Ultrasonographic evaluation of Hand and Wrist joint involvement in Rheumatoid arthritis and its association with disease activity markers in a Tertiary Care Centre, Chennai.

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KEYWORDS

Rheumatoid arthritis, Ultrasound, MRI, Doppler, CFS.

ABSTRACT

Introduction: Rheumatoid Arthritis (RA) is a chronic autoimmune disease affecting hand and wrist joints and also causing symmetrical joint synovitis. Radiography is used to measure bone and cartilage loss, although physical examinations are usually used to assess synovial inflammation. Both MRI and ultrasound are more sensitive than radiography in identifying synovitis. Various modalities to characterise the activity of joint inflammation include laboratory test like RF, ANA titer, CRP level and ESR.

Aim and Objectives: To assess the involvement of wrist and hand joints in RA using USG (which combines grayscale and PD imaging) and to associate the imaging findings with biomarkers of activity of disease (ESR, CRP and DAS scoring).

Materials and Methods: This cross-sectional study was conducted in the Department of Radiology at a tertiary care hospital, in Chennai. A total of sixty individuals, of all age and both genders, with RA who underwent USG and whose blood investigations shows increased inflammatory markers such as ESR and CRP were included in the study.

Results: Majority of cases belongs to age group 41 -50 years with female predominance. Mean ESR was 39.5 mm and mean CRP was 10.3 mg/dl. Mean RF titer was noted as 42.5 IU/ml, mean DAS score was 4.4 and mean CFS score was 4.9. On power Doppler findings, out of 600 MCP joints 12.2% of joints were abnormal, whereas out of 120 RC joints 55.8% of joints were abnormal. Out of 120 UC joints 42.5% of joints were abnormal. Mean CFS scores among the different DAS score and elevated CRP levels were noted as remarkably significant.

Conclusion: USG is better imaging modality than conventional radiography for early diagnosis of RA. CFS is found to be a better alternative for CRP, ESR followed by USG, the second better option and X rays being the least preference of option.

Introduction:

Rheumatoid Arthritis (RA) is a chronic systemic autoimmune disease identified by symmetrical joint synovitis and discomfort. It presents with a broad range of clinical presentations from a moderate, non-erosive disease to a severe form of inflammatory responses and destruction of joint spaces. Early in the course of the disease, hand and wrist joints are affected and few abnormalities appear in the initial two years of the condition.1

Proliferative synovitis leads to long term joint degeneration, bone erosion, cartilage degradation and disability in RA. One of the first pathologic changes that can be seen at the start of joint inflammation in RA is hyperemia caused by vasodilatation and angiogenesis, one of the essential conditions for the formation of pannus, is essential to start and maintain ance of synovitis.2 Laboratory tests, such as those for RF, ANA titer, CRP level and ESR have been used to characterise the activity of joint inflammation in RA.3

Radiography is used to measure bone and cartilage loss, although physical examinations are usually used to assess synovial inflammation. However, to control the outcome of diseases like RA, timely therapeutic management and for development of new effective medications, early radiological diagnosis is need of the hour.4

When imaging individuals with RA, radiographs have historically been the go - to method. Features that may be noticed on radiographs include swelling of soft

tissue, osteopenia of periarticular area, loss of joint space, subluxation of joints and bony erosions. On radiographs, however, data about synovium is far more difficult to evaluate. When it comes to identifying synovitis, both MRI and ultrasound are more sensitive than radiography. 5

In the realm of rheumatology, ultrasound (US/USG) is an imaging technology that has garnered a lot of interest recently. It has improved the ability to monitor activity of disease and make it easier to diagnose RA due to technical advancements and widespread availability.6 It is also helpful in differentiating between soft tissue edema in major and minor joints as well as in the diagnosis of popliteal cysts.7,8 The primary impediment to the use of USG in rheumatologic evaluation has been absence of standardised procedures for assessing and recording normal and aberrant joint structure.

