

Original Research Article

Role of imaging in evaluation and management of juvenile idiopathic arthritis: a prospective cohort study

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ABSTRACT

Background: This study was aimed to evaluate the role of imaging in diagnosis and management of juvenile idiopathic arthritis by comparing the evaluation findings of clinical and ultrasound of all 14 joints in arthritis affected patients under 16 years of age.

Methods: Prospectively study was done on patients in age group of 0-16years, who referred to radiology department based on clinical assessment. USG is done in both shoulder, elbow, wrist, hip, knee, ankle and subtalar joints of each patient to assess the following parameters Synovial hypertrophy, joint effusion, power doppler signal, tenosynovitis, enthesitis, cartilage thinning, bone erosions and bursitis.

Results: Out of 980 joints assessed 344 joints (35.1% of all joints) had clinical synovitis, while USG evidence was in 382 joints (38.9% of all joints). Among the 344 clinically positive joints (35.1% of all joints), 223 joints (64.8%) had features of synovitis in USG and the rest 121 (35.2%) joints were clinically positive turned out to be ultrasound negative. Out of 980 joints 636 joints (64.8%) were clinically negative, of these 159 joints (25%) was found to have synovitis in ultrasound and 477 joints (75%) turned out to be negative on ultrasound examination.

Conclusions: The sensitivity and specificity of ultrasound over clinical examination in shoulder joint was 47.6% and 89.1% respectively, in elbow joint 53.8% and 92.1%, in wrist joint 64.3% and 72.6%, in hip joint 65.1% and 64.9%, in knee joint 74.7% and 61.2%, in ankle joint 67.2% and 59.2% and in subtalar joint 56.7% and 71.8%, respectively.

Keywords: Chronic uveitis, Juvenile idiopathic arthritis, Rheumatologic disease, Synovitis

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common rheumatologic disease in children and is one of the most frequent chronic diseases of childhood. The etiology is not completely understood but is known to be multifactorial, with both genetic and environmental factors playing key roles. Without appropriate and early aggressive treatment, JIA may result in significant morbidity, such as leg-length discrepancy, joint contractures, permanent joint destruction, or blindness

from chronic uveitis. JIA is broadly defined as arthritis of one or more joints occurring for at least 6 weeks in a child younger than 16 years of age. Reliable documentation of the progress in therapeutic effectiveness makes it important to ensure that the methods used for assessing disease activity are accurate. Initially evaluation of the disease status in children with JIA is based on clinical and laboratory measures.¹

JIA occurs worldwide, with regional variations believed to be caused by differences in the distribution of HLA

alleles and environmental factors. Among developed nations, JIA has a yearly incidence rate of 2 to 20 cases per 100,000 people and a prevalence of 16 to 150 cases per 100,000 people.² The incidence of chronic arthritis in childhood ranged from 0.008 to 0.026 per 1000 children and the prevalence ranged from 0.07 to 4.01 per 1000 children in a comprehensive worldwide survey from 2002.³ The incidence of JIA is believed to vary widely in part because it is composed of a heterogeneous group of arthritides, which are diagnosed clinically. The disease tends to occur more frequently in children of European descent, with the lowest incidence among Japanese and Filipino children.²

Imaging in patients with JIA has historically relied on radiography, which allows the accurate assessment of chronic changes of JIA, including growth disturbances, periostitis, and joint malalignment. Both contrast material-enhanced magnetic resonance (MR) imaging and Doppler ultrasonography (US) are well suited for this application and are playing an increasingly important role in diagnosis, risk stratification, treatment monitoring, and problem solving. Contrast-enhanced MR imaging is the most sensitive technique for the detection of synovitis and is the only modality that can help detect bone marrow edema, both of which indicate active inflammation. US is more sensitive than radiography for the detection of synovial proliferation and effusions and is particularly useful in the evaluation of small peripheral joints. Contrast enhanced magnetic resonance imaging and doppler ultrasonography can help in detecting inflammatory lesions before permanent joint destruction occurs, and also helps in monitoring disease progression and treatment response to more effectively guide therapy.

The complexity of the temporomandibular and sacroiliac joints limits the usefulness of radiographic or US evaluation, and contrast-enhanced MR imaging is the preferred modality for evaluation of these structures.⁴ In this study, the role of imaging in evaluation and management of juvenile idiopathic arthritis by comparing the clinical evaluation findings and ultrasound evaluation findings of all 14 joints in arthritis affected patients under 16 years of age.

