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ROLE OF BONE MORPHOGENETIC PROTEIN- BMP-7 IN SPINE REMODELING IN AXIAL SPONDYLOARTHRITIS.

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ABSTRACT

The article presents the results of our own research devoted to the study of the marker of bone remodeling - BMP-7 in patients with axial spondyloarthritis. Based on the studies conducted, very high levels of BMP-7 were identified in patients with high disease activity, which indicates the development of syndesmophytes and the progression of spinal ossification.

According to the American Rheumatology Association, axial spondylitis occurs in 0.1-1.5% of cases among the population, it is based on autoimmune damage to the spine, sacroiliac joints , the disease has social significance leading to disability of young and middle-aged patients [1, 3, 4, 6] . The medical and social significance of the disease is associated with a high risk of developing early disability of the young population, which in turn leads to high economic costs, for this reason the disease is a very serious problem that requires its solution [5, 11].

Progressive spinal lesions are often the result of abnormal syndesmophyte formation, a bone neoplasm caused by chronic inflammation in patients with axial spondylitis (axSpA) [2, 9]. Bone morphogenetic proteins (BMPs) , which are members of the transforming growth factor-ß (TGF-ß) superfamily, also play a critical role in osteoblastic differentiation and bone function. They are important for skeletal development and joint morphogenesis, and according to various sources, they play a role in cartilage and bone homeostasis [10, 14] . BMPs are identified by their unique ability to induce ectopic cartilage development and bone formation in vivo. BMPs are also important in joint remodeling in arthritis, particularly in syndesmophyte formation in spondyloarthritis [12, 16] . Immunohistochemical staining has revealed active BMP signaling present in human enthesitis target cells in spondyloarthritis. Moreover, recombinant human BMPs were effective in inducing bone healing and improving spinal fusion. Overproduction of BMP-2 and BMP-7 has been reported in patients with axSpA. Although the mechanism of new bone formation in axSpA is not fully elucidated, various sources have suggested that BMP plays a significant role in spinal ankylosis and may be a therapeutic target in this pathology [10, 13, 15, 16] .

The study of the levels of proteins produced by osteoblasts are commonly used to assess the degree of bone formation, and the measurement of BMP -7 is one of the valuable assessments of osteoclast activity [2, 14] . The relationship between bone degradation markers (CTX - I) and radiographic progression of the spine in axSpA op and sana in many studies [2, 14, 11] . However, the role of the BMP - 7 marker and its relationship with disease activity and progression of structural changes in the spine in patients with axSpA has been poorly studied.

The aim of the study. To study the level of the biomarker BMP - 7 in patients with axial spondyloarthritis depending on the activity of the inflammatory process.

Materials and methods of research:

In the period from 2022 to 2025, 100 patients diagnosed with axSpA were examined in the 1st City Clinical Hospital of Tashkent , including 92 men and 8 women, the average duration of the disease was 8.29 ±2.66 years . The control group consisted of 30 healthy volunteers of the corresponding mean age. The diagnosis was made according to the modified New York and ASAS diagnostic criteria for axSpA . Patients were initially divided into two groups: group I consisted of 52 patients with axSpA with high activity according to ASDAS and group II consisted of 48 patients with low disease activity. The average age of patients in group I was 42.2±13.3 years and in group II 40.2±8.3 years .

