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Original article

Musculoskeletal ultrasonic findings in a group of children with Juvenile Idiopathic Arthritis

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Introduction: *The use of musculoskeletal ultrasonography (MSUS) for patients with Juvenile idiopathic arthritis (JIA) is gaining rising attention in the current clinical practice, being a simple non-invasive tool in diagnosing and assessing JIA patients. We sought to describe MSUS findings in a group of pediatric patients with JIA and correlate these findings to their clinical assessment.* ***Methods:*** *This cross-sectional included 60 JIA patients, aged 1-16 years, 40 were already diagnosed as JIA and on treatment and 20 were newly diagnosed at enrollment in the study They were subjected to clinical assessment and MSUS radiological assessment and were assessed by the 27-joint Juvenile Arthritis Disease Activity Score (JADAS27 score).* ***Results:*** *Oligoarticular was the commonest JIA subtype. Strong agreement was observed between MSUS features and clinical findings (kappa=0.937, P<0.001). Thirty-five cases were diagnosed as oligoarticular JIA, confirmed by MSUS examination at enrollment in 33, while 2 were reclassified as having polyarticular JIA. Also, clinically 22 cases were diagnosed to have polyarticular JIA, 18 of them were confirmed by MSUS examination at enrollment. In addition, significant moderate agreement was observed between the MSUS features and the JADAS27 score (kappa = 0.353, P = 0.003).* ***Conclusions:*** *MSUS is a valuable tool for the diagnosis and follow-up of synovitis in children with JIA.*

Keywords: juvenile idiopathic arthritis (JIA), Musculoskeletal ultrasonography (MSUS), 27-joint Juvenile Arthritis Disease Activity Score (JADAS27).

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a common chronic rheumatic disease in children and a major cause of acquired disability. Despite its diverse forms, all types of JIA share the hallmark of chronic synovial inflammation, which can lead to cartilage and bone damage, impaired physical function, and a diminished quality of life. Musculoskeletal ultrasonography (MSUS) has proven to be a reliable and effective diagnostic tool for chronic inflammatory joint diseases in adults and is now recognized as valuable for evaluating joints in children with JIA.[1]

In addition to being quick and affordable, MSUS allows for multisite assessment in a single session, doesn't require general anesthesia or sedation, and doesn't expose children to ionizing radiation. Moreover, it is the only imaging technique that can be combined with the clinic's standard procedure for patient evaluation.[2]

Musculoskeletal ultrasonographic findings in JIA may reveal joint involvement through signs such as bone erosions, cartilage thinning, synovial proliferation, and effusion. MSUS has shown greater sensitivity than clinical examination in detecting synovitis.[3] Additionally, it facilitates needle-guided procedures like aspiration or injection and provides quicker detection of synovial and bone abnormalities compared to traditional radiology. MSUS is also useful in evaluating tenosynovitis and enthesitis.[4]

The use of Doppler techniques further enhances MSUS by detecting synovial vascularization, which helps assess disease activity more effectively.[5]

The main aim of the current study was to describe MSUS findings in a cohort of pediatric patients with JIA and correlate these findings with clinical assessments.

METHODS

This cross-sectional study, conducted at Pediatric Allergy, Immunology, and Rheumatology Unit and the Radiology Department of Assiut University Children's Hospital between January 2020 and June 2022, involved 60 JIA patients aged 1–16 years. These patients, newly or previously diagnosed, were presented with one or more painful joints with or without swelling for more than six weeks. A notable aspect of the study is that some patients were already on treatment, which may have affected the number of joints with disease involvement at the time of ultrasound evaluation compared to their initial diagnosis.

Exclusion criteria for the study included children above 16 years at the time of diagnosis and those with arthritis due to causes other than JIA, such as reactive arthritis, post-streptococcal arthritis, septic arthritis, systemic lupus erythematosus, dermatomyositis, malignancy, or post-traumatic synovitis.

The clinical evaluation incorporated:

1. Complete History Taking: Personal history: age, sex, history of chronic diseases (e.g., diabetes mellitus, hypertension), obesity, drug intake, previous surgeries, and comorbid diseases (e.g., renal or hepatic conditions).

*2. General Examination: for v*ital signs and complete systemic examination.

3. Musculoskeletal Examination: with focus on assessment of the severity of joint inflammation through three key parameters: joint swelling, pain or tenderness on motion, and the degree of limitation of movement.

4. The 27-joint Juvenile Arthritis Disease Activity score (JADAS-27):[6] It is a comprehensive tool used to assess disease activity in JIA, with a total score ranging from 0 to 57. It consists of four key components: The physician's global assessment of disease activity (PGA) using a 10-cm visual analogue scale (VAS). The parent's or patient's assessment of overall well-being, also on a 10-cm VAS. The evaluation of active arthritis, characterized by joint swelling or restricted movement accompanied by pain and tenderness, across 27 joints, including the hips, knees, ankles, cervical spine, elbows, wrists, and selected finger joints. The erythrocyte sedimentation rate (ESR), normalized to a 0–10 scale using the formula (ESR-20)/10.