METHODS

Based on prospective (cross sectional validity analysis design) study. Based on accuracy of clinical examination and Ultrasound on detecting synovial hypertrophy in JIA affected children authors prospectively studied 70 patients (in age group 0-16 years) from November 2013 to October 2015. All patients between age group 0-16yrs presenting with history, signs and symptoms of arthritis, proved to have JIA after clinical, biochemical and ultrasound evaluation are included.

The study procedure was approved by the Institutional ethical committee and written consent was obtained from the patients. Based on the results of existing literature and

with 95% confidence and 20% error minimum sample size was found to be 32.⁵

Authors prospectively studied 70 patients from November 2013 to October 2015 in age group of 0-16years. All the patients between 0-16 years of age who are referred to paediatric rheumatology department with signs and symptoms of arthritis are examined clinically by the Paediatric Rheumatologist. Both shoulder, elbow, wrist, hip, knee, ankle and subtalar joints of each patient are assessed and the following information like swelling, pain on movement/restricted movement, swelling and pain on movement/restricted movement. Biochemical analysis (especially the ESR and CRP) of these patients are also considered during their first visit before starting the treatment. USG is done to assess the following parameters like synovial hypertrophy, Joint effusion, power doppler signal, tenosynovitis, enthesitis, Cartilage thinning bone erosions, bursitis.

Statistical analysis

Validity parameters namely sensitivity, specificity and accuracy of USG compared with clinical examination will be computed. Distribution of cases by grading the severity of involvement of the joint.

RESULTS

According to the statistical calculation, 32 cases were needed for the study with 95% confidence and 20% error minimum. However, authors could get only 32 cases during the three years period (2013-15) of the study. Distribution according to clinical presentation and ultrasound appearances of joint involvement (n=980) is depicted in Figure 1.

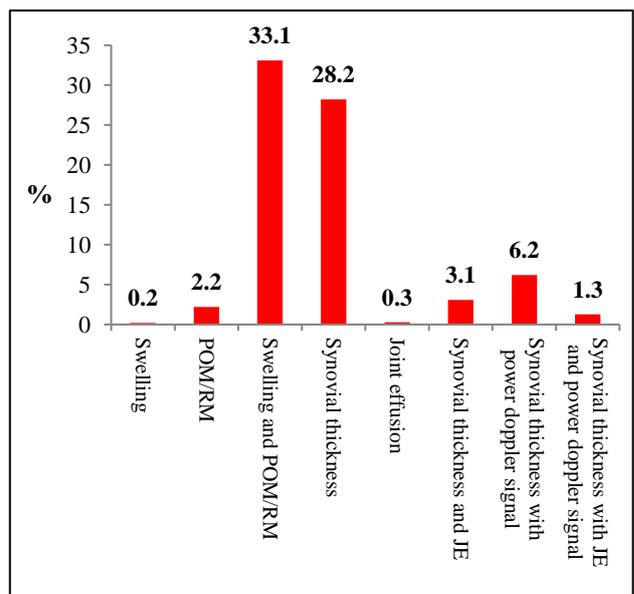


Figure 1: Distribution according to clinical presentation and ultrasound appearances of joint involvement (n=980).

In present study, the age of the patients ranged from 0-18 years, with peak incidence between 11-15 years of age (42.9%), with slight (20%) female preponderance (Figure

2 and 3). This female predilection is distributed across all age groups. 34.4% (RF^{+ve} =3, RF^{-ve} =22) of affected patients had polyarthritis.

Table 1: Synovitis in specific joints: concordance and discordance between ultrasound and clinical evaluation (n=140).

Joints	Concordance and discordance between ultrasound and clinical evaluation of synovitis	Number	Percentage
Shoulder joint	Clinically and US absent	106	75.7
	Clinically present, US absent	11	7.9
	Clinically absent, US present	13	9.3
	Clinically and US present	10	7.1
Elbow joint	Clinically and US absent	93	66.4
	Clinically present, US absent	18	12.9
	Clinically absent, US present	8	5.7
	Clinically and US present	21	15
Wrist joint	Clinically and US absent	61	43.6
	Clinically present, US absent	20	14.3
	Clinically absent, US present	23	16.4
	Clinically and US present	36	25.7
Hip joint	Clinically and US absent	63	45
	Clinically present, US absent	15	10.7
	Clinically absent, US present	34	24.3
	Clinically and US present	28	20
Knee joint	Clinically and US absent	30	21.4
	Clinically present, US absent	23	16.4
	Clinically absent, US present	19	13.6
	Clinically and US present	68	48.6
Ankle joint	Clinically and US absent	45	32.1
	Clinically present, US absent	21	15
	Clinically absent, US present	31	22.2
	Clinically and US present	43	30.7
Subtalar joint	Clinically and US absent	73	52.1
	Clinically present, US absent	13	9.3
	Clinically absent, US present	37	26.5
	Clinically and US present	17	12.1

