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The Relationship of Rheumatoid Factor with Disease Activity in Patients with Rheumatoid Arthritis

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Abstract: ***Objective: The aim of the present study was to evaluate if the presence of rheumatoid factor is associated with disease activity in rheumatoid arthritis patients. Material and Methods: This is a cross-sectional study that analyzes 70 patients with rheumatoid arthritis. Physical examination of the joints and the laboratory tests are requested for the patients such as rheumatoid factor and the erythrocyte sedimentation rate. Rheumatoid arthritis activity was assessed according to Disease Activity Score 28. Results: Patients with positive rheumatoid factor were 54 (77.1 %) and 16 (22.9 %) patients were seronegative. Patients with high disease activity scorer were 41 (58.6 %), moderate disease activities were 16 (22.8 %) patients and low disease activities were 13 (18.6 %) patients. Conclusions: Rheumatoid factor is important factor in disease activity in patients with rheumatoid arthritis and may help physician to diagnose and evaluate prognosis in rheumatoid arthritis patients.***

Keywords: rheumatoid arthritis, rheumatoid factor, seronegative, disease activity, joints

1. Introduction

Rheumatoid arthritis (RA) is a classic autoimmune disorder, with chronic inflammation of the synovial membrane and deterioration of cartilage and bone in the affected joints [1]. These processes eventually trigger joint deformities, functional impairment, and poor quality-of-life. [2], [3]. The diagnosis of rheumatoid arthritis is based on clinical manifestations of joints and serological markers [4]. Rheumatoid arthritis patients are characterized by presenting some circulating auto antibodies in their serum. In clinical practice the most common diagnostic test is rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) and is generally accepted by the majority of rheumatologists and recommended by the European League of Arthritis and Rheumatism (EULAR) [5]. These autoantibodies are valuable biomarkers for the diagnosis of rheumatoid arhritis, articular manifestations and disease activity [6]. High titer of IgM-RF and IgA-RF have also considerable prognostic value because they are associated with the severe forms of rheumatoid arthritis, such as radiological erosions, more rapid disease progression, worse outcome and extra-articular manifestations [7], [8], [9].

The aim of the present study was to evaluate if the presence of rheumatoid factor is associated with disease activity in rheumatoid arthritis patients.

2. Material and Methods

This is a cross-sectional study involving 70 patients with rheumatoid arthritis. All patients fulfill the criteria of American College of Rheumatology (ACR) and the European League against Rheumatism (EULAR) for the diagnosis of rheumatoid arthritis [10]. These patients were hospitalized in the clinic of Rheumatology or followed as outpatients. The patients in this study were recruited from outpatient consultations in the Rheumatology clinic. All patients had been treated with disease-modifying anti-rheumatic drugs in function of disease activity, as is usual in clinical practice.

Exclusion Criteria

We have excluded all patients with positive anti-cyclic citrullinated peptide antibody and all patients who had positive both serological markers, rheumatoid factor and anti-cyclic citrullinated peptide antibody.

Serologic Analysis

Serum samples for rheumatoid factor and erythrocyte sedimentation rate (ESR) were obtained. Rheumatoid factor was measured using a standard nephelometry. It was considered to be positive at a cut-off value of 20 u/ml. Erythrocyte sedimentation rate was measured using the Westergren method.

Disease Activity Score

Rheumatoid arthritis activity was evaluated according to" Disease Activity Score" of 28 joints (DAS 28) with 3 variables (tender and swollen joint counts plus value of ESR) [11].We used the EULAR activity criteria, based on the DAS 28 (clinical remission values below 2.6, low activity between 2.6 to 3.2, moderate activity from 3.2 to 5.1 and high activity values over 5.1) [12].

To determine the relation of rheumatoid factor with disease activity in rheumatoid arthritis, the patients are classified into two groups. The first group included patients with positive rheumatoid factor who had high disease activity scorer, moderate and low disease activity scorer and the second group were patients seronegative who had high disease activity scorer, moderate and low disease activity scorer.

3. Statistical Analysis

Continuous variables were expressed as mean values and their respective standard deviations. Categorical variables were presented in absolute values and their respective percentages. Differences between the categorical variables were assessed with Chi square test.The P value ≤ 0,05 was considered a statistically significant. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 19.0.

