Migration Letters

Volume: 20, No: S8(2023), pp. 1520-1528

ISSN: 1741-8984 (Print) ISSN: 1741-8992 (Online)

www.migrationletters.com

Assessment of the Level of Interleukin-17 in Patients with Axial Spondyloarthritis

Lobarhon Rikhsieva[1], Nargiza Abdurakhmanova[2], Khalmurad Akhmedov[3], Shaira Musayeva[4], Sagdiyana Buranova[5], Abdurashid Botirbekov[6]

Abstract

The article presents data from our own studies on the study of the level of pro-inflammatory cytokine - interleukin-17 in patients with axial spondylitis. The level of interleukin-17 was studied in two groups: in patients with spinal ankylosis and in patients without spinal ankylosing, as well as in healthy individuals. The level of interleukin-17 was also compared with the clinical and functional signs of the disease. According to the results of the studies, an increase in the level of interleukin-17 was revealed by 10.5 times compared with 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 lesions and clinical and functional signs of the disease, which once again proves its pathogenetic significance in the development of ankylosis.

Keywords: *Interleukin -17, axial spondylitis, BASDAI, ASDAS.*

Introduction

Axial spondyloarthritis (axSpApA) is an autoimmune disease closely associated with HLA-B27 that affects the spine, sacroiliac joints and ultimately leads to ankylosing and disability in patients [1, 3, 9, 10, 17].

Over the past two to three decades, advances in immunological research have led to increased understanding of the pathogenesis of axSpA, repeatedly emphasizing a key role in cytokine dysregulation and overproduction [9, 13, 19, 22]. There are a lot of works devoted to the pro-inflammatory cytokine - tumor necrosis factor (TNF-α), scientists have revealed its direct involvement 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 such as interleukin 17 (IL-17), interleukin-23 (IL-23) were identified, 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 family of cytokines consists of 6 proteins (from IL -17 A to IL -17 F) and 5 receptors (from IL -17

[1] Tashkent Medical Academy
[2] Tashkent Medical Academy
[3] Tashkent Medical Academy
[4] Center for the development of professional qualification of medical workers
[5] Tashkent Medical Academy
[6] Tashkent Medical Academy

RA to IL -17 RE) [4, 8]. IL-17 is mainly produced by T-helper cells 17 (TH17), but can be produced by other cells as well [20]. IL-17 affects various cells such as endothelial cells, fibroblasts, macrophages, osteoblasts, which in turn lead to inflammatory responses and bone formation [15]. A convincing influence of IL-17 in the pathogenesis of axSpA was the high efficiency of monoclonal antibodies blocking interleukin-17 in the treatment of this disease [11, 18, 20, 21, 23].

The study of the level of IL-17 in patients with axSpA with a combination of both pathologies is of particular interest.

Materials and methods of research:

period from 2021-2023, 63 patients diagnosed with axSpA were examined in the 3-city clinical hospital 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 corresponding average 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 ankylosing. Spinal lesion 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 was based on the assessment of the level of IL-17 and C-reactive protein. The mean age of patients in group I was 43.2±13.3 years and in group II 39.5±8.3 years . The activity of the disease was studied using the BASDAI and ASDAS scales , the pain syndrome was assessed using the 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 samples of patient sera, a quantitative enzyme-linked immunosorbent assay was used using reagents from Elabscience (USA) according to the instructions attached to the kit.

Statistical processing of the study 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.

The 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 of which led to ankylosing of the spine (Fig. 1). Thus, the IL-17 indices were 1.8 times higher than the data of the comparison group and 10.5 times higher than the results of practically healthy volunteers ($p <0.001$);