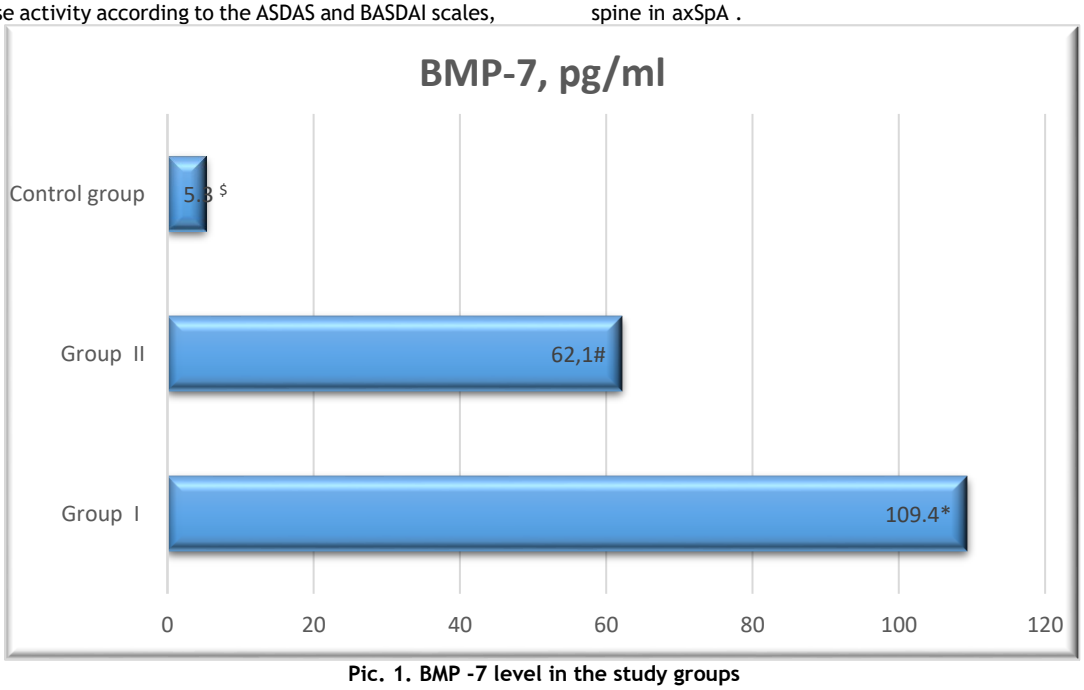
All patients underwent in-depth clinical and laboratory tests , including BMP -7 studies , X-ray studies, and testing using various scales.

Statistical processing of the research results was carried out using the Microsoft Office Excel 2013 and Statisti c a applications on a personal computer.

Research results.

The main complaint of patients in both groups was morning stiffness, which was observed in 88.6% of patients in Group I and 49.5% of patients in Group II; Back pain was noted in 95.1% of patients in Group I and 53.01% of patients in Group II; Joint swelling (in patients with the peripheral form of the disease) was observed in 56.1% of patients in Group I and 36.4% of patients in Group II; Limitation of motion was detected in 74.3% of patients in Group I and 40.2% of patients in Group II. When analyzing the level of disease activity according to the ASDAS and BASDAI scales, extremely high activity was noted in Group I - 4.4±0.71 points and 5.6±1.2 points, and low activity - 2.01±0.57 points and 3.3±0.75 points in Group II.