5. Musculoskeletal Ultrasonography evaluation: used for imaging assessments, performed with the Philips Affiniti 50 G machine. A linear transducer (6–18 MHz for grayscale, 12.5 MHz for power Doppler) was utilized, with a pulse repetition frequency of 500–750 MHz. A low-wall filter and gain adjustment ensured that no signals appeared on or below the bone surface. Pathological findings were aligned with the Outcome Measures in Rheumatology Clinical Trials (OMERACT) Special Interest Group's definitions for MSUS in rheumatology.[7]

Ethical considerations

The study adhered to the ethical requirements set forth by Assiut University's Ethical Committee (IRB No. 17100979). Informed written consent was obtained from the patients or their parents after thoroughly explaining the study's objectives.

Statistical analysis

Data were analyzed using SPSS version 22 (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA). Descriptive statistics included mean, standard deviation (SD), median (range), and frequency (number and percentage). Categorical data were compared using Chi-square (χ^2) or Fisher's Exact tests. The correlation between variables was assessed using the Spearman rho correlation test. The strength of agreement was evaluated through Cohen's kappa and weighted kappa statistics, following the benchmarks established by Landis and Koch.[8] *P*-value set significant at 0.05.

RESULTS

The mean age of the study participants was 8.77 ± 3.14 years (range: 3-15 years), with 50% of the children under 9 years old and a male-to-female ratio of 2:1. A positive family history of rheumatoid arthritis or JIA was noted in four cases (6.7%), as shown in Table 2. Among the 60 JIA patients, 40 were already diagnosed as JIA and already on treatment and 20 were newly diagnosed. Thirty-five patients were diagnosed as oligoarticular JIA, 22 polyarticular JIA (8 of whom were RF positive), 2 systemic JIA, and 1 had enthesitis-related arthritis.

Musculoskeletal ultrasound assessment indicated that synovial thickening (mm) and synovial effusion were significantly higher in oligoarticular JIA patients (P=0.010 and 0.031, respectively), while the grades of synovial effusion

were comparable between the two JIA subtypes (P=0.306). Additionally, patients with oligoarticular JIA exhibited more positive Doppler activity (P<0.001), with moderate Doppler activity being more common in this group compared to polyarticular JIA (P=0.008), as detailed in Table 3.
There was a significant positive correlation between the inflammatory marker ESR at the first hour and both synovial thickening (r=0.455, p<0.001) and synovial effusion (r=0.333, p=0.009), as well as with Doppler activity (r=0.628, P<0.001). Furthermore, there was a significant moderate agreement between MSUS features and the JADAS score among the studied patients (kappa = 0.353, P = 0.003). Figure 1 demonstrates a strong agreement between MSUS findings and clinical assessments (kappa = 0.937, P < 0.001).

Clinical examination identified 35 cases of oligoarticular JIA, and MSUS confirmed that 33 of these patients had oligoarticular JIA, while 2 were reclassified as having polyarticular JIA. In the case of polyarticular JIA, clinical examination identified 22 patients, and MSUS confirmed that 18 of these were accurately diagnosed, with 4 patients identified as having oligoarticular JIA instead.

Table 1. MSUS pathological findings in JIA.[7]

Synovitis	Presence of joint effusion and/or synovial hypertrophy – identified in each joint as an area of hypoechoic or anechoic intra-articular material, compressible and displaceable, with absence of power doppler signal (joint effusion) 0: Normal: ≤3 mm 1: Mild: >3 mm to ≤5 mm 2: Moderate/severe: >5 mm Or Presence of hypoechoic area of non-displaceable and poorly compressible material, with absence or presence of power doppler signal (synovial hypertrophy). It is graded as mild, moderate, or severe based on semiquantitative analysis using score from 0 to 3. 0: No synovitis 1: Mild synovitis in joint recess up to capsule but without causing its bulge. 2: Moderate synovitis in the entire joint recess causing bulging its capsule but without extension to bone diaphysis. 3: Severe synovitis in joint recess with bulging its capsule and extension to bone diaphysis.
Tenosynovitis	Abnormal anechoic and/or hypoechoic (relative to tendon fibers) tendon sheath widening which can be related both to the presence of tenosynovial abnormal fluid and/or hypertrophy. Doppler signal can be considered if seen in two perpendicular planes, within the peri-tendinous synovial sheath, excluding normal feeding vessels (i.e. vessels at the mesotenon or vinculae or vessels entering the synovial sheath from surrounding tissues).
Enthesopathy	Abnormal hypo-echoic (loss of normal fibrillar architecture) and/or thickened tendon or ligament at its bone attachment (may contains hyper-echoic foci consistent with calcification) seen in two perpendicular planes that may exhibit a doppler signal and/or bony changes such as enthesophytes, erosions, or irregularities.
Bone erosions	Intra-articular discontinuity of the bone surface that is visible in two perpendicular planes.
Doppler activity (Blood flow)	Presence of Power Doppler signals performed only in areas where grade 1 to 3 joint synovitis was detected. It is scored on a semiquantitative 4-grade scale: 0: No Doppler activity or No flow. 1: Mild (presence of single vessel dots or mild flow) 2: Moderate (presence of confluent vessel dots in less than half of the synovial area or moderate flow) 3: Severe (presence of confluent vessel dots in more than half of the synovial area)

