INFLUENCE OF INTERLEUKIN-17 ON SPINAL REMODELING IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Rikhsieva Lobarkhon Makhmudzhanovna, Abdurakhmanova Nargiza Mirza-Bakhtiyarkhonovna

Tashkent Medical Academy

Annotation

The article presents data from our own studies devoted to studying the level of the pro-inflammatory cytokine - interleukin-17 in patients with axial spondyloarthritis. The level of interleukin-17 was studied in two groups: in patients with spinal ankylosis and in patients without spinal ankylosis , as well as in healthy individuals. The level of interleukin-17 was also compared with clinical and functional signs of the disease. According to the research results, an increase in the level of interleukin-17 was revealed by 10.5 times compared to healthy individuals and by 1.8 times in patients with no signs of ankylosis. An increase in the level of interleukin-17 shows a high correlation with spinal damage and clinical and functional signs of the disease, which once again proves its pathogenetic significance in the development of ankylosis

Keywords: interleukin-17 , axial spondyloarthritis, BASDAI , ASDAS .

Axial spondyloarthritis (axSpA) is an autoimmune disease that is closely related to HLA-B27, affecting the spine, sacroiliac joints and ultimately leading to ankylosis and disability of patients [1, 3, 9, 10, 17].

Over the past two to three decades, advances in immunological research have led to an increased understanding of the pathogenesis of (axSpA), repeatedly emphasizing the key role in cytokine dysregulation and its overproduction [9, 13, 19, 22]. There are a lot of works devoted to the pro-inflammatory cytokine - tumor necrosis factor (TNF-α), scientists have identified its direct participation in the pathogenesis of axSpA and its inhibitors have begun to be widely used in the

treatment of axSpA [4, 10, 24]. But a decade later, other cytokines were identified, such as interleukin 17 (IL-17), interleukin-23 (IL-23), which play a direct role in the development of the disease [5, 8, 16, 18].

IL-17 was first described in 1993 in connection with the study of its effect on the production of IL-6 and IL-8 in rheumatoid arthritis [6, 20]. The IL -17 cytokine family consists of 6 proteins (IL -17 A to IL -17 F) and 5 receptors (IL -17 RA to IL -17 RE) [4, 8]. IL-17 is primarily produced by T helper 17 (TH17) cells, but can also be produced by other cells [20]. IL-17 affects various cells, such as endothelial cells, fibroblasts, macrophages, osteoblasts, which in turn lead to inflammatory reactions and bone tissue formation [15]. The convincing influence of IL-17 in the pathogenesis of axSpA was the high effectiveness of monoclonal antibodies blocking interleukin-17 in the treatment of AS [11, 18, 20, 21, 23].

Studying the level of IL-17 in patients with axSpA with a combination of both pathologies is of some interest.

Materials and research methods:

In the period from 2022 to 2023 years, 63 patients diagnosed with axSpA were examined in the 3-rd City clinical Hospital of the city of Tashkent, of which there were 48 men, 15 women, the average duration of the disease was 9.3 ± 2.4 years. The control group consisted of 30 healthy volunteers of the appropriate middle age. The diagnosis was made according to the modified New York criteria for the diagnosis of axSpA. The subjects were divided into two groups : Group I - 33 patients with axSpA, with signs of spinal ankylosis, Group II - 30 patients with axSpA, without signs of spinal ankylosis. Spinal involvement was determined using MRI/MSCT studies of the spine, mSASSS index , CTX-II marker, disease activity using interleukin-17. The dynamics of systemic inflammation indicators were based on assessing the level of IL-17 and C-reactive protein. The average age of patients in group I was 43.2±13.3 years and in group II 39.5±8.3 years . Disease activity was studied using the BASDAI and ASDAS scales , pain syndrome was assessed using a visual analogue scale (VAS). All patients underwent in-depth

clinical, laboratory, and immunological studies, including IL-17A. To measure the content of IL-17A in the obtained patient serum samples, a quantitative enzyme immunoassay method was used using Elabscience reagents (USA) according to the instructions supplied with the kit.

