

## Original Research Article

# Comparative study of DAS-28 ESR and DAS-28 CRP in determining the severity of disease activity in patients with rheumatoid arthritis

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## ABSTRACT

**Background:** Rheumatoid arthritis is a systemic and chronic disease. Combined indicators, such as disease activity score or DAS-28, can be used to categorize quantitative disease activity status and recovery. But in this calculation there is no difference between using ESR or CRP. Some studies have showed that using CRP instead of ESR will cause the severity of the disease to be underestimated. The aim of this study was to comparison of DAS-28 ESR and DAS-28 CRP in determining the severity of disease activity in patients with rheumatoid arthritis.

**Methods:** This study was a cross-sectional and descriptive-analytical study on patients with rheumatoid arthritis who referred to the rheumatology clinic of Imam Khomeini Hospital. 200 patients from the target community who referred to the rheumatology clinic were randomly selected and studied. Relevant questionnaires including demographic information such as age, sex, cigar consumption were completed from the study.

**Results:** In this study, 200 patients with RA who met the inclusion criteria were randomly selected and evaluated. The results showed that the mean age of participants in the study was  $50.38 \pm 12.82$  and those in the age range of 18. They were up to 90 years old and 20% of the people were men and the rest were women. The study on alcohol and cigarette use in patients showed that 3 cases (1.5%) of patients had a history of alcohol consumption and 9 cases (4.5%) had a history of smoking. Examination of DAS28 in individuals showed that the mean of DAS28 in terms of CRP in patients is lower than the mean score of DAS28 in terms of ESR DAS28 showed less disease activity in terms of CRP and this difference was statistically significant ( $p=0.001$ ). There was no significant relationship between gender, age and serum albumin level with DAS28 score based on ESR and CRP. There was no statistically significant relationship between VAS in patients and DAS28.

**Conclusions:** According to the results of the present study and previous studies, it seems that if CRP is used to determine the severity of the disease, it is better to use a new scoring criterion for patients.

**Keywords:** DAS28-CRP, DAS28-ESR, Rheumatoid arthritis

## INTRODUCTION

Rheumatoid arthritis is a systemic and chronic disease and its prevalence in the world is about one percent and it usually occurs in middle aged adolescents and also in the first, third to fifth decades and is more common in women. The prevalence of rheumatoid arthritis is about 0.5 to 1 percent of the population (between 0.3 and 1.2 percent) and women are almost three times more likely to be infected than men. The prevalence increases with age

and the difference between men and women in older age groups was decreased. The beginning of the disease is more common in the fourth and fifth decades of life and were occurred in 80% of all patients between the ages of 35 and 50.<sup>1-3</sup>

These are just some of the symptoms of rheumatoid arthritis: morning joint hardness, joint swelling, joint pain, weakness and fatigue, rheumatoid nodules, symmetrical inflammatory polyarthritis, extra articular

manifestations (rheumatoid nodules, pulmonary fibrosis, vasculitis and serositis) and positive rheumatoid factor in the blood of 80% of patients are characteristic of the diseases.<sup>4-6</sup> Chronic synovitis is an inflammation that mostly effects the joints and causes cartilage destruction and bone damage. Rheumatoid arthritis has characteristics that distinguish it from other types of arthritis (inflammation of the joints). Arthritis, for example, is symmetrical, meaning that if one knee or arm is involved, the other side is more likely to be involved. The joints involved are the metacarpophalangeal, metatarsophalangeal, wrist and proximal interdigital joints. In some patients, the disease is mild and is associated with minimal joint damages in a short time, in some other, progressive and chronic lesions, are in the form of polyarthritis and cause joint dysfunction.<sup>7-9</sup>

