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Rheumatology

Musculoskeletal Ultrasound and Calprotectin Assessment in Patients with Rheumatoid Arthritis

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by autoimmune destruction of cartilage and bones, in which synovial hypertrophy is due to the infiltration of lymphocytes into synovial tissue and hyperproliferation of synovial fibroblasts. Calprotectin is involved in the pathophysiology of various pathological conditions, such as rheumatoid arthritis. There is a direct association between calprotectin expression and systemic autoimmunity development.
Aim of the work: To measure calprotectin and musculoskeletal ultrasound in patients with rheumatoid arthritis and evaluate the illness activity.
Patients and Methods: The American College of Rheumatology (ACR) criteria were used to diagnose fifty patients with rheumatoid arthritis in this research. All patients in this research have been collected from the Rheumatology and Rehabilitation Departments at Al Hussein and Bab El Sharia University Hospitals at Al-Azhar University in Cairo's outpatient clinics and inpatient units.
Result: There had been a statistically significant difference (p-value < 0.05) between study groups in terms of erythrocytic sedimentation rate and a statistically significant difference (p-value < 0.001) in terms of C reactive protein. Also, when it came to musculoskeletal ultrasound, there was a statistically significant difference (p-value < 0.001) between the groups tested. Calprotectin levels were found to differ statistically significantly (p-value < 0.001) between the groups tested.
Conclusion: There was a high level of calprotectin in patients having active rheumatoid arthritis, which was related to the musculoskeletal ultrasound finding, which might help us use it in the assessment of disease activity in rheumatoid patients.

Keywords: *Rheumatoid Arthritis; Calprotectin; Musculoskeletal Ultrasound.*

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INTRODUCTION

Rheumatoid arthritis (RA) is a rare chronic inflammatory autoimmune illness characterized by persistent synovial inflammation and the formation of bony abnormalities in joints.[1] Calprotectin levels are increased in both synovial fluid and synovial tissue in RA, and it is associated with a high concentration of the protein in immune cells around the damaged joint sites.[2] Calprotectin levels are higher in active disease and decrease following efficient therapy; it was demonstrated to be a more sensitive biomarker of disease activity in RA than the commonly employed acute-phase proteins, which are mostly of liver origin.[3] Ultrasonography of the musculoskeletal is a useful imaging method for assessing RA activity.[4]

This work aimed to measure calprotectin and musculoskeletal ultrasound in patients with rheumatoid arthritis and evaluate the activity of the disease.

PATIENTS AND METHODS

This ten-month cross-sectional study was conducted on 50 patients with rheumatoid arthritis at Al-Hussein University Hospital from March 2021 to October 2021. Before starting the study, the Ethics Committee at Al-Azhar University's Faculty of Medicine in Cairo, Egypt, gave their approval. Additionally, informed consent was obtained from every patient before recruitment for the use of their medical reports. The inclusion criteria were patients with RA who were 18–60 years old and met the ACR/EULAR criterion 2010. There were exclusion criteria that included patients having other autoimmune diseases that might affect calprotectin. All patients had a detailed medical history taken, which included their name, age, sex, alcohol, occupational, and drug history, and any comorbid

conditions they had. The erythrocyte sedimentation rate (ESR), complete blood count (CBC), rheumatoid factor (RF), C reactive protein (CRP), anti-CCP, and fecal calprotectin were among the investigations performed in the laboratory. Assesment of disease severity according to the German musculoskeletal ultrasound 7 score and calprotectin level.

Statistical analyses: The Statistical Package for the Social Sciences (SPSS) version 24 was used to analyze the data. The mean ± standard deviation (SD) has been employed to express quantitative data. Frequencies and percentages have been employed to express qualitative data.

The following tests have been performed:

The IBM SPSS program package version 20.0 was employed to analyze the data provided on the computer. (Armonk, NY: IBM Corp). Numbers and percentages were employed to describe qualitative data. The normality of the distribution has been checked using the Kolmogorov-Smirnov test. The range (min and max), mean, SD, median, and interquartile range (IQR) have been employed to characterize quantitative data. The significance of the acquired data has been assessed at a 5% level.

