BRITISH MEDICAL JOURNAL

British Medical Journal

Volume 1, No.1.1, January 2022

Internet address: http://ejournals.id/index.php/bmj
E-mail: info@ejournals.id
Published by British Medical Journal
Issued Bimonthly
3 knoll drive. London. N14 5LU United Kingdom
+44 7542 987055

Chief editor
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HIGH CONCENTRATION OF TUMOR NECROSIS FACTOR IN ANKYLOSING SPONDYLITIS PATIENTS AFTER COVID-19

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Abstract: The article is devoted to the study of clinical features, as well as the concentration of tumor necrosis factor in patients with ankylosing spondyloarthritis (AS) in the postcovid period. The patients were divided into two groups: the first group of patients with AS who had recovered from COVID-19, the second group of patients with AS who did not have a history of coronavirus infection COVID-19. Patients were given clinical characteristics and the level of tumor necrosis factor in the serum of all patients was investigated. In patients with AS in the postcovid period, a higher activity of the disease was noted , as well as a high level of tumor necrosis factor.

Keywords: COVID-19, ankylosing spondylitis, tumor necrosis factor, skew period.

In March 2020, the World Health Organization announced the COVID-19 pandemic [1,7,8], since then, according to WHO, to date, the number of cases has exceeded 265 million people, and the mortality rate has been more than 5 million (www.covid.stat.com). The rapid development and large-scale vaccination programs against SARS-CoV-2 give hope for success in the fight against the COVID-19 pandemic [9]. The COVID-19 pandemic is particularly difficult for patients with rheumatic diseases due to the immune-mediated disease, and the treatment they take can negatively affect the susceptibility or severity of viral infection [4,5].

Ankylosing spondylitis (AS) is a chronic, progressive inflammatory rheumatic disease that affects the axial skeleton, sacroiliac and peripheral joints, resulting in bone erosion that seriously affects the quality of life of patients [11]. Many patients with AS carry a heavy burden, and the disease itself carries significant direct and indirect socioeconomic costs [1].

Tumor necrosis factor-α (TNF-α) is a well-known inflammatory mediator that plays an important role in the pathogenesis of AS and its level in patients significantly exceeds these indicators in relation to healthy individuals [5,10]. It was found that TNF-α, is important in the development and spread of the inflammatory process in the joints and destroying their structure, it is overexpressed in the sacroiliac joints of patients with AS and leads to the rapid development of ankylosis [3,11].

As you know, studies on COVID-19 have shown that the virus in severe cases causes the activation of autoimmune processes and leads to the development of a "cytokine storm" [4,6]. The similarity in immunological processes between AS and COVID-19 raises many questions about the influence of infection on the course of both diseases. In this regard, the study of the level of the pro-inflammatory cytokine TNF-α in AS patients who have undergone COVID-19 is of particular interest.

Purpose of the study: to study the level of the pro-inflammatory cytokine TNF- α in patients who underwent COVID-19 against the background of AS , as well as the effect of coronavirus infection on the course of AS.

Materials and methods of research: In the period from 2020-2021, 77 patients with a diagnosis of ankylosing spondylitis (AS) were examined in the 3-city clinical hospital of Tashkent city (Uzbekistan). The control group consisted of 30 healthy volunteers of the corresponding middle age. The diagnosis of AS was made according to the modified New York criteria for the diagnosis of AS. The patients were divided into two groups: Group I - 46 patients with AS who underwent COVID-19 (43 men and 3 women) and Group II of 31 patients (26 men and 5 women) with AS per se, i.e. without previous COVID-19 infection . In the first group, the average age of patients was 38.5 ± 7.1 years, with the duration of the disease from 1 to 10 years (5.3 ± 2.6 years). The average age of patients in the second group was 37.1 ± 5.2 years with the duration of the disease from 1 to 8 years (4.6 ± 1.8 years).

instrumental studies, including a study of the level of TNF-α . The level of TNF-α was determined using a standard commercial test kit, ELISA method. Disease activity was assessed taking into account the BASDAI and ASDAS scales , pain syndrome was assessed using a visual analogue scale (VAS). All patients underwent PCR tests for the presence of acute coronavirus infection, as well as IHLA tests for the presence of antibodies to COVID-19.

Statistical processing of the research results was carried out using the applied programs Microsoft Office Excel 2013, "Statistica" on a personal computer.