A number of investigative methods for visualising the musculoskeletal syste m's superficial structures have been reported however, only a small number of these reports include per tinent guidelines for evaluating tenosynovitis and arthritis.9,10 USG technology advancements in recent years have resulted in notable gains in colour Doppler sensitivity, contrast and spatial resolution.

Equipment’s with improved phase locking circuits can suppress artefacts that manifest as tiny phase shifts resulting from powerful scatters. They include lower Pulsed repetition frequency (PRF) on Doppler and increased colour gain settings that are employed for areas with pulsation artefacts in order to alleviate the issue of the technique's excessive sensitivity to motion. These configurations lead to increased equipment compatibility with USG machines, resulting in simpler handling and reduced investigation time.

The vascularity of soft tissue is shown with power Doppler ultrasound (PD US), which improves the B-mode image quality. Studies show ultrasound diagnosis as more sensitive investigation for differentiating between synovitis and joint effusion as well as for measuring the level of inflammation.11,12

High- resolution USG (US) has become more popular in recent years as a means of measuring synovial inflammation.13The synovial thickness and blood flow alterations of joints during inflammatory arthritis can be objectively evaluated by US. 14

Keeping these in mind, purpose of this study was to assess the involvement of wrist and hand joints in RA using USG (which combines grayscale and PD imaging) and to associate the imaging findings with biomarkers of activity of disease (ESR, CRP and DAS scoring).

Materials and Methods:

This cross-sectional study was conducted in the Department of Radiology at a tertiary care hospital, in Chennai from October 2022 to March 2024 after approval from the IHEC. Study participants included a total of sixty individuals with RA who underwent USG in the department of radiology. Individuals of all age groups of both genders referred with clinical symptoms of inflammatory joint disease and whose blood investigations shows increased inflammatory markers such as ESR and CRP were included in the study.
Patients who did not meet ACR criteria, who were diagnosed with other autoimmune disorders and who did not wish to participate in the study were excluded.

The study was discussed with each participant individually and written informed consent was taken. They were also given the assurance that their identity and the identity of their child would be maintained in the strictest confidence.
A pre -structured proforma to evaluate all the cases for the demographics and clinical presentation was taken. Also, all the cases were subjected to ESR and CRP and the findings of the same were associated with the USG findings. All Ultrasound scans were done in GE LOGIQ P7 and P10 scanner with linear probe (High frequency). Associate the imaging findings with blood investigations and clinical scoring.

Results:

In the present study 60 cases were included. Among them majority, 33.3% (n=20) were in the age group of 41 -50 years followed by 51- 60 years (25 %, n=15), 31 - 40 years (20%, n=12), > 60 years (15%, n=9) and 18 - 30 years (6. 7%, n=4).

Majority of the cases were females 75% (n=45) and 25% were males (n=15)

61.7% (n=37) had RA for about 1-3 years, 20% (n=12) of cases had RA for < 1 year and 18.3% (n=11) of cases had RA for more than 3 years. Mean duration of RA was reported as 2.3 years.

In this study 51.7% (n=31) cases were on methotrexate, 23.3% (n=14) on hydroxychloroquine and 1.7% (n=1) on steroids. Mean ESR of the study participants was 39.5 mm, mean CRP as 10.3 mg/ dl, mean RF titre was reported as 42.5 IU/ ml and mean DAS score among the study participants was 4.4.

Mean CFS score among the study subjects was reported as 4.9 . Notably, in our study X ray was abnormal in 31.7% (n=19) cases however the rest 68. 3% (n=41) of cases had normal X ray. USG was abnormal in 91.7% (n=55) of cases whereas 8. 3 % (n=5) cases had normal USG.

Bone erosion was detected in only 25% (n=15) by X ray whereas in 75 % (n=45) cases no bony erosion was detected on X ray. Bone erosion by USG was detected in 51.7% (n=31) cases only whereas in 48.3% (n=29) cases no bone erosion was detected by USG.

On assessing the power Doppler findings, out of 600 metacarpopharyngeal (MCP) joints 12.2 % (n=73) of joints were found to be abnormal and among them 9% (n=54), 3% (n=18) and 0.2% (n=1) of cases had grade 1, grade 2 and grade 3 erosion, respectively.