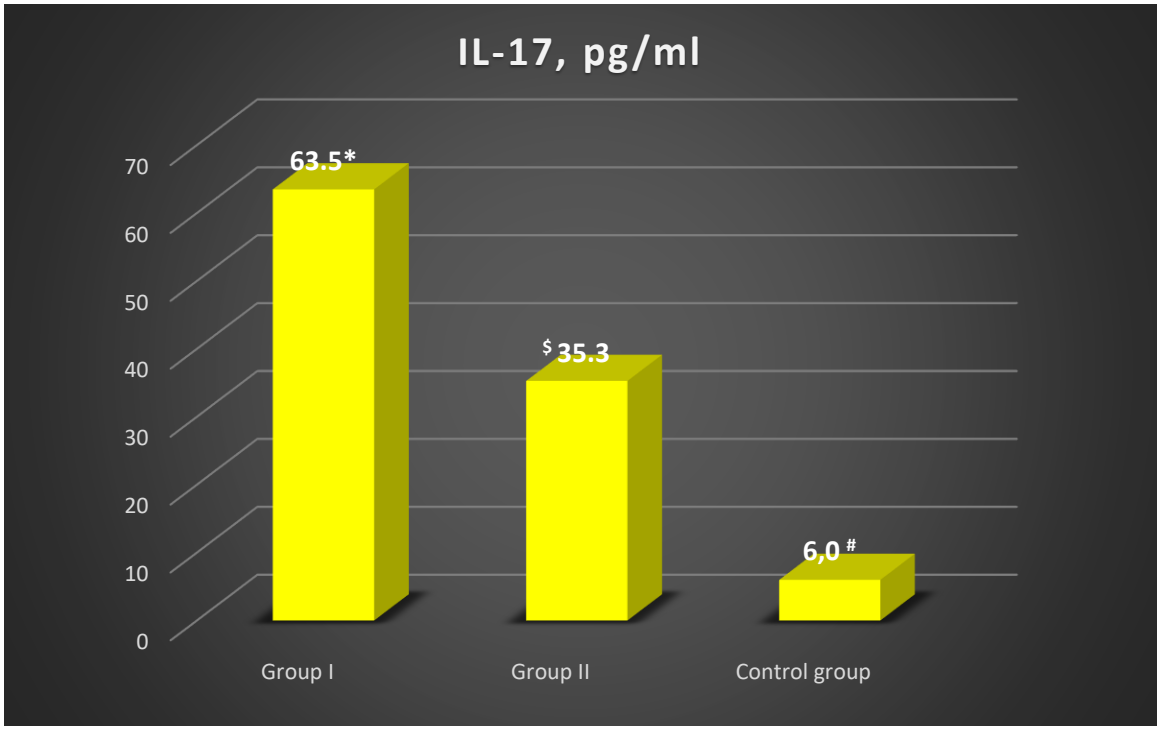
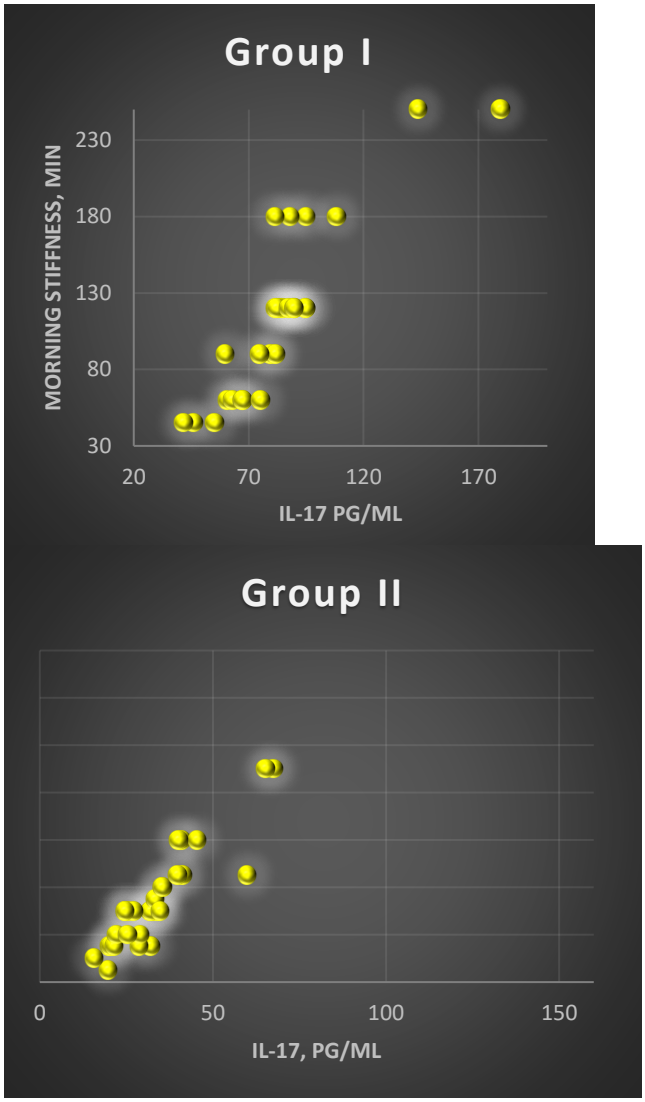