4. Results

70 Rheumatoid Arthritis patients were included. The mean (±SD) age of the patients was 46.17 (±8.75) years. The mean (±SD) duration of disease was 9.21 (±3.54) years. Female patients are 46 (66%) and male patients are 24 (34 %). The most common treatments received included combination of methotrexate, prednisone and nonsteroidal anti-inflammatory drugs 36 (51 %), followed by the combination of hydroxychloroquine, prednisone and nonsteroidal anti-inflammatory drugs 18 (26%), leflunomide, prednisone and nonsteroidal anti-inflammatory drugs 16 (23%).

Patients with positive rheumatoid factor were 54 (77.1 %) and 16 (22.9 %) patients were seronegative. Patients with high disease activity scorer were 41 (58.6 %), moderate disease activities were 16 (22.8 %) patients and low disease activity were 13 (18.6 %) patients **(table 1)**. In patients with rheumatoid factor positive, 37 (68.5 %) patients had high disease activity, 11 (20.4 %) patients had moderate disease activity and 6 (11 %) patients had low disease activity. The frequency of rheumatoid factor was higher in rheumatoid arthritis patients with high disease activity versus patients with low and moderate disease activity. In patients seronegative, 4 (25 %) patients were high disease activity, 5 (31.25 %) patients were moderate disease activity and 7 (43.75 %) were low disease activity. Patients with positive rheumatoid factor were 54 (100.0 %) of whom 52 (68.5%) represent high disease activity, while in the other group of 16 (100.0 %) patients seronegative who do not have positive rheumatoid factor positive only 4 (25 %) patients have high disease activity **(table 2)**. High disease activity scorer in patients with positive rheumatoid factor were significant versus patients with negative rheumatoid factor **P** = 0.0001.

Table 1: Frequency of patients with rheumatoid factor (RF) positive and seronegative patients in relation to disease activity (DAS 28)

RF	*Seonegative*	*DAS 28*
*37(68.5%)**	4 (25%)	High
11 (20.4 %)	5 (31.25 %)	Moderate
6 (11.1 %)	7 (43.75%)	Low

*****Absolute numbers and row percentage (in parentheses).

Table 2: The Relationship between of patients with rheumatoid factor (RF) positive and seronegative patients in relation to disease activity (DAS 28)

Patients' Group	*Total*	*Moderate and Low DAS 28*	*High DAS 28*	*P value*
RF	54(100%)*	17(31.5%)	37(68.5%)	0.0001
Seronegative	16(100%)	12(75%)	4(25%)	

*****Absolute numbers and row percentage (in parentheses).

5. Discussion

In the present study we evaluated the relationship of rheumatoid factor with disease activity in patients with rheumatoid arthritis. The determination of this serological marker appeared to be important for prognosis and disease activity of rheumatoid arthritis [13], [14], [15], [16], [17]. In this study the frequency of rheumatoid factor was greater in rheumatoid arthritis patients with high disease activity versus patients with low and moderate disease activity and we have found a strong relation between the presence of rheumatoid factor and high rheumatoid arthritis activity. Some previous studies have demonstrated stronger correlations between rheumatoid factor and disease activity parameters [18], [19]**.** IgM rheumatoid factor was a better predictor of disease severity [20]. There was a positive correlation between rheumatoid factor and increased erythrocyte sedimentation rate and C-reactive protein [21]. In other study the authors have found good correlations between rheumatoid factor titres and both the C-reactive protein and the number of swollen joints [22]. Rheumatoid factor is prognostically useful and one recent study revealed that rheumatoid factor titer reflected rheumatoid arthritis disease activity [23]. High serum levels of rheumatoid factor are a hallmark of rheumatoid arthritis and can be used to monitor disease activity [24]. In other study the presence of rheumatoid factor has been proved to be predictive of radiological disease progression, which is a clinical hallmark of aggressive disease [25]. Another study has reported that the presence of rheumatoid factor is predictive of high disease activity in rheumatoid arthritis and is an indicator of severe and erosive disease [26]. In our study, patients with positive rheumatoid factor had more high disease activity compared to seronegative patients. The greater prevalence of rheumatoid factor in patients with higher DAS 28 supports the hypothesis that this autoantibody could be associated with a active disease. We recommended using the combination rheumatoid factor in clinical practice for better diagnostic or even therapeutic options.

6. Study Limitations

The patients in our study were selected from a university hospital center, which could potentially be prone to selection bias by including patients with more severe stages of the disease compared to patients at the community level. However, we tried to minimize this bias by recruiting also all the patients from the hospitals outpatient consultation clinics. Another limitation maybe the small sample size.

7. Conclusions

Rheumatoid factor is important factor in disease activity in patients with rheumatoid arthritis and may help physician to diagnose and evaluate prognosis in rheumatoid arthritis patients.

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