

## ORIGINAL ARTICLE

# A Study of the Relation Between Clinical Parameters of Rheumatoid Arthritis with Ultrasonographic Findings in Joints and a Comparison of Ultrasonography with Conventional Radiography

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## Abstract

**Background:** Ultrasonography is a safe and effective method which detects synovitis and erosions in joints early, while conventional radiography (CR) detects changes at later stages. These ultrasonographic findings have a relation with clinical parameters which help in predicting outcome.

**Materials and Methods:** 60 patients of diagnosed rheumatoid arthritis (RA) (ACR-EULAR 2010 criteria) were subjected to clinical examination, laboratory investigations, CR and ultrasonography. Data was compiled in Epi Info version 7 software and tests of significance were applied.

**Results:** Mean tender and swollen joint counts were 18.61+6.51 and 9.56+3.94 respectively. USG detected joint changes in 90% patients while CR could do so in 33.3%. 85% patients with a normal CR had an abnormal USG. On USG, tenosynovitis was found in 48.33% patients, synovial thickening with vascularity in 73.33%, synovial effusion in 40%. USG detected erosions in 14(23.33%) patients, while CR did so in 5(8.33%), a statistically significant finding. 80% of patients with less joint counts had positive USG findings and in them, joints other than those clinically involved were also found affected. Out of 16 patients of early RA who had a normal CR, 87.5% had positive findings on USG. 92.86% of patients having erosions on USG had a positive C reactive protein (CRP). 60.4% patients with synovial thickening had a positive CRP. In all the patients who had erosions on USG, anti CCP levels were of high titre, found to be significant. (P=0.022).

**Conclusion:** USG can detect inflammatory arthritis and synovitis in RA better than CR in both early and established cases. USG findings may be seen in clinically uninvolved joints. Detection of erosions is also significantly better by USG as compared to CR. USG changes correlated with anti CCP and CRP.

greater diagnostic sensitivity and facilitate early diagnosis in articular disorders. Ultrasonography (USG) is an inexpensive, safe and easily performed imaging modality which is useful in detection of soft tissue abnormalities that cannot be detected on clinical examination. It is a reliable technique that detects synovial thickening, synovitis and more erosions than radiography, especially in early RA.<sup>2</sup> This study was conducted to elucidate findings on ultrasonography of joints in diagnosed patients of RA and to correlate these with clinical aspects such as joint counts, inflammatory and immunological markers which are taken as individual parameters of disease activity. Ultrasonography was compared with CR in early and established cases of RA.

## Materials and Methods

It was a cross sectional observational study conducted over a period of two years in a tertiary care teaching hospital in Western India. The study was approved by Institute ethics committee. A written informed consent was taken from each participant.

Sixty patients above 16 years of age who came to Medicine and Rheumatology outpatient department and medical wards with rheumatoid arthritis diagnosed on the basis of American College of Rheumatology – European League Against Rheumatism (ACR-EULAR) 2010 criteria were included in the study. A score of more than 6 is required to diagnose RA clinically.<sup>1</sup>

## Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease which causes erosive and destructive arthritis and extraarticular manifestations, leading to disability and mortality.<sup>1</sup>

Nowadays, emphasis is on early diagnosis and prompt treatment of RA so that deformities are delayed or prevented. Imaging studies help in corroborating the diagnosis and also evaluating disease activity.<sup>2</sup> Conventional radiography (CR) is most appropriate in later or advanced stages of the disease.<sup>2</sup> In most inflammatory

disorders, early radiography is rarely helpful in diagnosis as it may be normal. The earliest changes in joints are synovial thickening and vascularity which cannot be picked up by CR. The joint damage and loss of function in RA occur early. Radiographic outcome studies have shown that 70% of patients with recent onset RA develop bony erosions within the first 3 years.<sup>3</sup> Hence, additional imaging techniques have now arrived on the scene, which possess

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**Table 1: Findings on x-ray of joints among the study population**

Finding	No. of patients	Percentage
Erosions	5	8.33%
Periarticular osteopenia	15	25%
Joint space reduction	3	5%
Normal X ray	40	66.67%

**Table 2: Ultrasonography (USG) positivity in joints**

USG	Patients
Positive	54 (90%)
Negative	6(10%)
Total	60 (100%)

Non articular disease, connective tissue diseases such as systemic lupus erythematosus, systemic sclerosis, polymyositis, mixed connective tissue disease, seronegative spondyloarthropathies and crystal arthropathies were reliably excluded clinically.