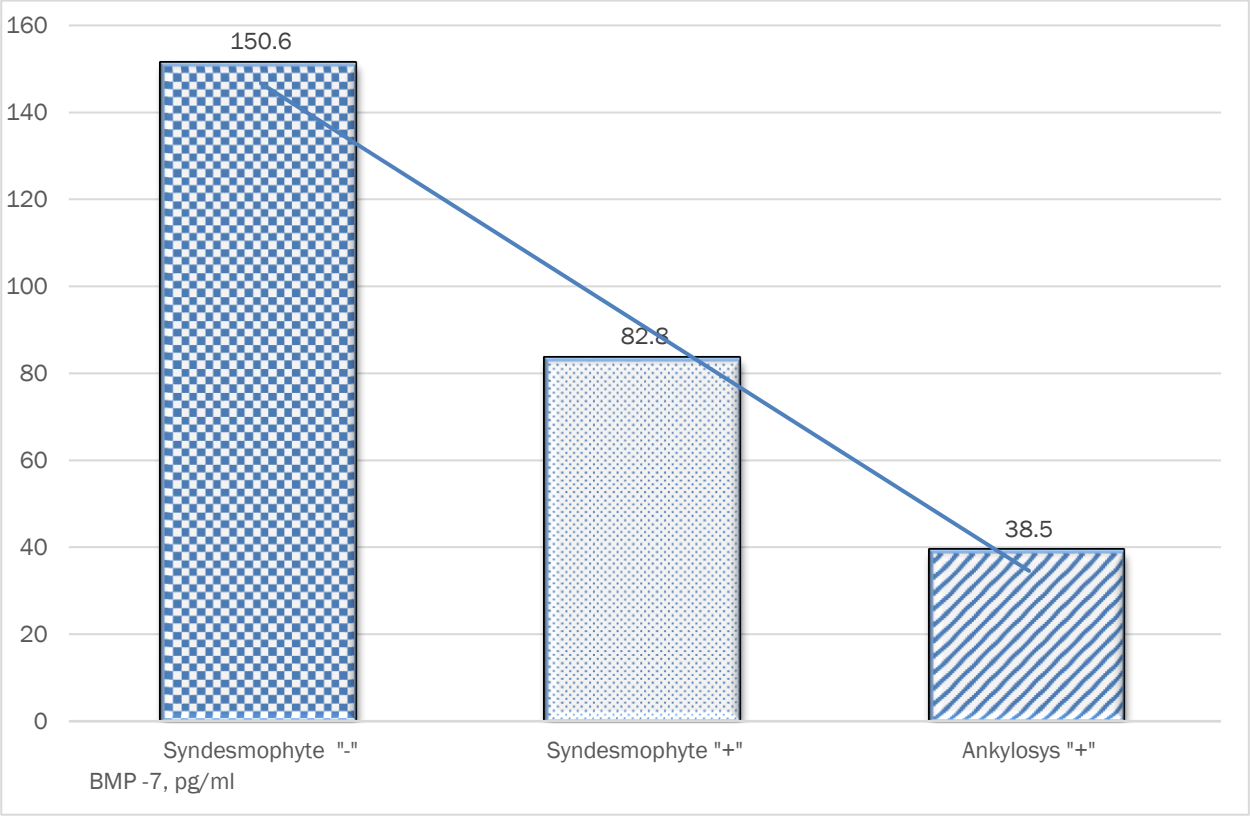
The study of the BMP -7 marker showed that in Group I it was 109.4±16.5 p g/mL ($p < 0.05$) in group II 62.1±5.18 and in the control group 5.3±2.8 n g/mL (Pic. 1). BMP -7 significantly exceeded in patients I groups compared with reference values, which indicates degradation of cartilage and pronounced progression of damage to the bone-structural elements of the spine in axSpA .



Pic. 1. BMP -7 level in the study groups

Note: reliable differences in the indices $p < 0.05$: * - between groups I and II ; $ - between I and the control group; # - between II and the control group.

The most interesting fact in the study of BMP -7 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 time passed, a decrease in its level in the blood was observed. 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 cartilaginous part is replaced by bone tissue and the level of BMP -7 in the blood decreases. To confirm this idea, we studied the concentration of BMP -7 in patients with axSpA in the context of the presence and absence of ankylosis and syndesmophytes in the spine according to radiological data (Pic. 2).