Research results:

Clinical studies have shown that the majority of patients with AS suffered from COVID-19 asymptomatically or with little or no symptoms with a mild or moderately severe form of the disease. In most cases, the presence of IgG antibodies to Covid-19 was a coincidence for patients.

Examination of patients in both comparison groups showed the presence of major complaints, such as morning stiffness, which was observed in 100% of patients in both groups; nocturnal back pain was noted by 85% of patients in group I and 66% of patients in group II. Objective examination of patients revealed the presence of severe pain in the spine, the intensity of which was assessed using VAS and in group I was 9.1 ± 2.4 cm and 6.4 ± 1.8 cm in patients of group II ($p < 0.05$) ... Laboratory studies showed an average erythrocyte sedimentation rate (ESR) in group I of 43.3 ± 4.1 mm / h and 31.7 ± 6.4 mm / h in group II ($p < 0.05$) . The level of C-reactive protein (CRP) was increased in both groups (11.4 ± 3.2 mg / L and 9.9 ± 5.1 mg / L) , which indicated a high activity of AS in both study groups ($p > 0.05$). The concentration level of antibodies to COVID-19 IgG averaged 5.5 ± 3.1 AU / mL in the first group, and in the second group it was in the limit of reference values.

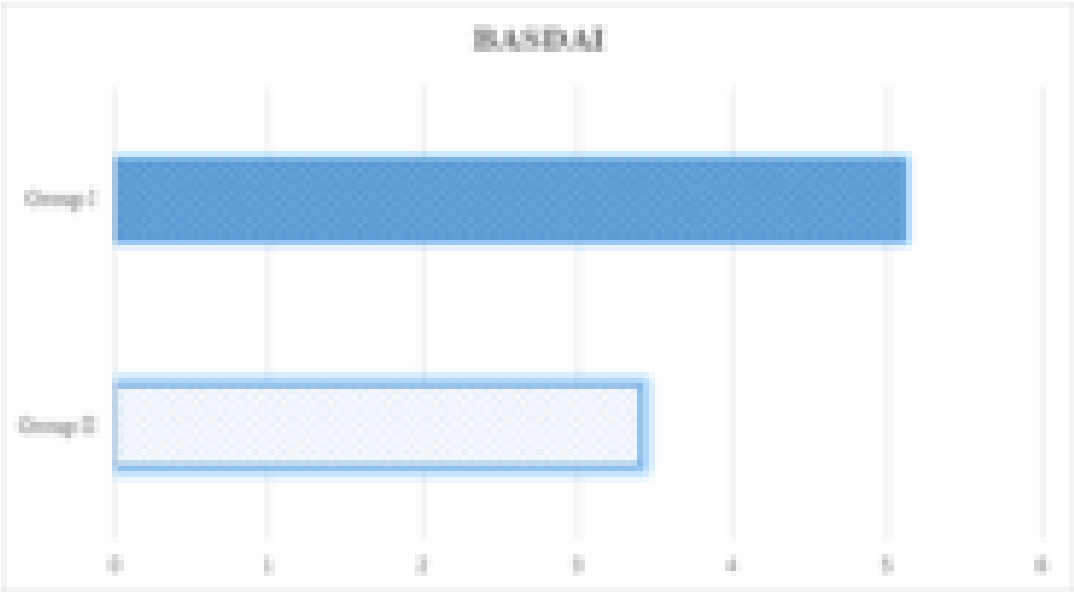

Fig 1. Disease activity according to the BASDAI scale in both groups.

The study of AS activity using the BASDAI scale showed an average level of 5.1 ± 1.7 points in group I and 3.4 ± 2.1 points in group II ($p < 0.05$) (Fig. 1). And the study of activity on the ASDAS scale showed an average level of 4.0 ± 1.7 points in group I and 2.5 ± 0.8 points in group II ($p < 0.02$), which indicates a very high activity of the pathological process in group I.