Also, it was seen on power Doppler findings that, out of 120 radiocarpal (RC) joints 55.8% (n=67) of joints were found to be abnormal and among them 13.3% (n=16), 30% (n=36) and 12.5% (n=15) of cases had grade 1, grade 2 and grade 3 erosion, respectively.

While, out of 120 ulnocarpal (UC) joints 42.5 % (n=51) joints were found to be abnormal and among them 30% (n=36), 11.7% (n=14) and 0.9% (n=1) of cases had grade 1, grade 2 and grade 3 erosion, respectively.

On assessing the CFS scores with the Disease activity score (DAS), CFS score was found to be increased with increasing DAS score. Mean CFS scores among the different DAS score was noted as remarkably significant as shown in the following table 1.

DAS 28	Frequency (%)	CFS (Mean±SD)	p value
< 2.6	9 (15)	1.2± 1.4	<0. 0001*
2.6-3. 2	12 (20)	3.1± 3.5	
3.3-5. 1	17 (28.3)	5.6± 4.7	
>5. 1	22 (36.7)	7.1± 2.8	

*Significant **Table 1: DAS vs CFS scores**

On assessing the CFS scores with the Rheumatoid arthritis (RA) titer, CFS score increased with positive RF cases. However, the difference in mean CFS among the cases with positive and negative RF was not significant as shown in the following table 2.

RF	Frequency (%)	CFS (Mean±SD)	p value
Positive	32 (53.3)	5.3± 4.2	0.1466
Negative	28 (46.7)	4.2± 4.5	

Table 2: RF vs CFS scores

On assessing the CFS scores with the C- Reactive protein (CRP) levels, CFS scoreincreased with increasing CRP levels score. Mean CFS scores among the different CRP levels were noted as remarkably significant as shown in the following table 3.

CRP levels	Frequency (%)	CFS (Mean±SD)	p value
≤ 6 mg/dl	37 (61.7)	3.7± 3.5	<0. 0001*
>6 mg/ dl	23 (38.3)	6.7± 4.6	

*Significant **Table 3: CRP vs CFS scores**

Following are clinical and radiological images of cases found in our study,

Figure 1: Clinical picture of a 57 yr old female RA patient showing Z deformity (Hitchhiker deformity) at thumb with swollen proximal interphalangeal joint.

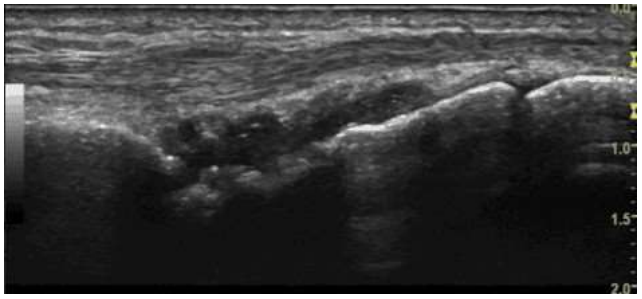

Figure 2: USG grayscale image of a 57 yr old female showing cortical erosions and synovial hypertrophy at 3rd MCP joint.