Fig 1. The concentration of IL-17A in the studied groups

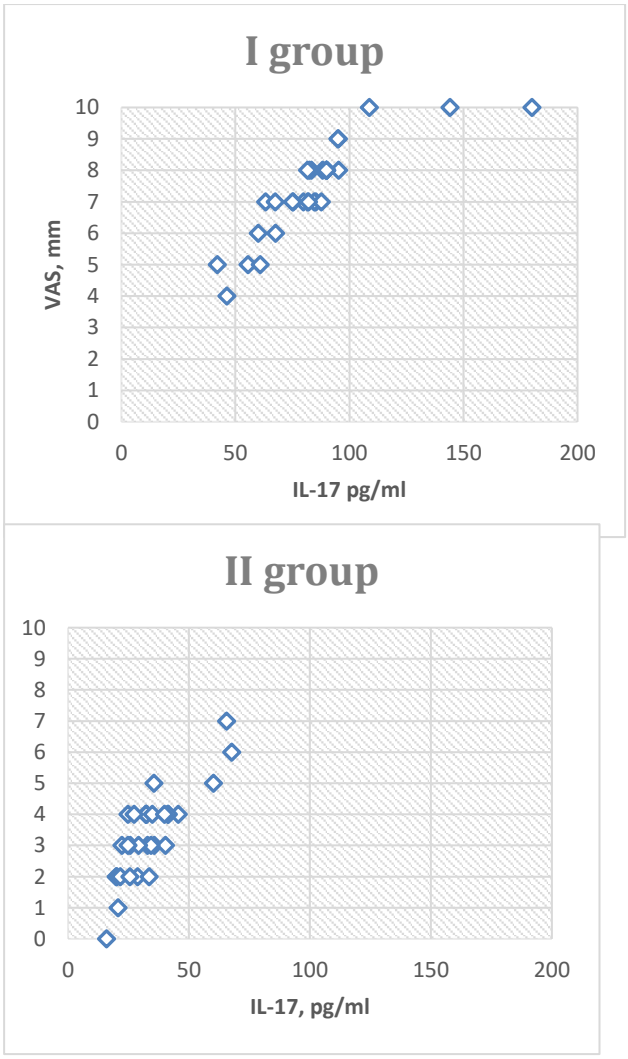
(Significant differences in indicators : * p <0.001 - group I in relation to the control group, $ group I in relation to II and control group; # p <0.05 between II and control group).