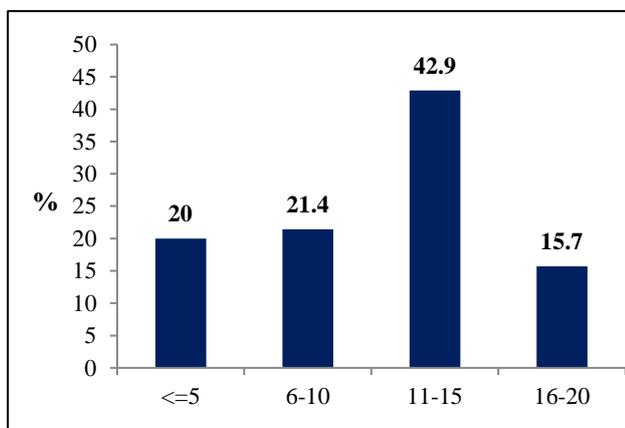


Figure 2: Percentage of distribution of sample according to age.

Next commonest was the systemic onset JIA with 31.4% incidence. Out of 70 patients 58.6% were injected intraarticular steroids as part of the treatment. A total of 980 joints (B/L shoulder, elbow, wrist, hip, knee, ankle and subtalar joints of 70 patients) were assessed both clinically and by using ultrasound scan. Out of these 344 joints (35.1% of all joints) had clinical synovitis, while ultrasound examination revealed evidence of synovitis in 382 joints (38.9% of all joints). Among the 344 clinically positive joints 223 joints (64.8%) had features of synovitis on ultrasound also and the rest 121 (35.2%) joints which were clinically positive turned out to be ultrasound negative. Out of 980 joints 636 joints (64.8%) were clinically negative, of these 159 joints (25%) was found to have ultrasound synovitis and 477 joints (75%) turned out to be negative on ultrasound examination (Table 1).

Of all the 7 major joints shoulder (82.8%) had the highest percentage of agreement followed by elbow joint (81.4). Ankle (62.8%) and hip (65%) joint shows the least agreement of all joints.

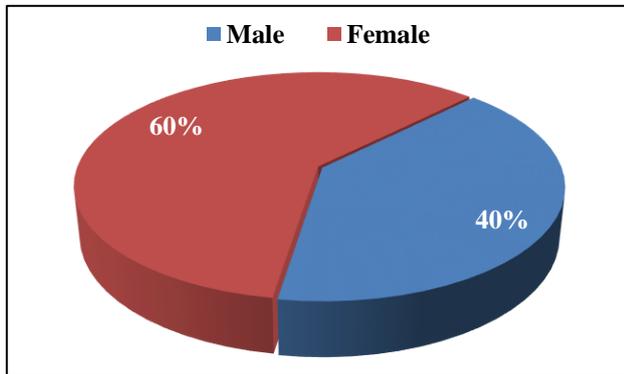


Figure 3: Percentage distribution of the sample according to gender.

Hip joint being a deeper joint is very difficult to assess clinically resulting in many clinically absent and ultrasound synovitis present joints. Ankle joint (37.2%) subtalar joint (31.4%) and knee joint (35%) have high percentage of disagreement because other factors like enthesitis, tenosynovitis and bursitis in these joints can mimic joint synovitis. 4.3% of 140 ankle joints had ultrasound detected tenosynovitis, followed by wrist joint (3.6%). 1% of ankle joints and 1.4% of knee joints had bursitis and 1.4% of ankle joints had enthesitis. Suspicious cartilage damage was recorded in the subtalar joint of a patient who was advised MRI for further evaluation but failed to follow up. There was no ultrasound detected bone erosions in this group of patients.

