T-lymphocytes, T-helpers and T-suppressors with the activation of natural killers and the preservation of the B-cell immunity. According to various authors, with COVID-19 disease, a decrease in natural killer cells by almost half [1, 7, 11] is characteristic, but in our study, the opposite phenomenon was found and an increase in their number compared to the group who did not have coronavirus infection.

In the study of the humoral link of the immune system, an increase in IgG was revealed in both groups, which is typical for AS, but in addition, after suffering COVID-19, there is a slight increase IgA , IgM which is consistent with the work of foreign authors [5, 9, 10] .

CONCLUSIONS:

1. The clinical course of AS in patients who underwent COVID -19 is characterized by a more pronounced intensity of pain in the articular syndrome, high activity of the disease according to the BASDAI and ASDAS scales .
2. An analysis of the immune status of AS patients who underwent COVID-19 showed a variety of changes at the level of both cellular and humoral parts of the immune system.
3. The course of AS in patients with COVID - 19 is associated with certain immunological changes . Yes , it accompanied T- cell deficiency link immunity (CD 3+, CD 4+, CD8+), which reflects depth autoimmune process and burdening systemic inflammation .

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