The performed tests were:

1- Mann Whitney test: To compare two studied groups with abnormally distributed quantitative variables

2- Spearman coefficient: To establish a link between the two quantitative variables that are abnormally distributed.

RESULTS

	No.	%
Sex		
Male	14	28.0
Female	36	72.0
Age (years)		
≤40	34	68.0
>40	16	32.0
Min. – Max.	19.0 – 59.0	
Mean ± SD.	36.56 ± 10.41	
Median (IQR)	35.50 (29.0 – 42.0)	

The study's patients were distributed based on demographic data (n = 50)
IQR: Inter quartile range SD: Standard deviation

Table 1: Regarding description of demographic data

This table shows that among the studied cases, there were 14 (28 %) males, 36 (72%) females, 34 (68%) had ≤40 years old, 16 (32%) had >40 years old and mean of age (years) 36.56 (±10.41 SD).

Risk factors	No.	%
No	28	56.0
Yes	22	44.0

Table 2: The cases studied were distributed based on risk factors (n = 50)

This table demonstrates that 22 (44%) of the cases investigated had risk factors.

CBC	Min. – Max.	Mean ± SD.	Median (IQR)
ESR	20.0 – 80.0	49.76 ± 14.74	51.50 (40.0 – 60.0)
CRP	0.0 – 48.0	13.44 ± 12.34	6.0 (6.0 – 24.0)

Table 3: Descriptive analysis of the studied cases based on CBC (n = 50)

This table shows that the mean of ESR 49.76 (±14.74 SD) and mean of CRP 13.44 (± 12.34 SD).

	No.	%
RF		
Negative	21	42.0
Positive	29	58.0
ANTICCP		
Min. – Max.	8.0 – 200.0	
Mean ± SD.	75.92 ± 74.07	
Median (IQR)	62.50 (8.0 – 130.0)	

IQR: Inter quartile range SD: Standard deviation

Table 4: Distribution of the studied cases according to RF and ANTICCP (n = 50)

This table shows that there were 29 (58%) were positive RF and mean of ANTICCP was 75.92 (± 74.07 SD).

Musculoskeletal Ultrasound German 7 score	Min. – Max.	Mean ± SD.	Median (IQR)
GS synovitis	2.0 – 20.0	7.50 ± 4.84	6.0 (4.0 – 10.0)
PD synovitis	0.0 – 14.0	3.50 ± 3.06	2.0 (2.0 – 5.0)
GS tenosynovitis	0.0 – 4.0	0.34 ± 0.82	0.0 (0.0 – 0.0)
Erosions	0.0 – 3.0	0.28 ± 0.70	0.0 (0.0 – 0.0)

Table 5: Descriptive analysis of the studied cases based on Musculoskeletal Ultrasound German 7 score (n = 50)

This table shows that according to Musculoskeletal Ultrasound German 7 score, the mean of GS synovitis 7.50 (± 4.84 SD), mean of PD synovitis 3.50 (± 3.06 SD), GS tenosynovitis 0.34(± 0.82 SD) and mean of erosions 0.28 (±0.70 SD).

	Min. – Max.	Mean ± SD.	Median (IQR)
Stool calprotectin	10.0 – 100.0	41.08 ± 24.27	36.0 (22.0 – 60.0)

Table 6: Descriptive analysis of the studied cases based on stool calprotectin (n = 50)

This table shows that among the studied cases the mean of stool calprotectin 41.08 (± 24.27 SD).