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

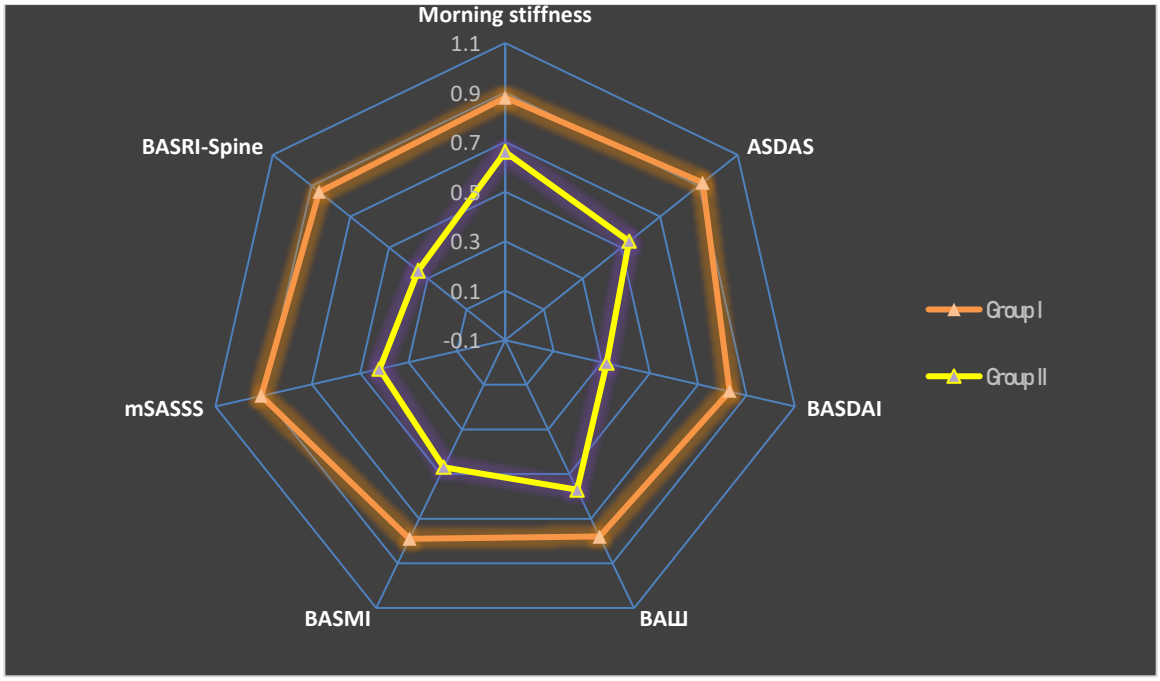


Rice. 2. Correlation between the level of IL-17 and the duration of morning stiffness in the studied groups.

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.).



Rice. 3. Correlation between the level of IL-17 and pain syndrome according to VAS in the studied groups.



Rice. 4. Correlation relationship between clinical and functional parameters 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, BASMI metrological index , radiological indices BASRI - SPINE, mSASSS , showed a strong positive correlation relationship in group I , which confirms its role in pathogenesis of axSpA (Fig. 4).

In axSpA, X-ray, MRI/MSCT signs and articular syndrome, determined on the basis of changes in the spine, are of some practical importance in the diagnosis of the disease, but it is difficult to diagnose due to the absence of specific changes in the early stages of the disease.

Based on the results of the study of MRI and MSCT of the spine, a cartography of the spine was compiled in patients A to C.

Table 1. MRI/MSCT signs of changes in the spine in patients with axSpA.

MRI/MSCT signs	axSpA % (n=51)
Romanus-type spondylitis (bone marrow edema in the corners of the vertebral bodies, osteitis)	58.9
Anderson-type spondylitis (diffuse unevenly expressed edema, osteitis)	5.8
Edema of the bone marrow "trough-shaped" form, osteitis	0
erosion	50.9
Arthritis of the synovial joints of the spine	3 9.2
Inflammatory swelling in the ligaments of the spine	2 9.4
Ossification of ligaments	23.5
Fatty degeneration of the bone marrow	35.3

Zones of osteosclerosis	37.2
Osteoporosis of the vertebral bodies	74.5
Syndesmophytes	37.2
Narrowing of the intervertebral fissure	33.3
Formation of bone bridges between the vertebrae and ankylosis	27.4

According to the results obtained by cartography, as can be seen from Table 1, in all patients with axSpA, i.e. in 100% of cases, multilevel changes were revealed in the lumbar spine. One of the initial changes in the spine in axSpA was the damage to the cartilaginous part in the form of arthritis of the synovial joints of the spine, which many specialists did not pay attention to. An important point was also the lesion of the ligamentous apparatus, which began with inflammatory changes and ended with ossification. Erosion of the vertebral bodies was also a common finding in patients with axSpA. Post-inflammatory fatty degeneration of the bone marrow was characteristic of a long-term inflammatory process in the body of the spine. Narrowing of the intervertebral space, formation of bone bridges, syndesmophytosis, ankylosis were typical for the late stages of the disease.

When studying inflammatory changes in the body of the spine, spondylitis of the Romanus and Anderson type was revealed, which is typical for patients.

Discussion:

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

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 ankylosis of the spine, very high concentrations of IL-17A were observed, which affected the clinical picture of the disease and the high activity of the disease. A high level of IL-17A positively correlated with radiological indices (BASRI - Spine, mSASSS) of axSpA, which indicates 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, a higher activity of the disease on several scales at once, and a pronounced intensity of the pain syndrome.

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 and contribute to high disease activity.

2. The conducted studies showed the need to optimize the algorithm for diagnosing axSpA lesions with the additional inclusion of markers such as IL-17 to predict the rate of ankylosis.

3. Spinal cartography can facilitate early radiological diagnosis of axSpA.

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