A clinical evaluation was done to record swollen and tender joint counts, pain and deformities. Laboratory investigations such as complete blood counts, haemoglobin, blood indices, quantitative rheumatoid factor (RF) by immunoturbidimetry, anti cyclic citrullinated polypeptide (CCP) by ELISA method, erythrocyte sedimentation rate (ESR), quantitative C reactive protein by immunoturbidimetry (CRP) (normal range <3 mg/dl), renal functions, liver functions, blood sugar, electrocardiogram, chest x-ray was done. The normal ranges of RF and anti CCP were : < 15IU/ml and < 5U/ml respectively.

X-rays of hands and feet in posteroanterior and oblique views were done in all patients and evaluated for periarticular osteopenia, erosions and joint space reduction. Ultrasonography (USG) of all involved joints and of wrist, metacarpophalangeal (MCP), proximal interphalangeal (PIP) and metatarsophalangeal joints (MTP) was done using Aloka Prosound alpha 6 machine with 7-12 MHz transducer in longitudinal and transverse planes, in dorsal and palmar aspects. Presence of active synovitis, inflammation within joint, effusion, synovial thickening, width and vascularity, erosions and inflammation of soft tissue around joint was studied by using Grey scale and Power Doppler. Clinical, biochemical and radiological data in qualitative and quantitative form was compiled

**Table 3: Detailed USG findings in joints**

USG	Frequency
Tenosynovitis	29 (48.33%)
Synovial thickening	44 (73.33%)
Synovial effusion	24 (40%)
Erosions	14 (23.33%)

**Table 4: Comparison between CR and USG findings in joints**

	USG positive	USG negative	Total
CR positive	20(100%)	0	20
CR negative	34(85%)	6(15%)	40
Total	54(90%)	6(10%)	60

and analysed using Epi Info Version7 software and the mean and standard deviation were calculated. Chi square and Fishers exact test were applied as test of significance. Comparison between findings of USG and CR was done and analysed by agreement and kappa coefficient tests.

## Results

Mean age of the patients was 41.13 ± 12.98 years and maximum number of patients were between 31 and 50 years of age (34 patients, 56.66%). 50 patients (83.33%) were females and 10 (16.66%) were males. Among the symptoms exhibited by patients, pain (60% having severe pain of VAS > 5), swelling, early morning stiffness (100%) and presence of functional disability and deformities were the important ones. 48 patients had involvement of small joints mainly PIP, MCP and wrists (80%). 55 patients (91.66%) had a tender joint count (TJC) more than/equal to 10 and only 5(8.33%) had a tender joint count of <10. Mean TJC was 18.61+ 6.51 joints. 37 patients (61.66%) had a swollen joint count (SJC) of less than/equal to 10 and 23(38.33%) had an SJC more than 10. Mean SJC was 9.56+ 3.94 joints.

Out of 60 patients included in the study, 20 (33.33%) had positive X ray findings. Among them, 5(25%) patients had erosions, 15(75%) had periarticular osteopenia and 3 had joint space reduction(5%), many patients having more than one finding. So, out of the 60 patients, only 5(8.33%) showed erosions on X-ray (Table 1).