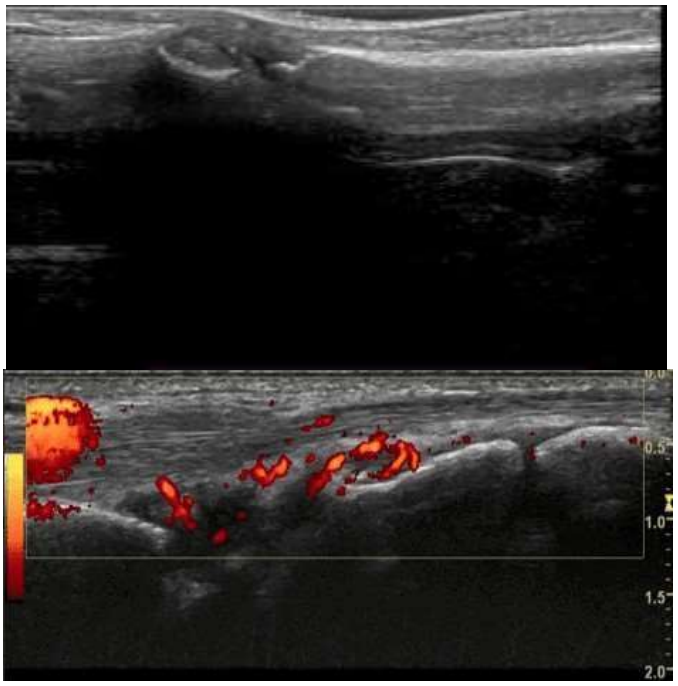

Figure 3: PDUS Image of a 57 yr old female showing increased synovial vascularity and hypertrophy at 3rd MCP joint.

Figure 4: USG grayscale image of a 57 yr old female showing cortical erosion at 2nd MCP joint

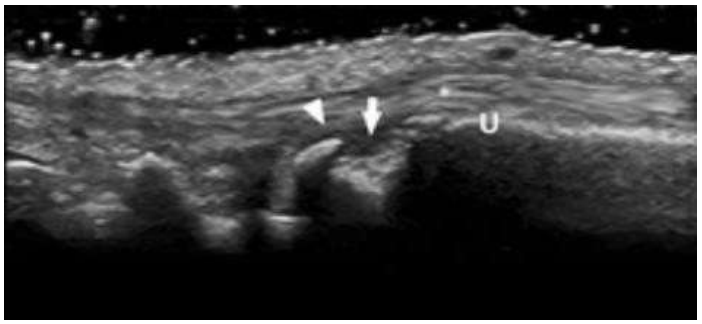

Figure 5: USG grayscale image of 48 yr old male RA patient showing cortical erosion at ulnar styloid at wrist joint

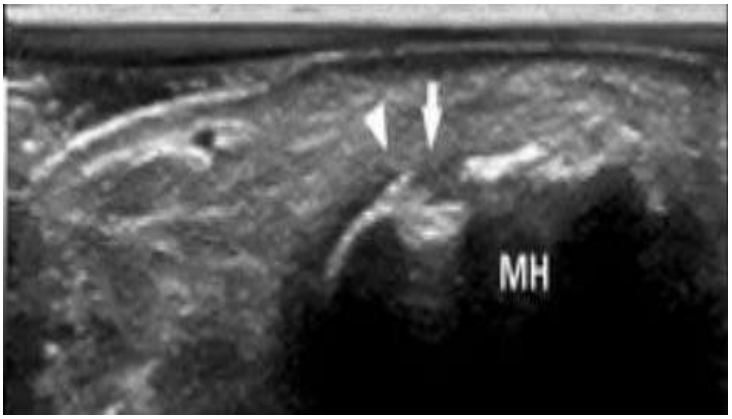

Figure 6: USG grayscale image of 48 yr old male RA patient showing cortical erosions at metatarsal head at 2nd MCP joint.

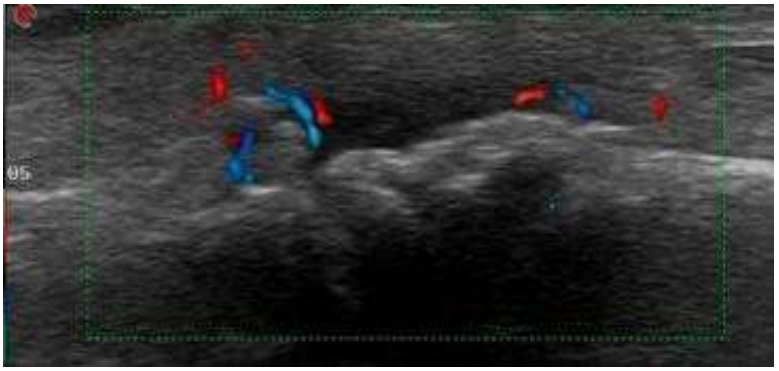

Figure 7: USG grayscale with colour Doppler image of 60 yr old female RA patient showing hypertrophy of synovium at MCP joint