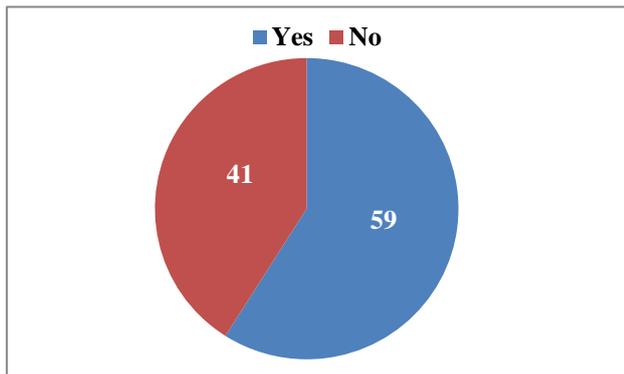


Figure 4: Percentage distribution of the sample according to number of joints injected.

Out of 70 patients, 58.6% were injected with intra-articular steroids as the part of treatment (Figure 4). These injections included both guided and non-guided technique as per the rheumatologist preference. Most of the knee, ankle, elbow and wrist joints were injected without guidance depending on ease of access and joints like shoulder and hip were injected under ultrasound or

fluoroscopic guidance, to assure proper positioning of needle tip within the joint space and to avoid complication like subcutaneous atrophy due to extravasation of steroids.

DISCUSSION

Ultrasound is the most practical and rapid method of obtaining images of musculoskeletal system. In present study, the age of the patients ranged from 0-18 years, with peak incidence between 11-15 years of age (42.9%), with slight (20%) female preponderance. This female predilection is distributed across all age groups. 34.4% (RF⁺ve =3, RF⁻ve =22) of affected patients had polyarthritis. Next commonest was the systemic onset JIA with 31.4% incidence. Oligoarticular JIA was the least common and no patient was categorized under psoriatic and undifferentiated JIA. Out of 70 patients 58.6% were injected intraarticular steroids as part of the treatment. These injections included both guided and non-guided technique. A total of 980 joints (B/L shoulder, elbow, wrist, hip, knee, ankle and subtalar joints of 70 patients) were assessed both clinically and by using ultrasound scan. Out of these 344 joints (35.1% of all joints) had clinical synovitis, while ultrasound examination revealed evidence of synovitis in 382 joints (38.9% of all joints). Among the 344 clinically positive joints 223 joints (64.8%) had features of synovitis on ultrasound also and the rest 121 (35.2%) joints which were clinically positive turned out to be ultrasound negative. Out of 980 joints 636 joints (64.8%) were clinically negative, of these 159 joints (25%) was found to have ultrasound synovitis and 477 joints (75%) turned out to be negative on ultrasound examination.

Authors analysed the concordance and discordance between ultrasound and clinical evaluation of synovitis in 140 shoulder, elbow, wrist, hip, knee, ankle and subtalar joints. Of 140 shoulder joints, 21 joints (15%) had clinical synovitis, of which 11 joints (7.9%) did not reveal ultrasound synovitis while the rest 10 joints (7.1%) showed ultrasound synovitis. Of the 10 joints which showed ultrasound synovitis only 6 joints had power doppler signal presence. 119 joints (85%) were clinically negative, of which 13 joints (9.3%) turned out to be ultrasound positive. 8 joints out of 13 ultrasound positive clinical negative joints showed power doppler signal presence. There is 82.8% agreement between clinical and ultrasound examination. 39 (27.9%) of 140 elbow joints had clinical synovitis, of which 21 joints (15%) revealed ultrasound synovitis and the rest 18 joints (12.9%) did not show ultrasound synovitis. Of this 21-ultrasound positive and clinical positive joints, 18 showed power doppler signal presence. 101 joints (72.1%) were clinically negative, of which 8 joints (5.7%) turned out to be ultrasound positive. Of the 8 clinically negative and ultrasound positive joints 3 had power doppler signal presence. The amount of agreement between clinical and ultrasound examination in elbow joint was 81.4%. 56 (40%) of 140 wrist joints had clinical synovitis, of which

20 (14.3%) did not show ultrasound synovitis while the rest 36 joints (25.7%) revealed ultrasound synovitis. Of the 36-ultrasound positive and clinical positive joints 18 showed power doppler signal presence. 84 joints (60%) were clinically negative, of which 23 (16.4%) joints had ultrasound synovitis. Of the 23 clinically negative and ultrasound positive joints 9 had power doppler signal presence. There was 63.9% agreement between clinical and ultrasound examination in wrist joint.