CRP and ESR measurements are also used to track disease activity and rate of response to treatment. Performing CBC and diff and basically examining kidney and liver function is beneficial because their results can affect other treatment options. Mild anemia due to chronic diseases is seen in 33-60% of patients with rheumatoid arthritis. However, in patients receiving corticosteroids or NSAIDs, the possibility of gastrointestinal bleeding should also be considered. Radiographs of the arms and legs (from the wrist down) should be taken to evaluate the erosive changes around the joint that are characterizes of rheumatoid arthritis. The presence of these changes may indicate a more aggressive form of rheumatoid arthritis.<sup>10-13</sup> The American College of Rumatology uses a scoring system to more quickly and accurately diagnose rheumatoid arthritis. In this rating, if the patient score reaches at least 6 points or more the disease is diagnosed as positive. In summary, this rating is as follows: the number of swollen, inflamed and diseased joints is rated up to 5 scores as follows: two or more large joints (1 point), one to three small joints (2 points), 4 to 10 small joints (3 points), 10 joints with at least one small joint (5 points). A positive blood test is also important in this diagnosis and adds to the scores: 1- at least one positive result in Rf or Anti CCP (two to three points depending on the severity) 2- at least one abnormal result in CRP or ESR indicators (one point). In general, according to the definitions of the European Rumatology League (EULAR) and the Asia-Pacific Rumatology Association (APLAR), the DAS-28 score is higher than 5.1 defined as an active disease, less than 3.2 as a low activity disease and less than 2.6 as a disease with minimal activity. A mathematical formula is used to calculate DAS-28, which although this formula differs in the use of CRP and ESR, but in determining the cut off of this calculation does not differentiate between the use of ESR or CRP.

$$\text{DAS28-ESR} = 0.56 * \sqrt{(t28)} + 0.28 * \sqrt{(sw28)} + 0.70 * \text{Ln}(\text{ESR}) + 0.014 * \text{VAS}$$

$$\text{DAS28-CRP} = 0.56 * \sqrt{(t28)} + 0.28 * \sqrt{(sw28)} + 0.36 * \text{Ln}(\text{CRP}+1) + 0.014 * \text{VAS} + 0.96$$

However, studies like COMET and PRIZE showed that using CRP as the equivalent of ESR will cause the severity of the disease to be underestimated and a significant number of patients who are candidates for treatment intensification will be excluded. Therefore, providing a new definition of DAS-28 scoring with respect to the use of ESR or CRP is seems necessary. Treatment should begin after rheumatoid arthritis diagnosis and initial assessments of patients. There are new methods in treatment of rheumatoid arthritis. The goals of treatment included minimizing joint pain and swelling, preventing deformity (such as ulnar deviation) and radiological destruction of the joint (such as erosions), maintaining a person's quality of life (personal and work) and controlling extra articular manifestations. Due to the importance of the subject and the lack of similar studies in this field in the province and the country, the purpose of this study was to compare DAS-28 ESR and DAS-28 CRP in determining the severity of disease activity in patients with rheumatoid arthritis who referred to Ardabil city hospital during 2017-2018.

## METHODS

### Study design

This was a descriptive cross-sectional study that was performed in Imam Khomeini Hospital in Ardabil city between 2017 and 2018.

According to the patient list, 200 patients who had received at least one biological anti rheumatic drug (DMARD) for at least 3 months were randomly selected and entered the study.

### Data collection and analysis

Data collection tools were checklist including demographic characteristics of samples and test results and DAS28, which was calculated by the mathematical formula based on ESR and CRP amounts. After coding, the data were entered into SPSS 22 and analyzed using descriptive statistical methods in the form of tables and graphs and analytical statistical methods using t-test and Chi-square test for the relationship between quantitative and qualitative data analyzed. Significance level less than 0.05 was considered significant.

