CHANGES IN C-TELOPEPTIDE COLLAGEN-II LEVEL IN PATIENTS WITH ANKYLOSING SPONDYLOARTHRITIS AFTER COVID-19.

Khalmurad. S. Akhmedov, Lobarxon M. Rixsiyeva, Nargiza M. Abdurahmanova, Abdurashid N. Botirbekov, Ikhtiyor A. Turaev, Sardor S Raximov.

Tashkent Medical Academy, Tashkent, 100109, Uzbekistan

ABSTRACT

The article presents the results of our own studies on the study of CTX-II in patients with ankylosing spondylitis (AS) who underwent COVID-19. Based on the studies, very high levels of CTX-II were found in patients with AS after COVID-19, which indicates the destruction of the cartilaginous part of the spine and damage to bone and structural elements as a result of the progression of the disease against the background of a coronavirus infection.

Keywords: *COVID-19, ankylosing spondylitis, spine, C-telopeptide collagen-II.*

INTRODUCTION

The coronavirus infection, which began its spread in December 2019, has now spread to all countries of the world, over a three-year period, COVID -19 contributed to over 6.6 million deaths around the planet [1,7,8]. It is well known that COVID -19 is not only has a severe effect on the condition of patients, affecting many organs and systems, but also affects the course of those somatic diseases that were observed in patients in the premorbid period [10,15]. At the same time, patients who had previously suffered from ankylosing spondylitis (AS) for many years turned out to be in a more vulnerable state in relation to patients who did not recover from COVID -19 [1,3,4].

Progressive spinal involvement is often the result of abnormal syndesmophyte formation of bone neoplasm caused by chronic inflammation in patients with AS [2, 5] . With AS in the spine, two opposite processes occur in parallel - pathological growth of the bone, against the background of loss of bone mass [6,9,12] . A very interesting point is that the pathology of this disease differs

from the pathology of other joints in that it is characterized by a greater tendency to damage cartilaginous joints, including intervertebral discs, facet and sternocostal joints [10,13,14] . The study of the level of proteins produced by osteoblasts is commonly used to assess the degree of bone formation, as well as the measurement of C - telopeptide collagen - I (CTX-I) is one of the most valuable measures of osteoclast activity, while C is a telopeptide collagen II (CTX-II) specifically reflects cartilage degradation [5, 7, 9,11] . Relationship between markers of bone degradation (CTX - I) and radiological progression of the spine in AS has been described in many studies. However, the role of the cartilage degradation marker (CTX-II), its relationship with the activity of the disease and the progression of structural changes in the spine in patients with AS has been little studied, and the impact of COVID -19 has not been studied at all .

The aim of the study. The study of the level of the biomarker of cartilage degradation - CTX - II in patients with ankylosing spondylitis who underwent COVID-19.

MATERIALS AND METHODS

In the period from 2020-2022, 211 patients with a diagnosis of AS were examined in the Clinical Hospital # 3 of Tashkent city 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 old. 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 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. Patients with a peripheral form of the disease were excluded from the study.

All patients underwent in-depth clinical and laboratory tests, including CTX - II studies , X-ray studies, and testing using various scales. All patients underwent PCR, as well as ICLA tests for the presence of antibodies to COVID -19.

Microsoft Office Excel 2013 "Statistica" application programs have been used on a personal computer.

RESULTS.

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; restriction of movements in 74.3% of group IA, in 57.3% of group IB and in 40.2% of group II

The study of the CTX-II marker showed that in group IA it was 2.11±0.3 ng/mL ($p<0.001$), IB 1.46±0.14 ng/mL in group II 0.99±0.18 and in the control group 0.23±0.12 ng/mL (Fig. 1). CTX-II significantly exceeded the reference values, which indicated a significant increase in the level of CTX-II in the blood in patients of group IA compared with the reference values, which indicates cartilage degradation and a pronounced progression of damage to the bone-structural elements of the spine in AS due to COVID-19.

