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RESEARCH ARTICLE

Comparative Clinical and Immunological Characteristics of Seripositive And Seronegative Rheumathoid Arthritis

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Abstract: To study and compare the diversity and specific characteristics of the clinical course of seronegative and seropositive Rheum factor, anti-CCP positive, and anti-CCP negative variants of rheumatoid arthritis.

Methods: Information was collected from studies measuring visual analog scale (VAS) pain, disease activity score 28 (DAS28), X-ray of joints, tender joint count (TJC), swollen joint count (SJC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP).

Results: The study included 80 patients with rheumatoid arthritis divided into two equal groups: seropositive and seronegative RA. The mean age was comparable between groups (36.87± years in Group I vs. 37.65± years in Group II), with a clear predominance of female patients in both groups (80% and 90%, respectively). Articular involvement was the most common clinical form; however, systemic (articular-visceral) manifestations were more frequent in the seronegative group (47.5% vs. 35%). Anti-CCP positivity was significantly higher in the seronegative group (67%) compared to the seropositive group (27%). Disease activity analysis revealed that moderate activity predominated in the seropositive group (55%), whereas high disease activity was more common in the seronegative group (57.5%). Regarding disease staging, the established (advanced) stage was the most frequent in both groups (55% in Group I and 60% in Group II), while very early stages were rare or absent.

Key words: Rheumathoid factor, rheumatoid arthritis, joint, anti-CCP, C-reactive protein, DAS28.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by a chronic inflammatory response, with persistent synovitis leading to progressive deterioration and dysfunction of joints. Bone fragility in RA is caused by systemic inflammation, circulating autoantibodies, and the secretion of proinflammatory cytokines, which collectively have a detrimental effect on bone[1]. The prevalence of RA is approximately 1–2% of the global population, and it is three times more common in women than in men. Rheumatoid arthritis can occur at any age, but patients aged 40 to 50 are most susceptible. According to the World Health Organization Mortality Database, which covers 31 countries, rheumatoid arthritis accounts for nearly 18% of all deaths caused by various types of arthritis and other musculoskeletal diseases, but the exact cause of rheumatoid arthritis remains unknown [2]. A specific feature of RA is the presence of a positive rheumatoid factor (RF) in the blood of 80–90% of patients (IgG, IgM immune complexes). The clinical picture of 'classic' seropositive RA is difficult to differentiate from other joint diseases. At the onset, reliable diagnosis of RA can be challenging. In some patients, especially men, the disease may begin atypically with damage to large joints and without morning stiffness or RF. Seronegative RA is a form of the disease in which RF is not detected in serum or synovial fluid, and occurs in about 20% of patients [3].

Depending on the detection of anti-CCP, different RA subtypes show significant differences in immunological clinical presentation [4]. The presence of anti-CCP in peripheral blood indicates a predominant

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inflammatory component and B cell involvement, leading to the development of a progressive erosive process [5]. In anti-CCP negative subtypes, CD4+ cells play a significant role and the pathological process is characterized by a proliferative-fibrotic pattern.

Therefore, studying the distinctive features and differences in the clinical course of various immunological variants and subtypes of rheumatoid arthritis is of great importance. [6].

Purpose of the research

To study and compare the diversity and specific characteristics of the clinical course of seronegative, seropositive, anti-CCP positive, and anti-CCP negative variants of rheumatoid arthritis.

METHODS

The study included 80 patients aged 18 to 65 years diagnosed with rheumatoid arthritis according to the ACR/EULAR classification criteria, with no evidence of other rheumatologic diseases. The patients were managed either as inpatients or outpatients at the Republican Rheumatology Center under the 2nd Clinic of Tashkent Medical Academy, specifically in the departments of cardiorheumatology, rheumatology, and arthrology. Patient enrollment was conducted between April 2023 and January 2025.

The study population was divided into two groups:

- Group I consisted of 40 patients with confirmed seropositive rheumatoid arthritis (RF-positive).
- Group II consisted of 40 patients with confirmed seronegative rheumatoid arthritis (RF-negative).

All patients underwent the following evaluations:

- Collection of patient complaints and medical history (anamnesis), along with a comprehensive physical examination
- Laboratory investigations including complete blood count and biochemical blood analysis (ALT, AST, total protein, bilirubin, urea, creatinine), acute-phase inflammatory markers, and immunological tests (rheumatoid factor and anti-cyclic citrullinated peptide antibodies [anti-CCP])
- Urinalysis
- Radiography of the joints
- Electrocardiography (ECG)
- Additional instrumental diagnostic methods when clinically indicated

RESULTS

The mean age of patients in Group I was 36.87 years (range: 22–47 years). Among them, 32 (80%) were female and 8 (20%) were male. The number of patients aged 18–40 years was 23 (57.5%), while those aged 41 years and older accounted for 17 (42.5%). According to the clinical-anatomical classification, the articular form was observed in 26 patients, whereas the articular-visceral (systemic) form was identified in 14 patients.

The clinical characteristics of patients with rheumatoid arthritis (RA) are presented in table 1.