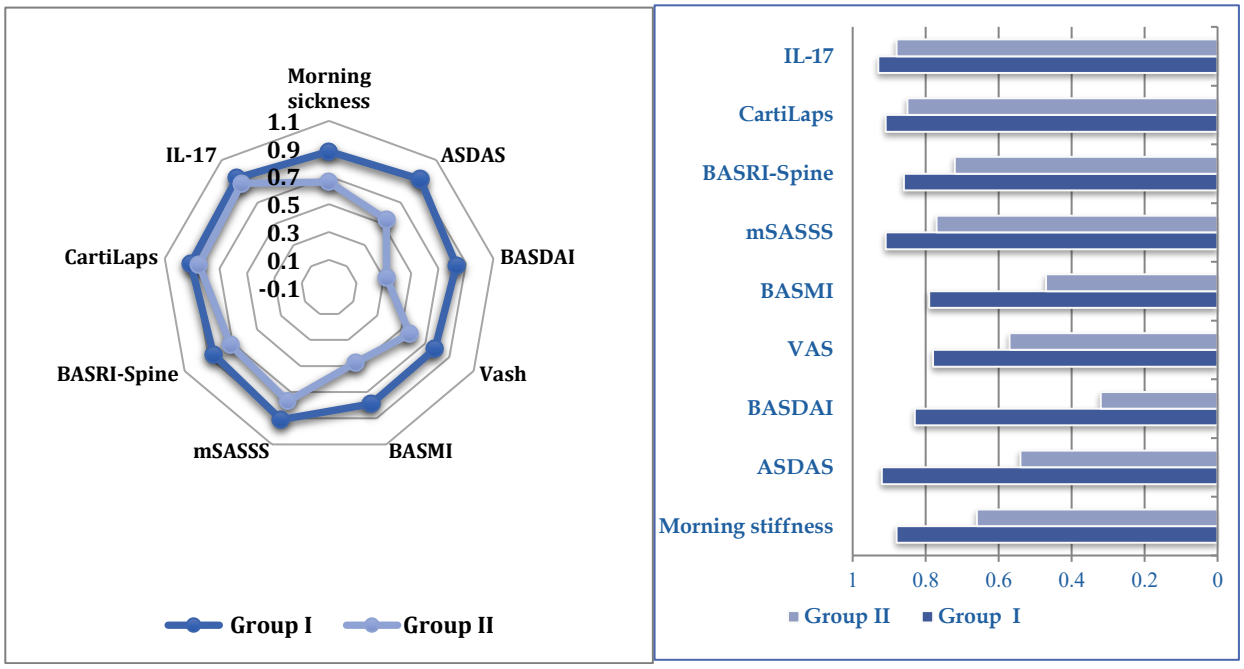


Pic. 2. Average level of BMP -7 in patients with AcS depending on the presence of ankylosis and syndesmophytosis of the spine.

Note: #*-p < 0.05 between measures

As it turned out, patients with spinal ankylosis had very low BMP -7 levels , moderate levels in patients with only syndesmophytes, and high levels in patients without signs of spinal ossification.

Conducting a correlation analysis between BMP -7 and the duration of the disease, IL-17A, radiological indices mSASSS , BASRI - Spine in patients with axSpA showed a strong positive relationship between the parameters (Pic. 3).



Pic. 3. Correlation analysis between BMP -7 clinical, laboratory, and radiological indices in patients with axSpA .

DISCUSSION

In axSpA , two opposing processes occur in the spine in parallel: pathological bone growth, against the background of bone loss , heterotopic cartilage and formation of new bone, which ultimately causes fusion and ankylosis of the joints [2, 10, 13, 15] . 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 the cartilaginous joints, including intervertebral discs, facet and sternocostal joints with their subsequent ossification [9, 11, 12, 14] .

Structural damage associated with the processes of degradation and resorption of cartilage and bone necessitates paying special attention to both the patient's symptoms and the structural damage to the joints associated with axial

spondyloarthritis [2, 14, 17]. One of the important moments in the progression of structural changes in the spine in axSpA is damage to the cartilaginous structure. Since articular cartilage consists of collagen fibers, the study of BMP -7 in axSpA aroused our interest.

The study of BMP -7 showed its very high numbers in patients with axSpA against the background of high disease activity , which indicates the progression of spinal damage. Our data show that the increase in BMP -7 , which indicates cartilage ossification, is associated with radiographic damage to the spine and directly correlates with IL-17A in patients with axSpA .

Thus, ankylosis of the spine against the background of high disease activity with an increase in the level of IL-17A is preceded by the breakdown of cartilage tissue with the formation of bone tissue in its place, and the study of the BMP -7 biomarker in the early stages of the disease can serve as an indicator of the prognosis of the progression of bone-structural changes in the spine.

CONCLUSION

1. In patients with axSpA with high disease activity, a significantly high level of BMP -7 was detected, which indicates the progression of the replacement of spinal cartilage tissue with bone and the rapid development of ankylosis.
2. The obtained data suggest that measurement of BMP -7 levels may be useful for monitoring and prognosticating spinal injuries in patients with axSpA .

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