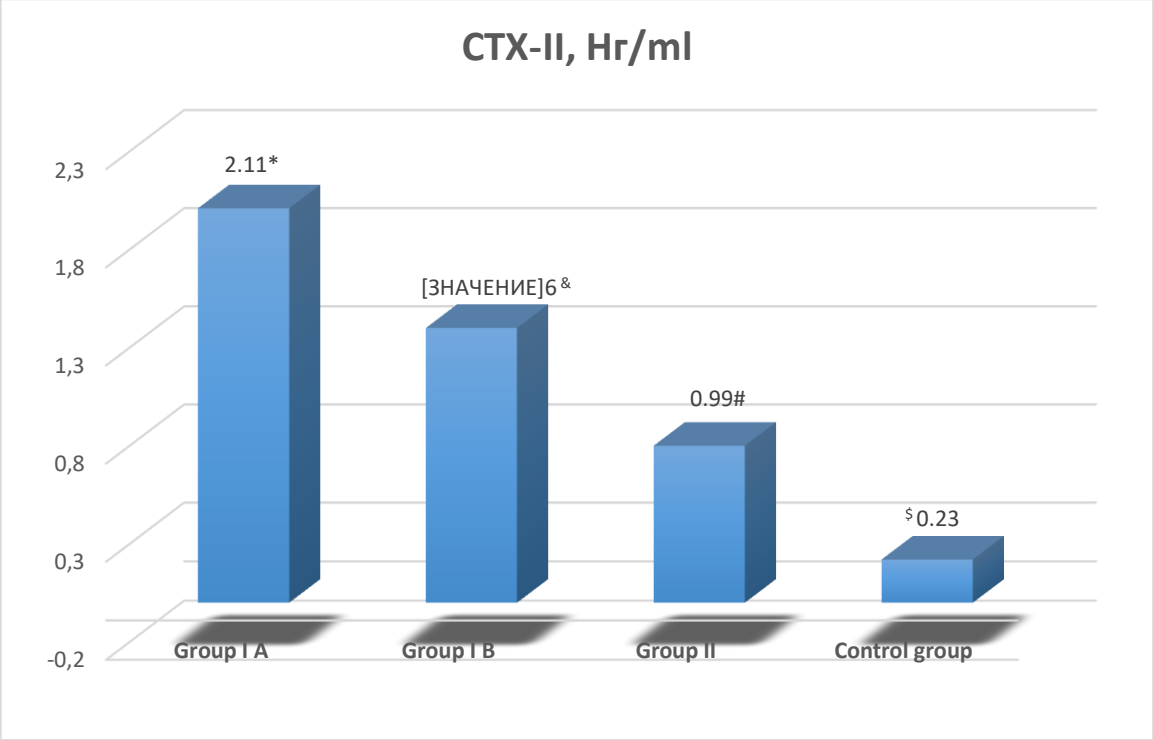

Fig.1. Level of CTX - II in the studied groups

Note: significant differences in p <0.001: * - 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.

The most interesting fact in the study of CTX - II was the identification of its relationship with the duration of the disease: in the first years of the disease, the highest concentration of this marker was observed, and as a long time passed, its level in the blood decreased. This fact may indicate that at the initial stages of the disease, the cartilaginous part of the spine is damaged and, as a result, cartilage decays with an increase in its concentration in the blood and, as the disease progresses, the replacement of the cartilage part with bone tissue and a decrease in the level of CTX- II in the blood (Fig. 2.). To confirm this idea, we studied the concentration of CTX - II in patients with AS in the context of the presence and absence of ankylosis and syndesmophytes in the spine according to radiological data (Fig. 3).