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

Research results:

Studies of both groups showed the presence of both axial and peripheral forms of joint damage.

A study of the concentration of IL-17A in blood serum showed significantly high numbers in group I (63.5 ± 49.4 pg /ml; p < 0.0 01 *) relative to group II (35.3 ±13.6 pg /ml; p < 0.0 01*) and control group (6.00 ±1.25 pg /ml; p < 0.0 01*), which indicates a more pronounced and persistent inflammatory process against the background which led to ankylosis of the spine (Fig.1). Thus, IL-17 values were 1.8 times higher than those of the comparison group and 10.5 times higher than the results of practically healthy volunteers (p <0.001);

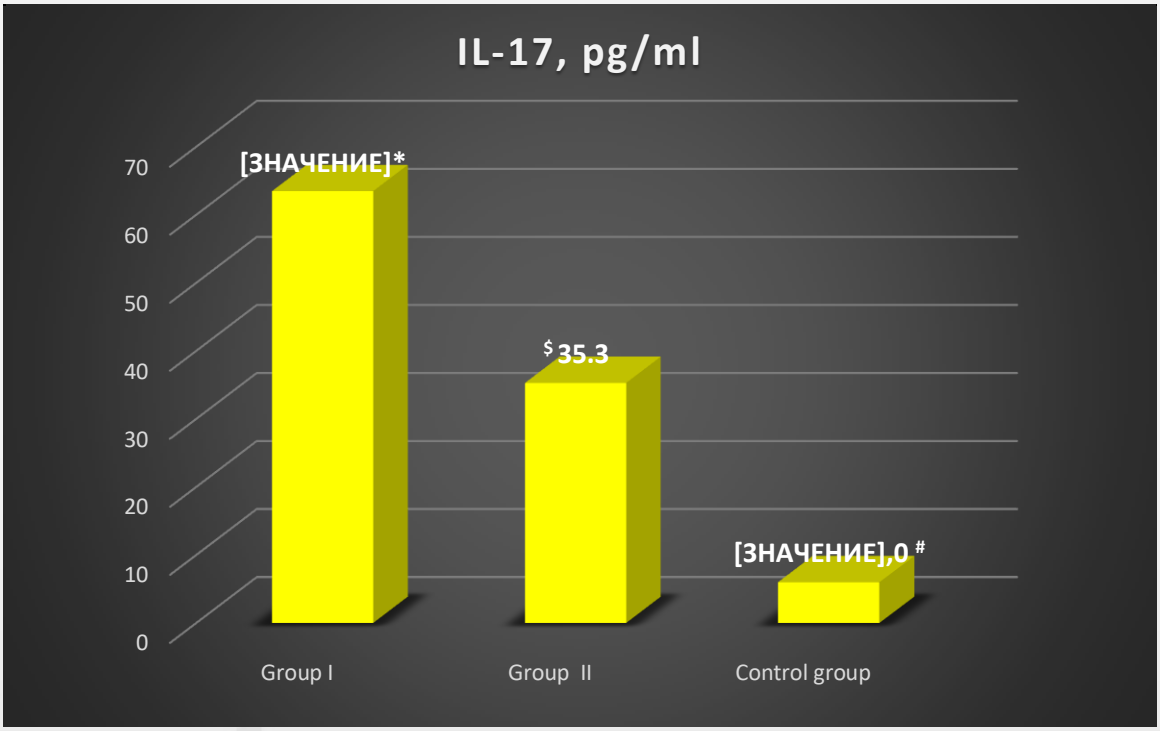

Fig. 1. Concentration of IL-17A in the study groups

(Significant differences in indicators : * p <0.001 - group I in relation to the control group, [group] I in relation to group II and the control group; # p <0.05 between group II and the control group).