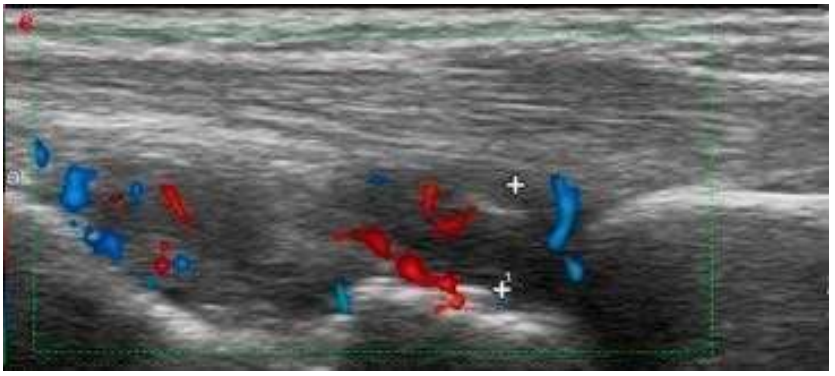

Figure 8: USG grayscale with colour Doppler image of 60 yrs old female RA patient showing increased vascularity at MCP joint suggesting synovitis

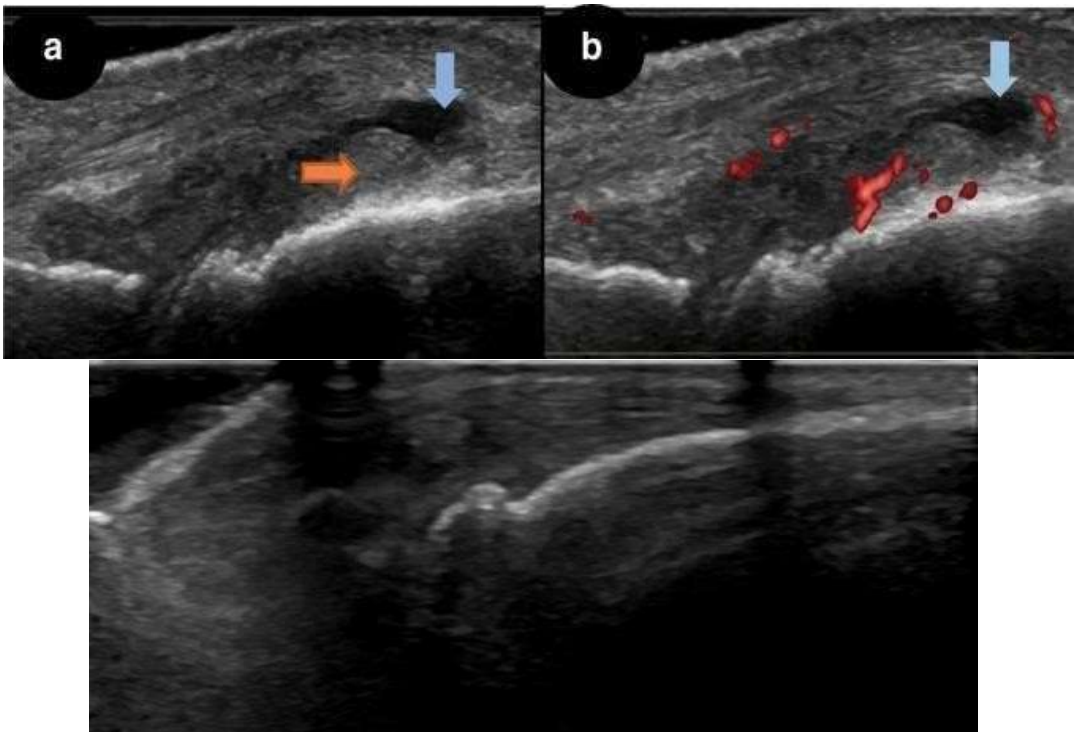

Figure 9: USG grayscale image of a 54 yr old male RA patient showing cortical erosions at MCP.