USG of MCP, wrist, PIP, MTP joints was done in all patients along with the clinically involved joints. Most of the findings were seen in wrist (radiocarpal) and MCP joints. Out of 60 patients, 54 (90%) had positive USG findings (Table 2). Many patients had

**Table 5: Comparison between detection of erosions by USG and CR (p=0.000367)**

	Not Detected by CR	Detected by CR	Total
Detected by USG	9	5	14
Not detected by USG	46	0	46
Total	55	5	60

**Table 6: Relation between joint counts and USG findings**

Joint count	USG		Total
	Negative	Positive	
<10	1	4	5
≥10	4	51	55
Total	6	54	60

more than one finding in them such as tenosynovitis, synovial thickening with vascularity (synovitis), synovial effusion and erosions. 6 patients had no findings on USG. Tenosynovitis was found in 29 (48.33%) patients, synovial thickening with vascularity in 44 patients (73.33%), synovial effusion in 24 (40%) and erosions in 14(23.33%) patients (Table 3).

USG could detect changes in joints of 90% patients while CR could do so in 33.3%. So USG was able to detect changes in three times the number of patients than CR could. These 54 patients with positive USG included all those 20 patients who had positive findings on CR and the 34 patients (85%) without findings on CR, thus adding to better detection ability of USG (Table 4).

In particular, USG could detect erosions in 14(23.33%) patients while CR could detect them in only 5(8.33%) patients, a result which was found statistically significant. (Fisher exact test significance value is 0.000367 and result is significant at p <.05) (Table 5).

Out of 5 patients having tender joint counts less than 10, 4(80%) had positive USG findings and in them, joints other than those clinically involved were also seen to be affected, thus further confirming a better contribution of USG in detecting inflammatory arthritis. Out of 55 patients having a joint count of more than 10, 51 (92.72%) had positive USG findings (Table 6).

Out of 21 patients of early RA, 19 had positive USG findings (90.48%), while only 5 had positive CR findings (23.81%). Earliest finding on CR was periarticular osteopenia; no erosions were noted. Out of those 16 patients

**Table 7: Relation between CR and USG findings in Early RA**

CR	USG		Total
	Positive	Negative	
Positive	5	0	5
Negative	14	2	16
Total	19	2	21

who had a normal CR, 14 (87.5%) had positive findings on USG. Out of the remaining 5 patients who had findings on CR, all of them had positive findings on USG, thus showing that USG could detect abnormalities in early RA much better than CR (Table 7).

Out of 45 patients with high titres of anti CCP, 41 (91.11%) had positive abnormalities on USG. Out of a total of 14 patients having erosions on USG, 13(92.86%) had a positive CRP. 60.4% patients with synovial thickening had a positive CRP. These findings indicate that ultrasound findings were related with inflammatory markers in a positive trend. In all the patients who had erosions on USG, anti CCP levels were of high titre (more than 3 times normal range). This finding was found to be significant. (P=0.022), showing that erosive disease correlated with anti CCP titres (Table 8).

## Discussion

In this study, the mean age of patients was  $41.13 \pm 12.98$  years and the female to male ratio was 5:1. In a study conducted in Brazil mean age was 47 years, with 11 males out of the 98 patients taken in the study, indicating that RA is commoner in females.<sup>4</sup> In the present study, mean tender joint count was  $18.61 \pm 6.51$  joints and mean swollen joint count was  $9.56 \pm 3.94$ . According to a study conducted in Brazil, the mean of tender and swollen joints involved was 13.87, similar to present study.<sup>4</sup>

In present study, 33.33% patients had positive CR findings. Out of them, 25% patients had erosions and 75% had periarticular osteopenia. So, out of the 60 patients, only 5(8.33%) showed erosions on CR. In a study carried out in Germany, CR could detect erosions in 4% of 128 patients.<sup>5</sup> In another study CR could detect erosions in established and diagnosed cases of RA as opposed to early ones.<sup>6</sup> In the present study, 90% patients had positive USG findings, while only 33.3% had positive CR findings. Many patients had more than one finding in them such as tenosynovitis, synovial