Table 1. Clinical characteristics of patients with rheumatoid arthritis (n = 80)

Groups / Parameters		Group I (Seropositive RA, n=40)	Group II (Seronegative RA, n=40)
Age	18-40 years	23 (57,5%)	22 (55 %)
	≥41 years	17 (42,5%)	18 (45%)

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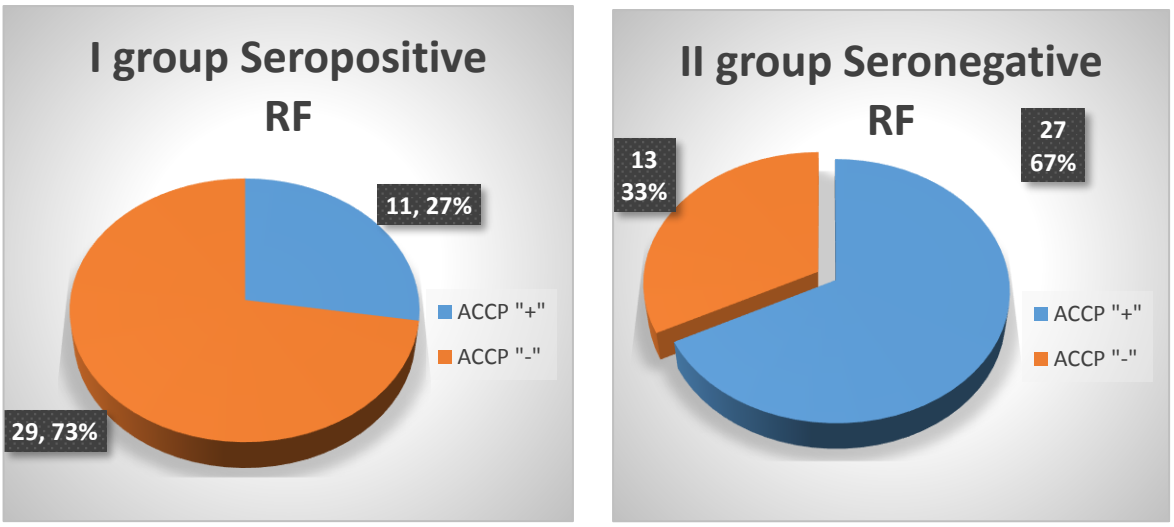
Sex	Female	32 (80%)	36 (90%)
	Male	8 (20%)	4 (10%)
Clinical-anatomical form	Articular form	26	21
	With systemic involvement (articular-visceral form)	14	19

In Group II, the mean age of patients was 37.65 years (range: 23–52 years). Among them, 36 (90%) were female and 4 (10%) were male. Patients aged 18–40 years accounted for 22 (55%), while those aged 41 years and older comprised 18 (45%). According to the clinical-anatomical classification, the articular form was observed in 21 patients, whereas the articular-visceral (systemic) form was recorded in 19 patients.

One of the key immunological factors in the disease is the presence of anti-cyclic citrullinated peptide antibodies (anti-CCP, referred to as SSPA). In Group I (n=40), 11 patients (27%) were anti-CCP positive, while 29 patients (73%) were anti-CCP negative. In Group II (n=40), 27 patients (67%) were anti-CCP positive, whereas 13 patients (33%) were anti-CCP negative (figure 1).

Figure 1. Distribution of patients according to anti-CCP (anti-CCP) status



The distribution of patients according to disease activity levels differed between the groups (figure 2).

In Group I, patients with low disease activity (grade 1) accounted for 2 cases (5%), while the majority had moderate disease activity, comprising 22 patients (55%). High disease activity was identified in 16 patients (40%).

In Group II, notable differences were observed compared to Group I. Although the number of patients with low disease activity was slightly lower, comprising 1 patient (2.5%), the