### DAS28 calculation formula

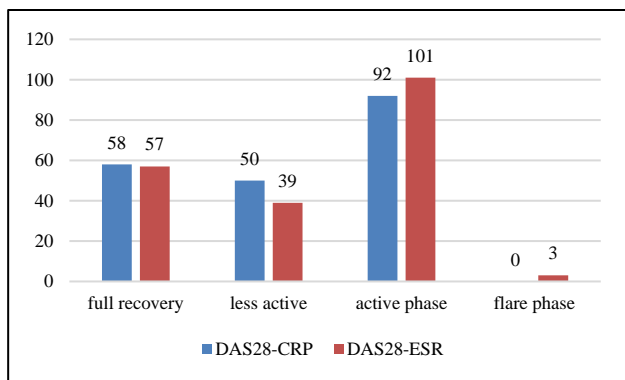
$\text{DAS28} - 4(\text{CRP}) = 0.56 * \sqrt{(TJC)} + 0.28 * \sqrt{(SJC)} + 0.36 * \text{Ln}(\text{CRP}+1) + 0.014 * (\text{VAS}) + \text{GH} + 0.96$ . This formula shows the correlation between the studied factors in the rheumatoid arthritis group. Patients with definitive diagnosis of rheumatoid arthritis and patients who have been treated with DMARD for at least 3 months and patients due to unwillingness to participate and having comorbidities that alter ESR and CRP levels, such as infections and inflammatory diseases were excluded from the study.

**Classification of DAS28**

In this study, the rate of DAS28 was less than 2.6 as a disease with minimal activity, less than 3.2 as a disease with low activity, 3.2 to 1.5 as a disease in the active phase and more than 1.5 as a flare-up (flare) the disease was considered. This study was performed after approval by the ethics committee with the code IR.ARUMS.REC.1398.200 and written consent were obtained from all patients.

**RESULTS**

The average age of the participants was 50.38±12.82 and the subjects were in the age range of 18 to 90 years and 20% of the subjects were men (40 patients) and the rest (160) were women. There was no significant difference between men and women in terms of age. According to the DAS28 classification, 58 patients (29%) were in the minimal activity phase and 50 patients (25%) were in the inactive phase and 92 patients (46%) were in the active phase of the disease and no cases of disease were seen in the flare phase and the results showed that DAS28 based on ESR and CRP results showed less disease activity rate and this difference was statistically significant (p=0.001).



**Figure 1: Severity of disease based on DAS28-CRP and DAS28-ESR.**

**Table 1: Difference between DAS28-CRP and DAS28-ESR by gender of patients.**

Variables	Sex	Mean±SD	P value
DAS28-CRP	Male	2.96±0.8	0.26
	Female	3.13±0.83	
DAS28-ESR	Male	2.96±1.1	0.17
	Female	3.2±0.9	

In the ESR rate, 57 patients were in the active phase, 39 patients in the less active phase, 101 patients were in the active phase and 3 patients in the flare phase of disease and in terms of disease severity based on DAS28 ESR, results showed a significant relationship between ESR and disease severity (Figure 1). In CRP, 57 patients were in recovery phase, 39 patients in less active phase, 101 patients in active phase and 3 patients in flame phase,

according disease severity based on DAS28CRP results showed a significant relationship between CRP rate and disease severity. Examining the relationship between VAS in patients and the amount of DAS28 in terms of ESR and CRP, with p=0.097 in DAS28-CRP and p=0.32 in DAS28-ESR does not indicate a relationship between the patient’s view of his disease and the amount of DAS28. In the study of DAS28 results by sex of subjects, results showed that there was not a significant difference between gender and DAS28 score based on ESR and CRP (Table 1). In compare DAS-28 results by age of patients, results showed that there was not a significant correlation between patients’ age and DAS28 score based on ESR and CRP. Pearson correlation coefficient between patients’ serum albumin level and DAS28 score based on ESR and CRP showed that there was a significant correlation between them. This relationship is inverse so that with increasing DAS-28 score (increasing disease severity) the amount of serum albumin decreases. However, there is no significant difference between the severity of the disease based on the decrease in albumin by inclusion of ESR or CRP amounts in the DAS28 formula.

**DISCUSSION**

The average age of participants in the study was 50.38±12.82 and the subjects were in the age range of 18 to 90 years and in the study of Ahmadzadeh et al the average age of participants in the study was 49 years in range 22 to 76 years.<sup>14</sup>

In the study of Ahmadzadeh et al, 20% of the patients were men and the rest were women, which confirms the higher incidence of RA in women.<sup>14</sup>

Examination of DAS 28 in individuals showed that the average of DAS28 in terms of CRP in patients was lower than the average score of DAS28 in terms of ESR and most of patients were in the low activity phase of the disease.