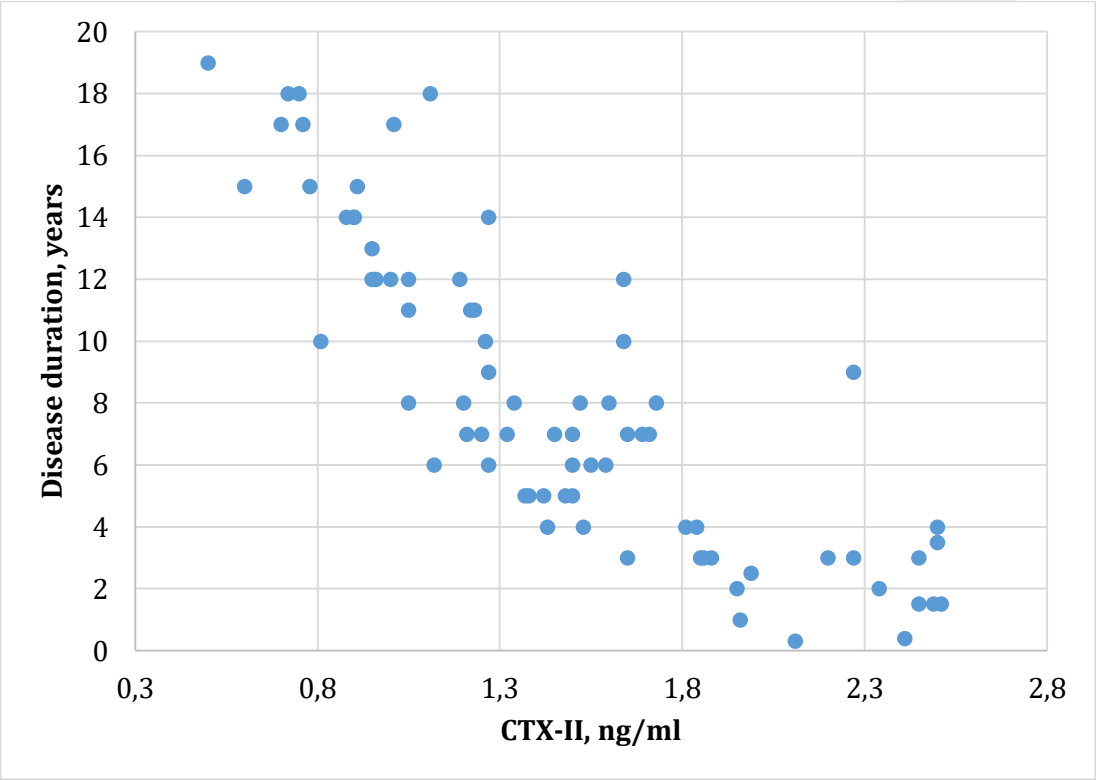

Fig.2. Comparison between disease duration and CTX - II levels in patients with AS .