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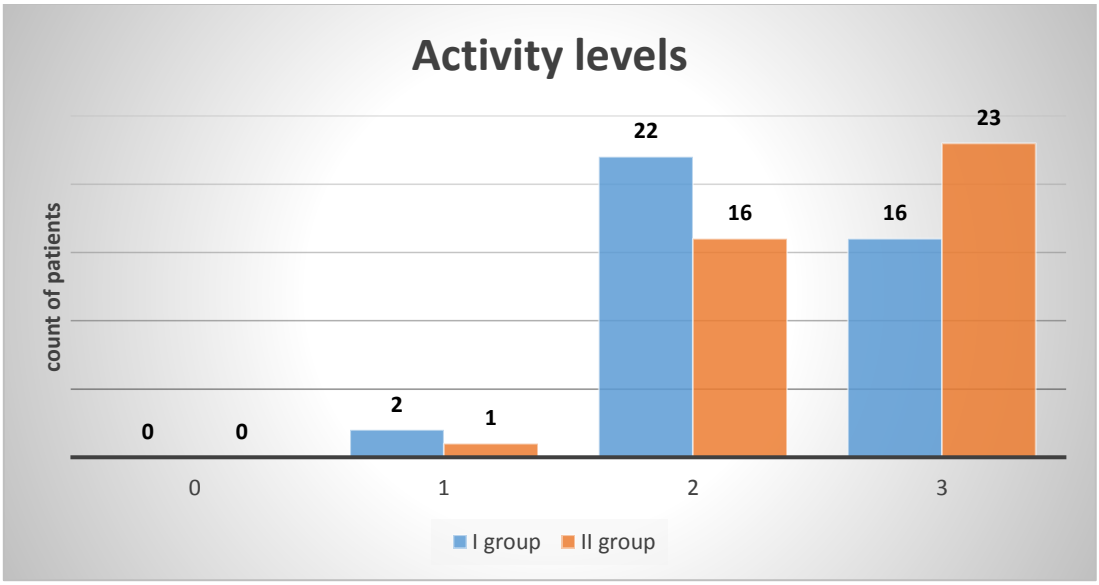
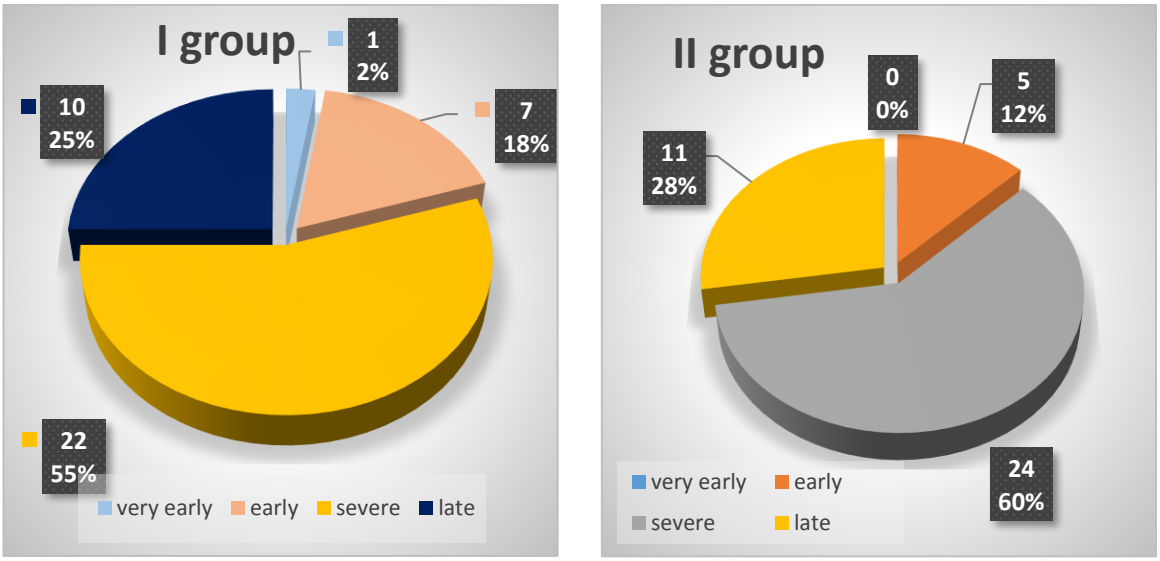
proportion of patients with moderate disease activity was also lower than in Group I, accounting for 16 patients (40%). In contrast, a higher proportion of patients exhibited high disease activity, totaling 23 patients (57.5%).

Figure 2. Frequency distribution of disease activity levels among patients in the study groups



The distribution of patients according to disease stage in the study groups is presented in figure 3

Figure 3. Distribution of patients according to disease stages



As shown in the figure above, the distribution of disease stages in both groups demonstrates that the established (advanced) stage predominated in each group.

In Group I, 1 patient (2%) was in the very early stage, 7 patients (18%) were in the early stage, 22 patients (55%) were in the established stage, and 10 patients (25%) were in the late stage.

In Group II, no patients were identified in the very early stage. The early stage was observed in 5 patients (12%), the established stage in 24 patients (60%), and the late stage in 11 patients (28%).

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DISCUSSION

The findings of this study demonstrate important clinical and immunological differences between seropositive and seronegative rheumatoid arthritis. Although traditionally seropositive RA is considered more severe, our results indicate that seronegative patients exhibited higher disease activity and more frequent systemic involvement. A notable observation is the higher prevalence of anti-CCP positivity in the seronegative group, suggesting that anti-CCP antibodies may serve as a more sensitive marker of disease severity and progression than rheumatoid factor alone. This aligns with current evidence indicating the role of anti-CCP in predicting erosive and aggressive disease course. The predominance of patients in the established stage in both groups reflects delayed diagnosis or late presentation, which remains a significant clinical issue. Early detection strategies should therefore be emphasized to prevent disease progression and joint damage.

CONCLUSION

Seronegative rheumatoid arthritis is characterized by higher disease activity, greater systemic involvement, and a higher frequency of anti-CCP positivity compared to seropositive RA. Despite similar demographic characteristics, the clinical course differs significantly between groups, highlighting the importance of comprehensive immunological assessment, particularly anti-CCP testing, in the diagnosis and prognosis of rheumatoid arthritis. Early identification and timely management remain crucial to improving patient outcomes.

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