Figure 10: USG grayscale with b-colour Doppler image of a 54 yr old male RA patient showing synovial effusion (blue arroe) and synovium hypertrophy (orange arrow) at MCP joint

Discussion:

In our study, 33% cases were in the age group of 41 -50 years followed by 51- 60 years (25 %), 31 - 40 years (20%), > 60 years (15%) and 18 - 30 years (6.7%). Females were (75%) and males were 25%. Total 61.7% had RA for about 1-3 years, 20% of cases had RA for < 1 year and 18.3% of cases had RA for more than 3 years. Mean duration of RA was reported as 2.3 years.

In this study 51.7%, 23.3% and 1.7% of cases were taking medications like methotrexate, hydroxychloroquine and steroids respectively. Mean ESR of the study participants was 39.5 mm, mean CRP as 10.3 mg/dl and mean RF titre was 42.5 IU/ml. Mean DAS score among the study participants was 4.4 and mean CFS score among the study subjects was 4.9.

Notably, in this study X ray was abnormal in 31.7% of cases however 68.3% of cases had normal X ray. USG was abnormal in 91.7% of cases and 8.3% of cases had normal USG. In 25% of cases only the b one erosion was detected by X ray and in 75% of cases there was no bony erosion detected. In 51.7% of cases only, the bone erosion was detected by USG and in 48. 3% of cases there was no bony erosion.

On assessing the power Doppler findings, out of 600 MCP joints 12.2 % of joints were found to be abnormal and among them 9%, 3% and 0. 2% of cases had grade 1, grade 2 and grade 3 erosion respectively. Among the RC joint, out of 120 55.8 % of RC joints were abnormal and among them 13.3%, 30% and 12.5% of cases had grade 1, grade 2 and grade 3 erosion respectively. On assessing the power Doppler findings, out of 120 UC joints 42.5 % of joints were abnormal and among them 30%, 11.7% and 0.9 % of cases had grade 1, grade 2 and grade 3erosions respectively. On assessing the CFS scores with DAS scores, CFS score was found to be increased with increasing DAS score.

Also, it was found that, CFS score increased with positive RF cases. On assessing the CFS scores with the CRP levels, CFS score increased with increasing CRP levels score.

Findings of the present study were comparable with the findings of Klauser A et al[15] who evaluated the value of CE CDUS in RA individuals' appraisal of the intraarticular vascularisation (IAV) of their finger joints. Neither CE nor unenhanced CDUS revealed any IAV in healthy joints. In 8% of 83 sedentary joints, 52% of moderately moving joints, and 58% of active joints, unenh anced CDUS revealed the presence of IAV. IAV was found using CE CDUS in all 55 activeRA joints, 98% of 60 moderately active RA joints, and 49% of passive RA joints. Through the use of CE CDUS, it was possible to see changes in IAV between joints that were either inactive or moderately active, as well as between joints that were active or moderately active.

In another study, Terslev L et al[16] revealed a significantly substantial correlation between post -contrast MRI scores and USG indicators of inflammation. In comparison to the other groups, the group without joint swelling had significantly different mean values for the two parameters color reaction and the RI. When comparing mean RI values between the groups with and without joint soreness, there was a remarkable difference. Also, Terslev L et al [17] assessed Sn and Sp of DUS in order to

diagnose RA in the hands and wrists and, if feasible, to establish a threshold value for our USG measurements of colour fraction, RI, and inflammation. AUC for both the colour fraction and the RI, according to pooled combined analysis, was 0.84. The colour fraction cutoff was 0. 01, and the RI cutoff was 0. 83. Sn and Sp for colour fraction were, at the se cutoff thresholds, 0.92 and 0.73, accordingly. A Sn of 0.72 and a Sp of 0.70 were discovered for RI. The results of the analysis of the wrist and small joints were fairly comparable.