**Table 8: Relation between erosions on USG and anti CCP titres (p value = 0.022)**

Erosions on USG	Anti - CCP		Total
	<3 times	>3 times	
Present	0	14 (100%)	14
Absent	15	31	46
Total	15	45	60

thickening with vascularity (synovitis), synovial effusion and erosions. CR cannot detect signs of inflammation, synovitis, tenosynovitis and effusions. In the present study, USG could detect erosions in 23.33% patients as opposed to 8.33% detected on CR, a result found highly significant. In a study by Saigal R et al, out of total 57 patients evaluated, 94.7% had abnormal findings on USG as compared to only 29.82% having radiographic abnormalities. USG could detect erosions in 50% patients in that study while CR detected them in 24% patients only.<sup>7</sup> Hence in that study, USG detected erosions in almost twice the number of patients than CR did which is comparable to our study.

In present study, out of 40 patients with a negative CR, 34 patients (85%) showed USG findings in them, while 20 patients had a positive CR and USG both. In the study done by Saigal et al, the positive USG included all of the 17 subjects with radiographic changes and 37 cases without radiographic changes, thus adding to the better disease detection ability of USG.<sup>7</sup> According to a study done by Weidekamm C et al, USG could detect 46% of articular changes, which was 20% more than plain radiography.<sup>8</sup> In a study done by Szkudlarek M et al, with MRI as the reference method, the sensitivity of USG for the detection of bone erosions in the toe joints was 0.79, while it was 0.32 for radiography.<sup>9</sup> In our study, out of 5 patients having tender joint counts less than 10, 4(80%) had positive USG findings and in them, joints other than those clinically involved were also seen to be affected, thus further confirming a better contribution of USG in detecting inflammatory arthritis. In a study done by Szkudlarek M et al, with MRI as the reference method, USG had higher sensitivity and accuracy in detecting inflammation in joints than clinical examination.<sup>9</sup> Therefore, USG appears to have a better disease detection as compared to conventional radiography.

In the present study, erosions could be correlated with titres of anti CCP

and the correlation was statistically significant. Similar results were found in a study conducted by Samanci N et al.<sup>10</sup> In another study, associations with radiological progression rate, and extra-articular manifestations showed 98% specificity of anti-CCP with radiological findings.<sup>11</sup>

In the present study, 92.86% patients who had erosions on USG had a positive CRP and 60.4% patients with synovial thickening had a positive CRP. The association of acute phase reactants with erosive disease, at least on CR, is well known. In a study by Saigal et al, when ultrasound findings (cumulative flow signal score, CFS) were analyzed for correlation with various variables, the significant correlation was obtained between CFS and CRP levels.<sup>7</sup>

Out of 21 patients of early RA, 19 had positive USG findings (90.48%), while only 5 had positive CR findings (23.81%). Out of those 16 patients who had a normal CR, 14 had positive findings on USG, thus showing that USG was considerably better than conventional radiography in detecting changes in joints in early RA. In a study by Ostergaard M, it was concluded that CR, the traditional gold standard for imaging in RA, is not able to detect early disease manifestations such as inflammatory changes in the soft tissues (synovitis, tenosynovitis, enthesitis etc.) and the earliest stages of bone erosion. In contrast, ultrasonography (US) allows direct visualization of early inflammatory and destructive joint changes, and have several documented and potential applications in RA patients.<sup>12</sup>

Hence one can conclude that USG can detect inflammatory changes in a high percentage of patients having less joint counts and these can be seen in clinically uninvolved joints. This helps in confirming the diagnosis of RA in situations where it is doubtful, as in asymmetric clinical involvement. USG can detect inflammatory arthritis and synovitis in RA better than CR in both early and established cases. Detection of erosions is also significantly better by USG as compared to CR. Various soft tissue abnormalities can be well documented by USG. There is a correlation between USG findings and CRP positivity. Erosions detected on USG are significantly correlated with high titres of anti CCP. Hence one can

try to predict erosive disease on basis of anti CCP titres.

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