When comparing the level of IL-17 and morning stiffness (Fig.2.), a clear relationship was revealed: the higher the level of this cytokine, the longer the morning stiffness; when conducting a correlation analysis between the two signs in two groups, a strong positive relationship was revealed: Group I r =0.88; Group II r =0.90

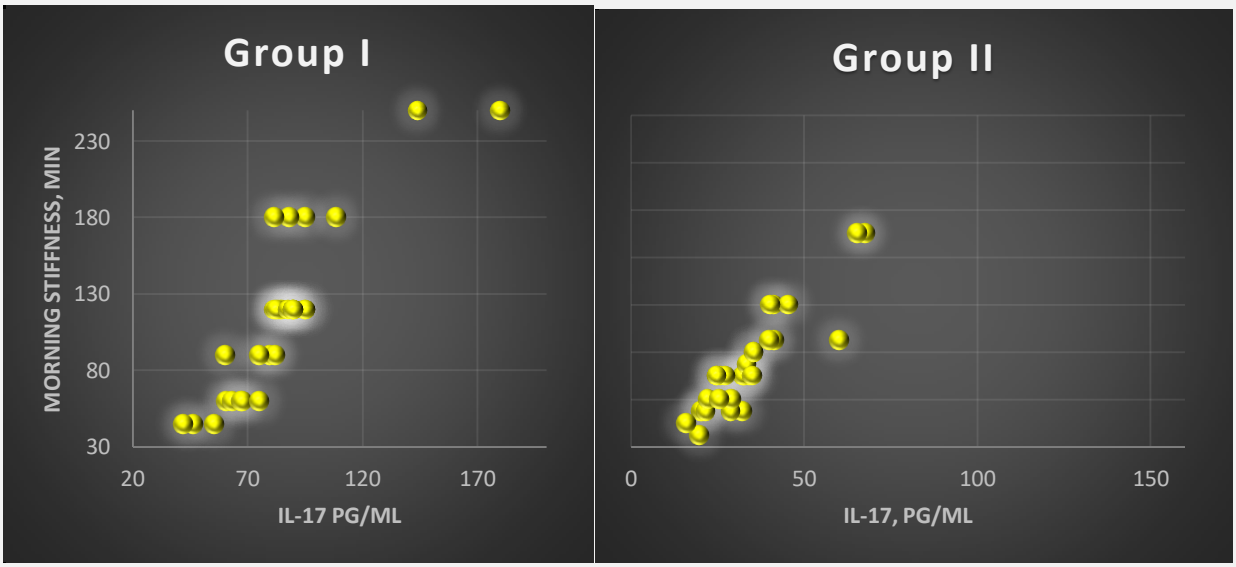

Fig. 2. The relationship between the level of IL-17 and the duration of morning stiffness in the study groups.

The study of the relationship between the concentration of IL-17 and pain syndrome according to VAS also showed the presence of a strong positive correlation in the studied groups: group I r = 0.84; Group II r =0.82 (Fig. 3).