	Min. – Max.	Mean ± SD.	Median (IQR)
DAS (disease activity score)	1.40 – 7.50	3.44 ± 1.58	3.05 (2.20 – 4.20)

Table 7: Descriptive analysis of the studied cases based on DAS (n = 50)

	N	Stool calprotectin			U	P
		Min. – Max.	Mean ± SD.	Median		
Age (years)						
≤40	34	10.0 – 100.0	40.21 ± 26.47	31.0	231.50	0.399
>40	16	10.0 – 78.0	42.94 ± 19.41	41.50		
Risk factors						
No	28	10.0 – 95.0	38.96 ± 23.0	32.50	277.0	0.544
Yes	22	10.0 – 100.0	43.77 ± 26.08	40.0		
RF						
Negative	21	10.0 – 90.0	33.95 ± 21.87	30.0	213.0	0.072
Positive	29	12.0 – 100.0	46.24 ± 24.97	40.0		

U: Mann Whitney test
p: p value is used to compare different categories

Table 8: Relation between stool calprotectin and different parameters (n = 50)

This table shows that there is insignificant relation between Stool calprotectin and (age, Risk factor and RF).

	Stool calprotectin	
	r_s	P
Age (years)	0.105	0.467
ESR	0.759*	<0.001*
CRP	0.696*	<0.001*
Anticcp	0.732*	<0.001*
GS synovitis	0.495*	<0.001*
PD synovitis	0.502*	<0.001*
GS tenosynovitis	0.231	0.107
Erosions	0.554*	<0.001*
DAS (disease activity score)	0.607*	<0.001*

r_s: Spearman coefficient
*: Statistically significant at p ≤0.05

Table (9): Correlation between stool calprotectin and various parameters (n = 50)

This table shows that there is strong association between stool calprotectin and (ESR, CRP, Anticcp, GS synovitis, PD synovitis and erosions).

DISCUSSION

The results of current study showed a statistically significant difference between studied markers like ESR and CRP, which are commonly employed to evaluate disease activity in patients with RA but may not necessarily represent continuing synovitis. As a result, rheumatologists searched for novel biomarkers with strong connections to inflammation and angiogenesis in RA patients [7].

Calprotectin levels were found to have a better correlation with rheumatoid arthritis sickness activity and joint damage in RA than standard inflammatory markers like ESR and CRP [5].

This cross-sectional study has been proposed to study the function of calprotectin in rheumatoid arthritis by measuring its use as an indicator of disease severity and activity in RA patients. Fifty individuals with RA were included in our study; all of them were diagnosed using the American College of Rheumatology's criteria.

Investigations that enable early and precise illness diagnosis, prediction of disease diagnosis, and responsive tracking of therapy results are required for ideal RA treatment. Traditional radiography has long been the imaging modality of choice for assessing RA illness, and it is still extensively employed in clinical and research settings [6].

It is efficient to detect bone anomalies like periarticular osteopenia, erosions or joint space narrowing (JSN) [11].

Radiographs may reveal symptoms of accumulated destruction, but they only provide limited data about the current state of disease activity in patients with RA[8].

The predominant inflammatory abnormality in RA is synovitis, which is correlated to joint and bone damage. It was found that traditional clinical and laboratory methods have inadequate sensitivity for detecting active synovitis [10].

In recent years, on the other hand, musculoskeletal ultrasound has been shown to be more specific and sensitive than clinical exam in defining synovitis. Inflammatory lesions observed in MRI in patients with RA had a strong association with US. It is used to assess treatment response since it is sensitive to alteration [8].

In order to determine inflamed joints, we used ultrasound assessments of disease activity in RA, which is a more sensitive method than a clinical evaluation [9].

We used the German US7 score in our study, which was developed by Backhaus and his colleagues in 2009 and involves an analysis of the most commonly afflicted joints in RA. It has demonstrated the value

and reliability of ultrasonography evaluation of inflammatory joints as an appropriate and effective method of tracking disease activity. In terms of correlation with the 78-joint score, this decreased 7-joint ultrasound score has become available, indicating that a new strategy to focus on a few joints delivers data about inflammatory activity in patients with RA that is equal to that of a thorough ultrasound examination [12].

CONCLUSION

In rheumatoid arthritis patients, there was a demonstrated significant association between calprotectin and laboratory markers of activity of the disease as well as ultrasonography synovitis and tenosynovitis scores.

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