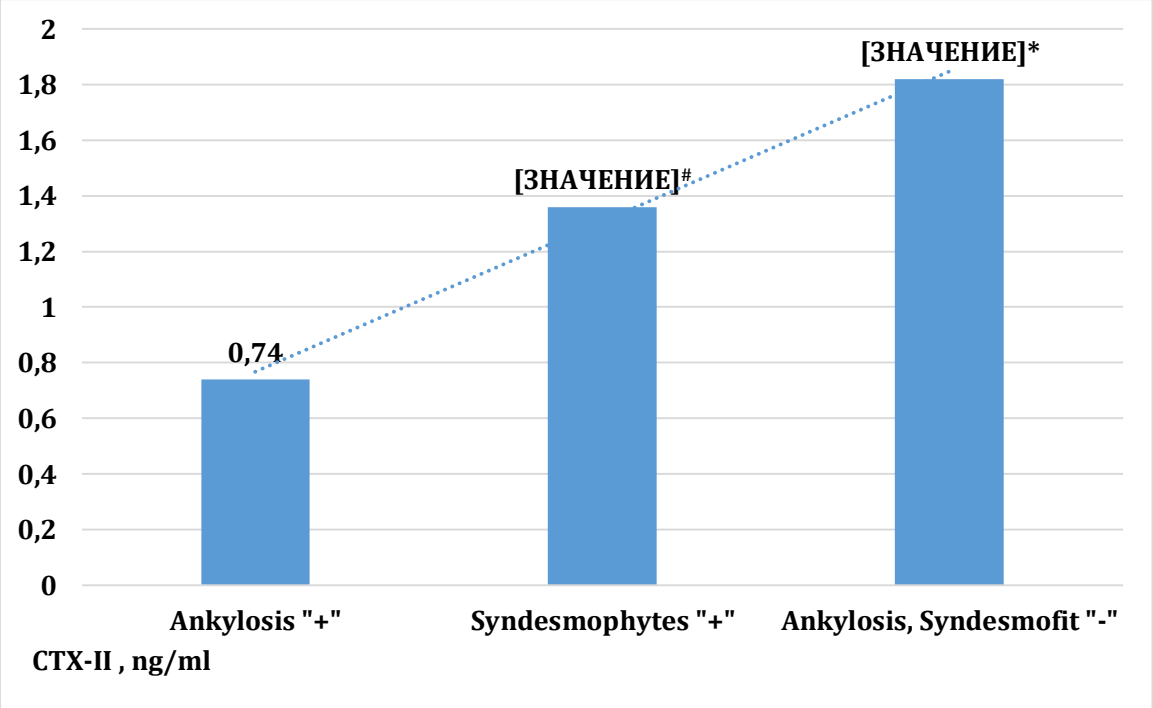

Fig.3. The average level of CTX - II in patients with AS, depending on the presence of ankylosis and syndesmophytosis of the spine.

Note: *p<0.05 between measures

As it turned out, patients with spinal ankylosis had very low CTX - II values , moderate in patients with syndesmophytes , and high in patients without signs of spinal ossification (Fig. 3).

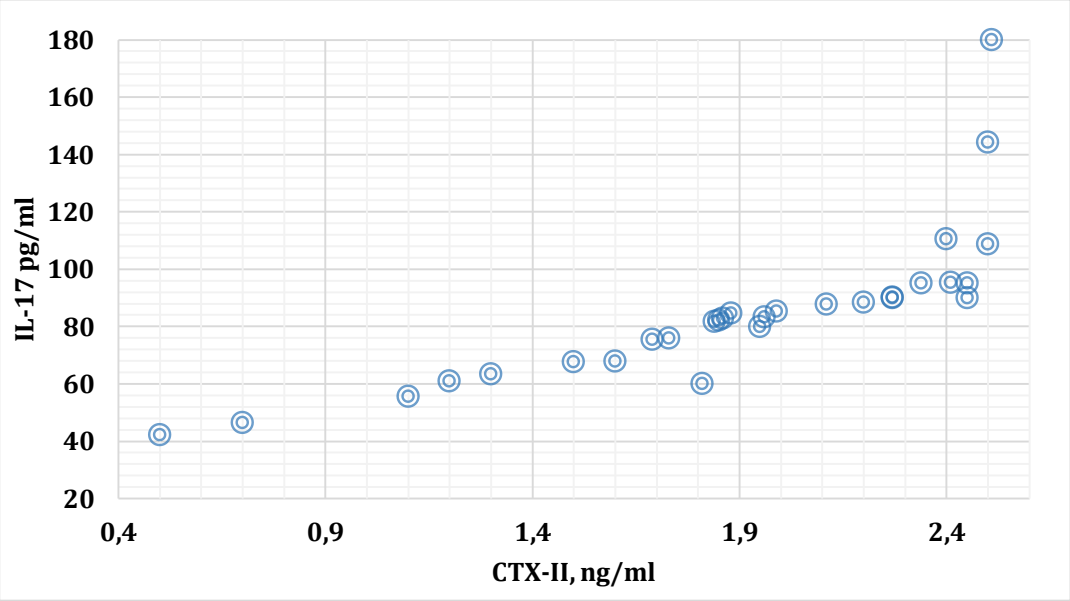

Fig.4. Associative analysis of the concentration of CTX - II and IL-17A in patients with AS who underwent COVID -19.

The study of the associative analysis of CTX - II and IL-17A showed the relationship between the two biomarkers in patients who underwent COVID -19. The higher was IL-17A, the higher was the concentration of CTX - II in the blood of patients who brought coronavirus infection (Fig. 4).

Conducting a correlation analysis between CTX - II and the duration of the disease, IL-17A, x-ray indices mSASS, BASRI - Spine in AS patients who underwent COVID -19 showed a strong positive relationship between the parameters (Fig. 5).