However, Heidari B et al[18] reported that ESR reductions predicted 97% of DAS28 respondents during the course of the treatment period; in contrast, a lack of Biomarkers reduction indicated 54% and 45% of non- responders, respectively. According to the DAS 28-CRP and DAS28 response criteria, changes in Biomarkers were generally 77% and 73% accurate in predicting treatment response, respectively. When predicting treatment response, CRP/ DAS 28 -CRP outperformed ESR/ DAS28 in terms ofspecificity but sensitivity. Hensor EMA et al [19] reported that when it comes to categorising RA cases with moderate or severe activity of disease, differ significantly. The ESR definition leads to a larger proportion of high DAS28, particularly in women. Their findings imply that improving agreement with DAS28-ESR could be achieved by changing the DAS28 -CRP definition. Important ramifications arise for therapy guided by DAS scores as well as meta -analyses.

Additionally, Carotti M et al[20] determined a cut- off value for CDUS RI and assessed blood flow using CDUS in wrist and fingersof RA individuals and healthy individuals. Fifty -nine percent of individuals with RA had flow. In 10.5% of the joints in the healthy subjects, there was measurable flow; specifically, 86.4% of the wrist, 11.1 % of the MCP, and 2 .2% of the PIP joints showed this. DUS is a helpful technique for identifying irregular blood flow in RA individuals' inflamed joints. Ahmed SF et al[21] sought to determine whether synovitis was present in individuals with recently developed RA and whether it was correlated with activity of disease. RA subjects showed a high Power Doppler Ultrasound (PD US) score and significantly increased synovial thickness, according to high resolution US imaging. DAS 28 significantly correlated with both the PD US score and synovial thickness in RA subjects. They asserted that high resolution US demonstrated synovitis in RA individuals.

However, Boedec ML et al [22] determined the variables influencing the concordance between Clinical joint examination (CJE) and US. They asserted that there is generally low concordance among CJE and US. Particularlyin the shoulders and metatarsophalangeal joints, US contributes information to CJE. When DAS 28 is low, B- US is less useful, and when the illness's duration is brief, PDUS is less useful. H Xiao et al[23] examined the usefulness of US in the diagnosis of RA - related synovitis. The results of the imaging methods (MRI and US) for diagnosing synovitis were reliable. Sn and Sp were 82.8%/85.8% and 98.2%/84.8%, respectively. Sn/Sp was 93.4%/ 93. 4% when the wrist cutoff was 5.2mm. The biochemical indicators like CRP, and DAS of 28 joints were all favourably correlated with the

average thickness of the synovial membrane; however, rheumatoid factor immu noglobulin A was negatively correlated. Ceponis A et al[24] asserted that PD evaluation of the wrist and the second and third MCP joints could bea practical and useful way to assess the clinical activity of RA.

Similarly, Nemoto T et al[25] conducted a study to see if standard clinical measurements could predict whether or not US synovitis will be present in RA cases and how severe it would be. SJC was not a good indicator of PD signal remission, but it was the most important predictor of PD score. Simple disease activity index (SDAI) remission, which had a 100% positive predictive value. They asserted that standard clinical measures canbe used to predict PD score and the lack of PD signals. Combining Steinbrocker' s stage, swollen joint counts (SJC) and SDAI allows for the estimation ofactivity of disease and the identification of instances that may require US due to synovitis. Son K M et al [26] assessed the discrepancy in the DAS28 in Korean RA cases based on the ESR versus CRP values. 82% of the cases included were female, with a mean age of 53 . The illness persisted for an average of 32.9 months. In 344 cases, there was agreement between the two groups when compared based on four DAS28 activity of disease categories. For RA individuals, the discrepancy between the ESR-based and CRP-based DAS28 may influence clinical treatment choices.

Notably, in this study, on assessing the CFS scores with the RA titer, CFS score was found to be increased with positive RF cases. However the difference in mean CFS among the cases with positive and negative RF was not significant. On assessing the CFS scores with the CRP levels, CFS score was found to be increased with increasing CRP levels score. Mean CFS scores among the different CRP levels were noted as remarkably significant. In another study, Minowa K et al [27] found the extent to which US plays a role in determining the presence of RA in routine clinical practice, as well as the factors that influence this diagnosis and the variations in prediction based on seropositivity. Of the 122 individuals, 52 had a diagnosis of RA.The greatest contribution to the diagnosis of seronegative RA was PD $\geq$ 1 for $\geq$1 joint; however, the European League against Rheumatism (EULAR) criteria had little bearing on the diagnosis. They asserted that US research aided in the clinical diagnosis of RA. The contributing factors change depending on whether seropositivity is present orabsent, and US complementation proved very helpful in cases of seronegative RA.