Of 140 hip joints, 43 (30.7%) had clinical synovitis, of which 28 (20%) joints had ultrasound synovitis while the rest 15 joints (10.7%) did not reveal ultrasound synovitis. Of the 28-ultrasound positive and clinical positive joints 17 had power doppler signal presence. 97 joints (65%) were clinically negative, of which 34 joints (24.3%) showed ultrasound synovitis. Of the 34 clinically negative and ultrasound positive joints 18 had power doppler signal presence. There was 35% disagreement between clinical and ultrasound examination in hip joint. 91 (65%) of 140 knee joints had clinical synovitis, of which 68 (48.6%) revealed ultrasound synovitis and the rest 23 joints (16.4%) did not show synovitis on ultrasound examination. Of the 68-ultrasound positive and clinical positive joints only 27 had power doppler signal presence. 49 joints (35%) of 140 knee joints were clinically negative, of which 19 (13.6%) showed ultrasound synovitis. Of the 19 clinically negative and ultrasound positive joints only 5 had power doppler signal presence. This data shows that there is 70% agreement between clinical and ultrasound examination in knee joint.

Of 140 ankle joints examined 64 (45.7%) had clinical synovitis, among which ultrasound synovitis was present in 43 joints (30.7%) and rest of 21 joints (15%) did not reveal synovitis on ultrasound examination. Of the 43-ultrasound positive and clinical positive joints only 16 had power doppler signal presence. 76 joints (54.3%) were clinically negative, among which 31 joints (22.2%) showed ultrasound synovitis. Of the 31 clinically negative and ultrasound positive joints only 7 had power doppler signal presence. There was 37.2% disagreement between the two modes of examination in ankle joint. 30 (21.4%) of 140 subtalar joints had clinical synovitis, of which 17 joints (12.1%) revealed ultrasound synovitis while the rest 13 joints (9.3%) did not reveal ultrasound synovitis. Of the 17 ultrasound positive and clinical positive joints 6 had power doppler signal presence. 101 joints (78.6%) were clinically negative, of which 37 joints (26.5%) showed ultrasound synovitis. Of the 37 clinically negative and ultrasound positive joints only 6 had power doppler signal presence.

Of all the 7 major joints shoulder (82.8%) had the highest percentage of agreement followed by elbow joint (81.4%). High percentage of agreement in Shoulder joint and elbow can be due to single observer bias because of a small sample size or shoulder being a ball and socket joint and elbow being a hinge joint is were easy to assess

clinically, so even minimal joint restriction can be made out easily. Ankle (62.8%) and hip (65%) joint shows the least agreement of all joints. Hip joint being a deeper joint is very difficult to assess clinically resulting in many clinically absent and ultrasound synovitis present joints. Ankle joint (37.2%) subtalar joint (31.4) and knee joint (35%) have high percentage of disagreement because other factors like enthesitis, tenosynovitis and bursitis in these joints can mimic joint synovitis. 4.3% of 140 ankle joints had ultrasound detected tenosynovitis, followed by wrist joint (3.6%). 1% of ankle joints and 1.4% of knee joints had bursitis and 1.4% of ankle joints had enthesitis. 159 (25%) of 382 ultrasound positive joints had subclinical synovitis. Subclinical synovitis was found to be more in deeper joints like hip (24.3%) followed by ankle, subtalar joint (22.1%) and wrist joint (18.4%). Elbow had the least percentage of subclinical synovitis (5.7%).

Authors computed the percentage of agreement between clinical and USG findings of 140 shoulder, elbow, wrist, hip, knee, ankle and subtalar joint. Elbow joint showed highest agreement among the joints (k-0.49-moderate agreement). All other joints showed fair agreement (shoulder- 0.35, wrist- 0.37, hip- 0.27, knee- 0.35, ankle- 0.26 and subtalar- 0.23) the p value of all joints was >0.05 suggesting that there is no disagreement between clinical and ultrasound findings. From these statistical values authors can presume that elbow joint being very superficial could be assessed accurately and easily as compared to rest of the joints, resulting in better clinical and ultrasound agreement. The subtalar joint being complex and close to ankle joint showed findings of clinical synovitis than what was observed sonologically. Stefano et al, concluded in his study that ultrasound is more sensitive than clinical evaluation in the assessment of subtalar joint in ankles with active disease.⁶ In his study 14% of ankles labelled as having subtalar joint involvement on clinical examination was found negative on ultrasound examination. MRI is the gold standard for assessing synovitis of all joints. Since most of the children have multiple joint involvement and all the major joints needs to be evaluated radiologically to upstage and downstage the disease it was not feasible to evaluate every joint with MRI. Taking clinical examination as the gold standard the sensitivity, specificity and accuracy of ultrasound examination for each joint were calculated separately, of which knee and ankle joint showed high sensitivity (74.7% and 67.2% respectively) whereas the specificity for these joints were low (61.2% and 59.2% respectively) as compared to elbow and shoulder joints which showed high specificity (92.1% and 89.1% respectively) and accuracy (81.4% and 83% respectively). The specificity for the ankle joint was the lowest compared rest of the joints; however, ankle joint showed 63% accuracy. The reasons for low sensitivity in some of the joints like shoulder (47.6%), elbow (53.8%) and subtalar (56.7%) could be due high false negatives (clinical positive and ultrasound negative), which can be due to early synovitis with less