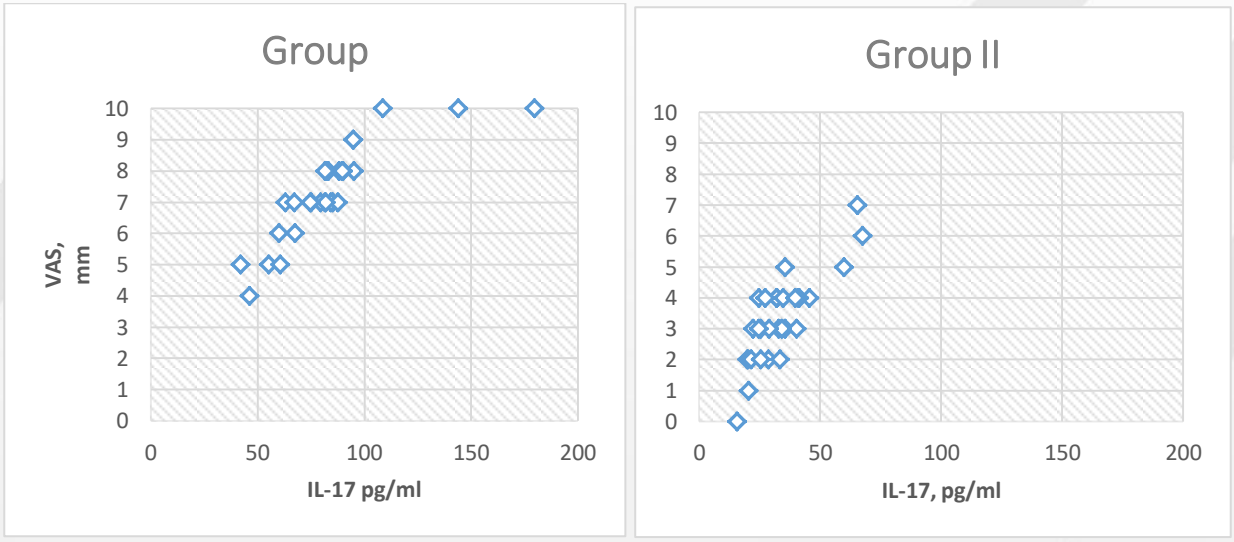

Fig. 3. The relationship between the level of IL-17 and pain syndrome according to VAS in the study groups.

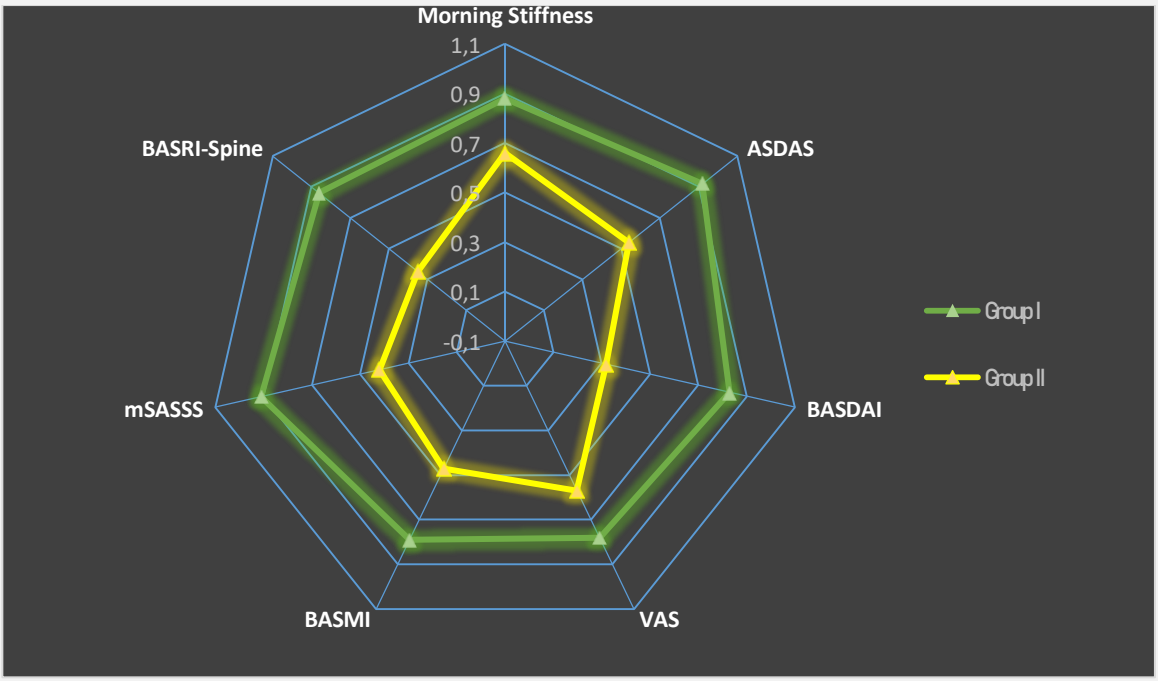

Fig. 4. Correlation between clinical and functional indicators of axSpA and IL-17A in the study groups.