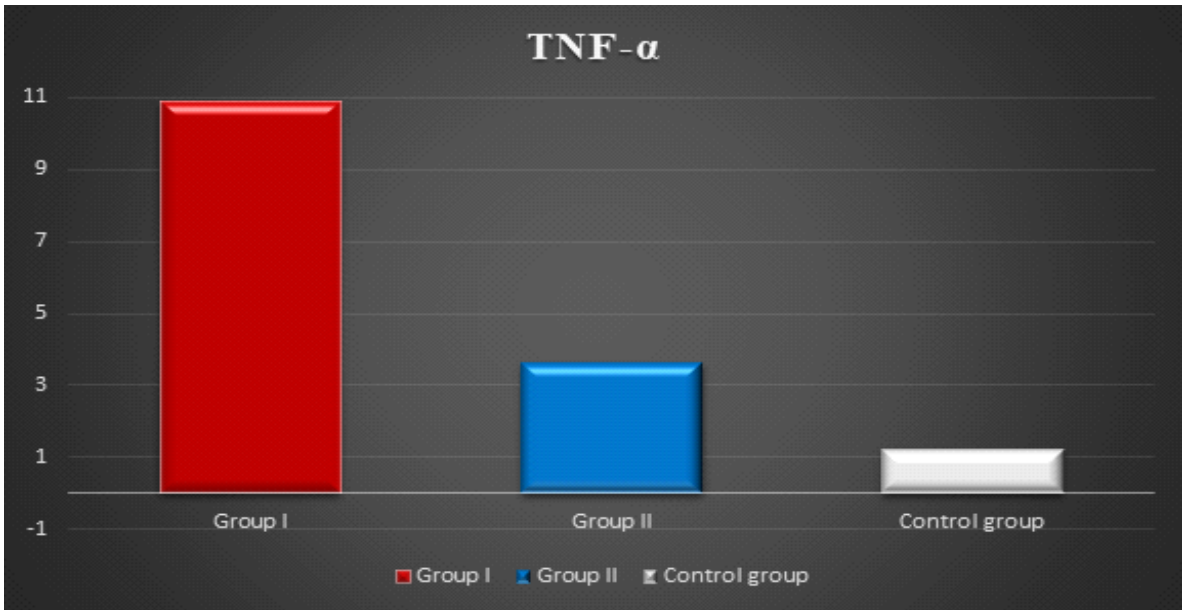

Fig. 2. The level of TNF-α in patients with AS (significant difference in indicators: * - in relation to the control group; # between groups I and II).

The study of the concentration of TNF-α in the blood serum showed significantly high numbers in group I (10.97 ± 4.1 pg / ml; p <0.05) relative to group II (3.6 ± 1.4 pg / ml; p < 0.05) and the control group (1.2 ± 0.5 pg / ml), which indicates a more pronounced inflammatory process against the background of the transferred COVID-19 (Pic. 2).

The results obtained indicate a persistent, statistically significant increase in the level of TNF-α in patients with AS, and this, in turn, leads to an increase in the activity of the disease.

Discussion:

In the development of COVID-19-associated lesions of internal organs, central importance is attached to the uncontrolled hyperproduction of cytokines, called the "cytokine storm" [10, 14]. The essence of this reaction of the immune system consists in the uncontrolled and non-protective function of overproduction of a wide range of pro-inflammatory cytokines, tumor necrosis factor α (TNFα), etc., which develops in response to viral infection [2,7,10]. This leads to systemic activation of inflammatory response cells [5]. The cytokine network plays an immunopathological role in both Covid-19 and AS, having a similar pathogenesis of the development of the autoimmune process [4,8]. the infection did not cause a severe course of COVID-19 in patients with AS. On the contrary, we came to the conclusion that taking basic drugs prevented the development of a severe course of the disease and a "cytokine storm". Nevertheless, the infectious process contributed to a persistent increase in proinflammatory cytokines such as TNF-α and other markers of inflammation , and they, in turn, contributed to the exacerbation of AS.

Conclusions:

1.The combined course of coronavirus infection and AS has similar immunological mechanisms of pathogenesis, accompanied by an increase in the concentration of various pro-inflammatory markers, including an increase in the level of TNF-α, and this, in turn, leads to an increase in the activity of the disease.

2.The clinical course of AS in patients who have undergone COVID-19 is characterized by a more pronounced intensity of pain on the VAS scale, high disease activity on the BASDAI and ASDAS scales.

3.Based on the results of the study, we recommend that in the case of the combined development of COVID-19 and AS not to cancel the intake of basic drugs in order to prevent the development of a "cytokine storm" and exacerbation of the course of the articular syndrome.

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