than 2mm synovial thickness but with clinical manifestations, partially or chronically treated synovitis and due to other coexisting factors mimicking joint synovitis like tenosynovitis, enthesitis and bursitis. Specificity can be low in some of the joints like ankle (59.2%), knee (61.2%) and hip (64.9%) due to more number (false positives) clinical absent and ultrasound present joints- subclinical synovitis.

Contrast enhanced ultrasound will be helpful in joints which are clinically positive and ultrasound negative, as synovial enhancement and synovial thickening less than 2mm could be easily assessed using contrast agents, thus obviating the need for MRI. Cimmino et al, in his study concluded that ultrasound contrast agents increase sensitivity of colour doppler examination by enhancing the blood scattering reflection.⁷ Previous studies were proved that Ultrasound contrast media can help in early detection and follow up of disease activity in Rheumatoid arthritis.⁸⁻¹¹

In present study ESR and CRP values assessed in the first visit was compared with the synovial thickness score (by addition of measured thickness of inflamed synovium in affected joints) and power doppler signal score (by addition of power doppler grades obtained in each joints). The mean ESR for 70 patients was 41.9 ± 23.6 and the mean CRP was 43.7 ± 16.9 . It was demonstrated that ESR and CRP values had no correlation with synovial thickness score but showed significant positive correlation with power doppler signal score ($r = 0.473$, $p = 0.001$ and $r = 0.185$, $p = 0.001$ respectively). This signifies that the patient with high disease severity (Power doppler signal grade 2 and 3) can have high ESR and CRP values. The relevance of ESR and CRP in clinical medicine were established as well.¹²⁻¹⁴ Wu et al, in his study concluded that ESR is a better parameter than CRP, but high initial CRP level can strongly predict treatment failure of the first remission.¹⁵

In present study authors also assessed the Pearson correlation between power doppler signal score and synovial thickness score and could demonstrate that there is a positive correlation between the two with $r = 0.731$ and $p = 0.001$. It signifies that those joints with increased synovial thickness measurements in each joint can have higher grades of power doppler signal presence. Twenty two patients out of 70 came for review ultrasound after their prescribed course of treatment. In these group of patients both pre-treatment and post treatment-clinical, ultrasound and power doppler binary joint count and semi quantitative joint score were assessed. Although most of the patients who underwent post treatment clinical assessment showed significant clinical improvement (binary clinical joint count p value = 0.002 and semiquantitative clinical joint score p value = 0.004), ultrasound assessment of these joints showed presence of residual disease (binary ultrasound joint count p value = 0.174 and semi quantitative ultrasound joint score p value = 0.080, Binary PDS joint count p value = 0.095 and semi

quantitative PDS joint score p value = 0.650), which signifies that ultrasound is a better choice in post treatment assessment of disease remission, since it detects subclinical synovitis. This can have implications in preventing joint damage or in modifying treatment.

Out of 70 patients, 58.6% were injected with intra-articular steroids as the part of treatment. These injections included both guided and non-guided technique as per the rheumatologist preference. Most of the knee, ankle, elbow and wrist joints were injected without guidance depending on ease of access and joints like shoulder & hip were injected under ultrasound or fluoroscopic guidance, to assure proper positioning of needle tip within the joint space and to avoid complication like subcutaneous atrophy due to extravasation of steroids.

CONCLUSION

The sensitivity and specificity of ultrasound over clinical examination in shoulder joint was 47.6% and 89.1% respectively, in elbow joint 53.8% and 92.1%, in wrist joint 64.3% and 72.6%, in hip joint 65.1% and 64.9%, in knee joint 74.7% and 61.2%, in ankle joint 67.2% and 59.2% and in subtalar joint 56.7% and 71.8%, respectively.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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