Medeiros MMDC et al [28] reported that out of the total 111 cases, 108 were female, aged 55.6 years, with an 11 - year illness history. The results of DAS28 - ESR remained greater than those of DAS 28 -CRP even after controlling for age, gender, rheumatoid factor, duration of disease, and Health Assesment Quessionare (HAQ). The agreement between SDAI and Clinical disease activity index (CDAI) was 95.8%. The length of the illness and HAQ were linked to the four indices. YousefA ME et al[29] established the relationship between the ESR and CRP levels in active RA subjects and various measures of activity of disease.

They propose reevaluating the relevance of and reliance on CRP as a marker of inflammatory in RA cases in routine practice, contending that it is not a reliable indicator of inflammatory activity in the clinical situation.

However, Ponikowska M et al [30] stated that higher CRP concentrations may lead to more severe cases of arthritis; thus, it's important to start effective disease - modifying antirheumatic therapy as soon as possible to stop the progression of harmful alterations. They observed that the existence of RF and ESR levels had no effecton the degree of joint inflammation. Das A et al [31] reported that there was significant agreement between the DAS 28 ESR and revised cutoff values of DAS 28 CRP when it came to identifying the participants' activity of disease. They asserted that DAS 28 CRP may be taken into account as a DAS 28 ESR substitute. Kamel SR et al [32] examined the function of US DAS in measuring RA - related joint inflammation and its relationship to disease indicators. The US DAS average was 5.2

A noteworthy association was discovered between USDAS and DAS28 as well as HAQ-DI. While USEC and SENS had a substantial association, US DAS and SENS had a modest correlation. They asserted that US DAS is a workable scoring system that may be applied to routine rheumatologic procedures. Disability and illness activities may be shown in US DAS.

In consistent with this study, Hetta WM et al [33] examined how useful US was in diagnosing synovitis in the wrist and hand joints of RA individuals. Whereas MRI only found synovial hypertrophy in 46 wrist joints, USG found it in 42. Within 30 wrist joints, PD found increased vascularity in 60% of them.Thirteen individuals' MCP joints had synovial activity (vascularity) identified by PD. US found that 27 MCP and 35 wrist joints had erosions. Tendinitis was identified in 8 tendons by MRI and 9 extensor tendon s by US. Ibrahim AM et al[34] showed, in comparison to laboratory studies, the value of US and PD in the identification of RA activity in the hands and wrist joints in a variety of age groups.

When it comes to identifying RA activity in connection with laboratory studies, US and PD are incredibly sensitive and specific. Thus, they can be applied as non-invasive techniques for identifying alterations in RA activity in the hand and wrist joints. In RA instances, US and PD are both reliable indicators of activity. Tharwat S etal[35] evaluated US-detected bone erosions in RA individuals and determined correlations between these findings and laboratory and clinical parameters. There were 57 female case s, the average age of cases was 43 years, and the median illness duration was 5 years. 19 instances lacked bone erosions while 41 did. The MCP joints werethe most commonly affected by eroded areas.

The two groups did not significantly differ in terms of age, gender, RF, or anti-CCP. The presence of synovitis, the synovitis score, swollen joint count, and tender

joint count all strongly linked with the bone erosion scores. They came to the conclusion that synovitis, inflammatory markers, and activity of disease are all linked to bone erosions that are detected by US and are commonly seen at the MCP joints in RA individuals.

Conclusion:

We infer that CFS is found to be a better alternative for CRP, ESR followed by USG, the second better option and X rays being the least preference of option. Hence CFS can be considered as an option of routine screening parameter for all cases with RA followed by USG. USG is better imaging modality than conventional radiography for early diagnosis of RA.

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Conflict of interest: Nil

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