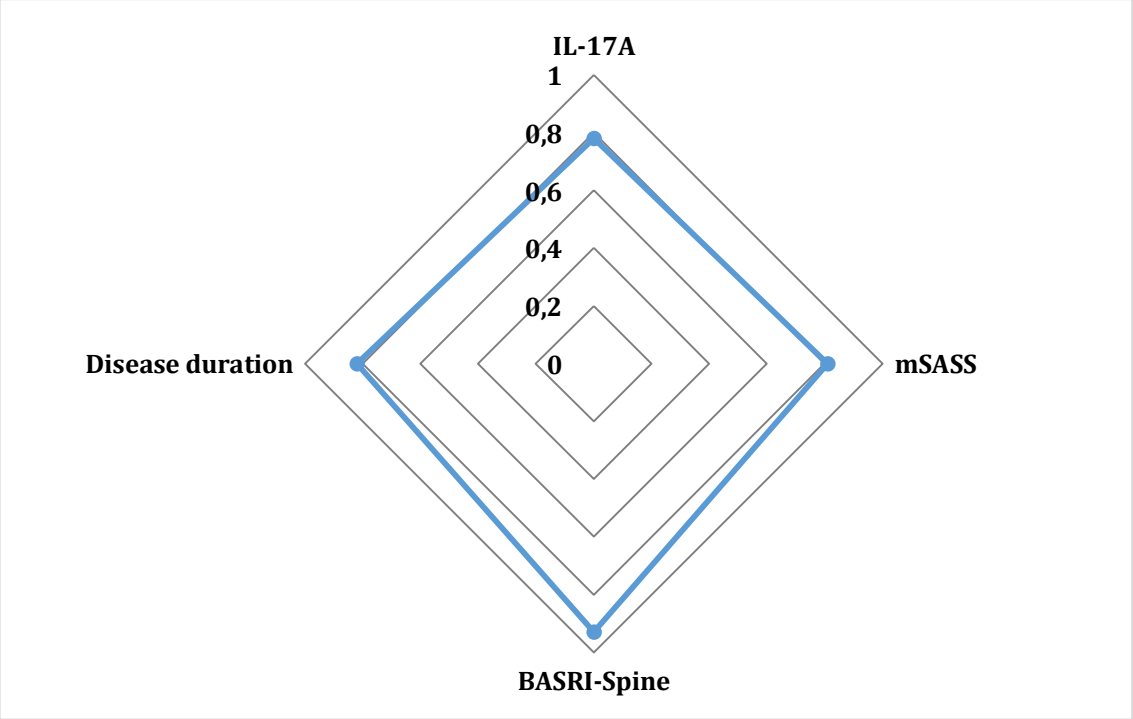

Fig.5. Correlation analysis between CTX - II and disease duration, IL-17A, radiographic indices in AS patients who underwent COVID -19.

DISCUSSION

Structural damage associated with the processes of degradation and resorption of cartilage and bone makes it necessary to pay special attention to both the symptoms of the patient and structural damage to the joints associated with ankylosing spondylitis [3,4,11]. One of the important points in the progression of structural changes in the spine in AS is the damage to the cartilaginous structure. Since articular cartilage consists of collagen fibers, the study of type II collagen C - telopeptide (CTX-II) in AS in patients with COVID-19 has aroused our interest.

The study of CTX-II showed its very high numbers in AS patients who underwent COVID-19, which indicates the progression of spinal lesions. Our data show that an increase in CTX-II, which is specifically indicative of cartilage degradation, is associated with radiographic spinal injury and directly correlates with IL-17A in AS patients with COVID -19.

Thus, ankylosing of the spine is preceded by the breakdown of cartilage tissue with the formation of bone in its place, and the study of the CTX-II biomarker in the early stages of the disease can serve as an indicator of the prognosis of the progression of bone and structural changes in the spine.

CONCLUSION:

1. In the study of patients with AS who underwent COVID-19, a significantly high level of CTX - II was revealed , which indicates the progression of the replacement of the cartilage tissue of the spine with bone and the rapid development of ankylosing.
2. Given the negative impact of coronavirus infection on the course of AS , it is recommended to optimize diagnostic and treatment measures in this group of patients.
3. The data obtained suggest that the measurement of CTX-II levels may be useful for monitoring and predicting spinal injuries in patients with AS.