Multivariate mathematical analysis showed between IL-17 and signs of activity (ASDAS , BASDAI), pain syndrome according to VAS, morning stiffness, metrological index BASMI , radiographic indices BASRI - SPINE, mSASSS,

showed a strong positive correlation in group I , which confirms its role in pathogenesis of axSpA (Fig. 4).

Discussion:

IL-17A also plays a key role in the pathogenesis of axSpA, having a high correlation with the activity and progression of the disease [2,7,12]. Studies of how this cytokine changes in the presence and absence of ankylosis and how it affects the clinical picture of both diseases aroused our special interest.

Our work presents data on the concentration of IL-17A in patients with axSpA and its effect on the clinical course of the disease. In axSpA patients with spinal ankylosis, very high concentrations of IL-17 A were observed, which affected the clinical picture of the disease and high disease activity. High levels of IL-17A positively correlated with radiographic indices (BASRI - Spine , mSASSS) of axSpA, indicating its prognostic significance. In the comparison group, an increase in IL-17A was also found, which is typical for axSpA, but the cytokine titer was almost two times lower than in the first group. If we compare the clinical and functional characteristics of both groups, we found a more pronounced limitation of functional activity, higher disease activity on several scales, and a pronounced intensity of pain.

Conclusions :

1. An increase in the level of interleukin-17 has a close relationship with spinal damage in patients with axSpA; an increase in its level can contribute to the progression of spinal ankylosis .
2. axSpA lesions with the additional inclusion of markers such as IL-17 to predict the rate of ankylosis .

Literature:

1. Гайдукова И.З., Ребров А.П., Апаркина А.В., Хондкарян Э.В. Концентрация интерлейкина-17А остается стабильно высокой у больных

анкилозирующим спондилитом, получающих ингибиторы фактора некроза опухоли-α в течение года // Терапевтический архив. 2017. №4.
2. Akhmedov, K. S., Rixsiyeva, L. M., Abdurahmanova, N. M., Botirbekov, A. N., Turaev, I. A., & Raximov, S. S. (2023). CHANGES IN C-TELOPEPTIDE COLLAGEN-II LEVEL IN PATIENTS WITH ANKYLOSING SPONDYLOARTHRITIS AFTER COVID-19. Journal of Modern Educational Achievements, 3(3), 78-87.
3. Axmedov Kh.S, Abdurakhmanova N.M, Zaripov S.S., & Turaev I.A. (2023). THE EFFECT OF CLIMATE-GEOGRAPHICAL FACTORS ON RHEUMATOID ARTHRITIS ACTIVITY. World Bulletin of Public Health, 18, 67-69. Retrieved from
4. 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.
5. 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
6. Abdurakhmanova N. M. High concentration of tumor necrosis factor in ankylosing spondylitis patients after COVID-19 //British medical journal. – 2022. – Т. 2. – №. 1.2.
7. Abdurakhmanova, N. M., & Ahmedov, K. S. (2022). Influence of accepting basic antirheumatic therapy for ankylosing spondyloarthritis on the clinical course Covid-19. ACADEMICIA: An International Multidisciplinary Research Journal, 12(7), 71-76.
8. Beringer A, Thiam N, Molle J, Bartosch B, Miossec P. Synergistic effect of interleukin-17 and tumour necrosis factor-α on inflammatory response in hepatocytes through interleukin-6-dependent and independent pathways. Clin Exp Immunol. 2018 Aug;193(2):221-233. doi: 10.1111/cei.13140. Epub 2018 May 31. PMID: 29676779; PMCID: PMC6046473.
9. Deveci H, Turk AC, Ozmen ZC, Demir AK, Say Coskun SU. Biological and genetic evaluation of IL-23/IL-17 pathway in ankylosing spondylitis patients. Cent Eur J Immunol. 2019;44(4):433-439. doi: 10.5114/ceji.2019.92805. Epub 2020 Jan 20. PMID: 32140056; PMCID: PMC7050057.
10. Dubash S, Bridgewood C, McGonagle D, Marzo-Ortega H. The advent of IL-17A blockade in ankylosing spondylitis: secukinumab, ixekizumab and beyond. Expert Rev Clin Immunol. 2019 Feb;15(2):123-134. doi: 10.1080/1744666X.2019.1561281. Epub 2019 Jan 8. PMID: 30576610.
11. Gravallese EM, Schett G. Effects of the IL-23-IL-17 pathway on bone in spondyloarthritis. Nat Rev Rheumatol. 2018 Nov;14(11):631-640.
12. Navarro-Compán V, Sepriano A, El-Zorkany B, van der Heijde D. Axial spondyloarthritis. Ann Rheum Dis. 2021 Dec;80(12):1511-1521. doi: 10.1136/annrheumdis-2021-221035. Epub 2021 Oct 6. PMID: 34615639.
13. Pedersen SJ, Maksymowych WP. The Pathogenesis of Ankylosing Spondylitis: an Update. Curr Rheumatol Rep. 2019 Nov 11;21(10):58.