In this study, the rate of DAS28 less than 2.6 defined as remission, less than 3.2 as inactive disease, 3.2 to 5.1 in active phase and more than 5.1 as flare-up (flare) the disease. Studies have shown that DAS28 shows less disease activity in terms of CRP and the number of patients in the recovery phase is more evaluated in DAS28-CRP and the number of patients in the flare phase is less evaluated in this criterion, this difference is statistically significant (p=0.001). In Madsen et al study, the average DAS28 in terms of CRP was lower than the DAS28 in terms of ESR.<sup>15</sup> This difference was considered statistically significant. Also in Matsui et al study, DAS28CRP showed most of patients were in the recovery phase, it seems that if DAS28-CRP is used, it may be patients in the acute phase or disease activity phase are not properly evaluated and do not receive appropriate treatment.<sup>13</sup> For this reason, in the study of Fleischmann et al, it is recommended to use low scores in the

evaluation of patients if DAS28 CRP is used.<sup>3</sup> Examination of DAS28 results by gender showed that there was no significant relationship between gender and DAS28 score based on ESR and CRP. The results show that in using DAS28 in terms of CRP or ESR, the difference in patient gender does not change the results. Comparison of DAS-28 results according to patients' age showed that there was no significant relationship between patients' age and DAS28 score based on ESR and CRP in similar studies there was no significant relationship between patients' age and disease severity in patients.<sup>3,14</sup> It seems that the factor like age is not related to disease progression if treated, however in the study of Oguro et al, a significant relationship between patients' age and positive effects on mania in patients treated with biologic drugs has been suggested.<sup>16</sup> It seems that the type of treatment received by patients can change the factors involved in the severity of the disease. Examination of ESR and CRP in terms of disease severity showed that there is a statistically significant relationship between these variables and DAS28 scores. The study of the relationship between VAS in patients and the level of DAS28 in terms of ESR and CRP showed that there is no relationship between patients' views of their disease and the level of DAS28. This indicates that VAS is unrealistic in patients and shows a lack of accurate insight into the severity of the disease in patients, also, in patients receiving drug therapy, the clinical signs that are effective in determining VAS may not be related to the test results. In the study of Kievit et al with the regression model, it was observed that VAS is associated with DAS28 at the beginning of the disease and improves after treatment independent of DAS28, although the accuracy of this claim is recommended by doing further studies.<sup>17</sup> Comparison of DAS-28 results in terms of patients' serum albumin level showed that there was a significant relationship between patients' serum albumin level and DAS28 score based on ESR and CRP. This relationship is inverse so that with increasing DAS-28 score (increasing disease severity) the serum albumin were decreased. In the study of Chen et al, the average serum albumin level in RA patients was lower than normal individuals and there was a significant relationship between disease severity and albumin level which indicates a decrease in albumin levels in patients with chronic diseases such as RA.<sup>18</sup>

The main limitation of this study was the lack of isolation of patients based on the type of drug used and different evaluation of patients from the severity of their disease.

## CONCLUSION

According to the results of the present study and previous studies, it seems that in term of using CRP to determine the severity of the disease, it is better to use a new scoring criterion for patients. This study also concluded that due to the weak correlation between VAS and DAS scores in RA patients and patients' wrong assessment of their disease status, it is better to use this criterion in patients

with more caution. The findings also showed that RA as a chronic disease can play an important role in reducing serum albumin levels.

## Recommendations

It is recommended that a prospective study be performed on changes in DAS28 levels by ESR and CRP during treatment to obtain a more general view of the use of DAS28 as a predictor in RA patients. It is also recommended that a study be performed to determine the scoring in terms of using DAS28-CRP to better assessment the severity of the disease by using this parameter.

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