Conflict of interest - The author declares no conflict of interest.

Financing - The study was performed without external funding.

Compliance with patient rights & principles of bioethics - All patients gave written informed con-sent to participate in the study.

Literature:

1. Abdurakhmanova N. M. et al. Modern methods of treatment of patients with ankylosing spondylitis //International Journal of Advance Scientific Research. – 2022. – Т. 2. – №. 11. – С. 112-118.
2. Abdurakhmanova N., Akhmedov Kh. Effect of pro-inflammatory cytokine-Interleukin- 6 on the course of ankylosing spondylitis in patients after COVID-19 //Annals of the Rheumatic Diseases. – 2022. – С. 1533-1533.
3. Abdurakhmanova N. M., Ahmedov K. S. Influence of accepting basic antirheumatic therapy for ankylosing spondyloarthritis on the clinical course COVID-19.

4. Akhmedov Kh.S. et al. Clinical and diagnostic significance of Anti-CD74 in Uzbek ankylosing spondylitis patients// Journal of Positive School Psychology. Vol 6. #6, 2022 p 9358-9364

5. Belov Boris Sergeevich, Karateev A.E. COVID-19: A new challenge for rheumatologists // Modern Rheumatology. -2020. -#2. -C.110-116 (Article in russian)

6. Descamps E, Molto A, Borderie D et al. Changes in bone formation regulator biomarkers in early axial spondyloarthritis // Rheumatology (Oxford). –2021 Mar 2;60(3):1185-1194. doi: 10.1093/rheumatology/keaa296. PMID: 32888036.

7. Erdes Sh.F., Korotaeva T.V. Progression of axial spondyloarthritis // Modern rheumatology. -2021. -No. 3. -FROM. 7-14. (Article in russian)

8. Fauny M. et al. Relationship between spinal structural damage on radiography and bone fragility on CT in ankylosing spondylitis patients // Scientific Reports. –2021. № 1 (11).

9. Garnero P., Sornay-Rendu E., Chapurlat R. The cartilage degradation marker, urinary CTX-II, is associated with the risk of incident total joint replacement in postmenopausal women. A 18 year evaluation of the OFELY prospective cohort // Osteoarthritis and Cartilage. -2020. No. 4 (28). pp. 468–474.

10. Gaydukova I. Z. et al. Biomarkers of bone remodeling in ankylosing spondylitis patients using nonsteroidal anti-inflammatory drugs: Results of an ETHICS research program // Terapevticheskii Arkhiv. –2017. № 12 (89). C. 185–189.

11. Mirza-Bakhtiyarkhonovna A. N. Features of the state of the cellular and humoral components of immune system in patients with ankylosing spondyloarthritis after COVID-19 //European Journal of Molecular & Clinical Medicine. – T. 9. – №. 08. – C. 2022.

12. Pedersen SJ et al. Circulating levels of interleukin-6, vascular endothelial growth factor, YKL-40, matrix metalloproteinase-3, and total aggrecan in spondyloarthritis patients during 3 years of treatment with TNF α inhibitors // Clinical Rheumatology. –2010. – No. 11 (29). - P. 1301–1309

13. Rakhimova MB, Akhmedov XS, Sadikova S, Khalmetova F. Endothelin-1 biomarker Features in Patients with Ankylosing spondylitis. Journal of Positive School Psychology 2022 . Vol 6. #6, - p.9369-9375

14. Rakhimbaeva GS, Shodiev UD Postcovid cerebro -asthenic syndrome. Journal of neurology and neurosurgical research. Vol.2 (2021), p. 6-11.

15. Tay SH, Yeo JG, Leong JY, Albani S, Arkachaisri T. Juvenile Spondyloarthritis : What More Do We Know About HLA-B27, Enthesitis , and New Bone Formation?. Front Med (Lausanne). – 2021;8:666772 . Published 2021 May 20. doi:10.3389/fmed.2021.666772