14. Rafael-Vidal C, Pérez N, Altabás I, Garcia S, Pego-Reigosa JM. Blocking IL-17: A Promising Strategy in the Treatment of Systemic Rheumatic Diseases. Int J Mol Sci. 2020 Sep 26;21(19):7100. doi: 10.3390/ijms21197100. PMID: 32993066;
15. Raiker R, Pakhchanian H et al. Axial spondyloarthritis may protect against poor outcomes in COVID-19: propensity score matched analysis of 9766 patients from a nationwide multi-centric research network. Clin Rheumatol. 2022;41(3):721-730. doi:10.1007/s10067-021-05979-y
16. Rakhimova MB, Kh.S. Akhmedov The impact of sequelae of COVID-19 on the course of ankylosing spondylitis. Central Asian journal of medicine. Vol. 2021. Issue 4., p.11
17. Ruiz de Morales JMG et al. Critical role of interleukin (IL)-17 in inflammatory and immune disorders: An updated review of the evidence focusing in controversies. Autoimmun Rev. 2020 Jan;19(1):102429.
18. Schinocca C, Rizzo C, Fasano S, Grasso G, La Barbera L, Ciccia F, Guggino G. Role of the IL-23/IL-17 Pathway in Rheumatic Diseases: An Overview. Front Immunol. 2021 Feb 22;12:637829. doi: 10.3389/fimmu.2021.637829.
19. Sieper J, Poddubnyy D. Axial spondyloarthritis. Lancet. 2017 Jul 1;390(10089):73-84. doi: 10.1016/S0140-6736(16)31591-4. Epub 2017 Jan 20.
20. Sieper J, Poddubnyy D, Miossec P. The IL-23-IL-17 pathway as a therapeutic target in axial spondyloarthritis. Nat Rev Rheumatol. 2019 Dec;15(12):747-757.
21. Sharip A, Kunz J. Understanding the Pathogenesis of Spondyloarthritis. Biomolecules. 2020 Oct 20;10(10):1461. doi: 10.3390/biom10101461.
22. Yin Y, Wang M, Liu M, Zhou E, Ren T, Chang X, He M, Zeng K, Guo Y, Wu J. Efficacy and safety of IL-17 inhibitors for the treatment of ankylosing spondylitis: a systematic review and meta-analysis. Arthritis Res Ther. 2020 May 12;22(1):111.
23. Ward MM, Deodhar A, Gensler LS et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Care Res (Hoboken). 2019 Oct;71(10):1285-1299. doi: 10.1002/acr.24025. Epub 2019