Table 2. Demographic characteristic of the studied JIA patients

Patients' characteristics	n=60	
Age (years)		
Mean ± SD	8.77 ± 3.14	
Median (range)	9 (3 – 15)	
Age groups		
<9 years	30	(50.0%)
≥9 years	30	(50.0%)
Male gender	40	(66.7%)
Positive family history	4	(6.7%)

Table 3. Comparison of MSUS features among JIA subtypes for the total number of examined joints (n=226).

MSUS features	JIA subtypes				P value
	Oligoarticular (n=35)		Polyarticular (n=22)		
Total number of examined joints	92		128		
Synovial thickening (mm)					0.010*
Mild	43	(46.7%)	66	(51.6%)	
Moderate	23	(25.0%)	46	(35.9)	
Severe	26	(28.3%)	16	(12.5)	
Number joints with effusion	90	(97.8%)	116	(90.6%)	0.031*
Effusion grades					0.306*
Mild	40	(44.4%)	64	(55.2%)	
Moderate	26	(28.9%)	28	(24.1%)	
Severe	24	(26.7%)	24	(20.7%)	
Number joints with erosion	0	(0.0%)	5	(3.9%)	0.076**
Tendinitis	0	(0.0%)	2	(1.6%)	0.511**
Positive Doppler activity	64	(69.6%)	52	(40.6%)	<0.001*
Doppler activity degree					0.008*
Mild	56	(87.5%)	52	(100.0%)	
Moderate	8	(12.5%)	0	(0.0%)	

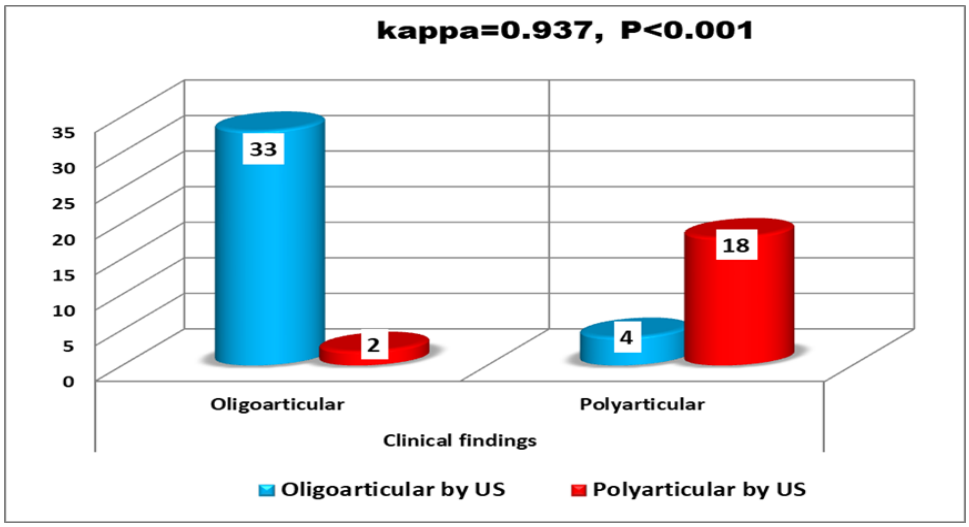

Figure 1: Bar graph showing the agreement between the MSUS features and clinical findings

Figure 2 Some ultrasound findings among the studied patients with JIA
A: Mild left hip joint synovitis; **B**: Right ankle with mild synovial thickness, minimal effusion and no doppler activity; **C**: Knee joint with moderate effusion; **D**: knee joint with mild synovial thickening and villous formation

DISCUSSION

Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children, characterized by chronic inflammation of the synovial membrane, which can lead to cartilage loss, bone damage, and long-term joint impairment if untreated.[9] High resolution devices as MSUS have become a key tool for evaluating JIA with more accurate evaluations of arthritis, tenosynovitis, and enthesitis compared to clinical examination alone.[10] MSUS offers a non-invasive, radiation-free way to visualize soft tissues in real time and guide procedures like fluid aspiration. While MSUS can reveal greater detail of soft tissues compared to MRI, it cannot penetrate bone and has limitations with deeper structures especially in older patients. Also, it is operator dependent and needs to be done by experienced personnel. MSUS provides valuable detail on tendons and joints, making it highly useful in managing JIA.[11]

The study reveals important demographic insights into JIA, with an average age of 8.77 years and 66.7% male predominance. Unlike studies by Mosa et al.,[12] and Al-Mayouf et al.,[13] which found that JIA affects females more frequently, this may reflect cultural tendencies in Upper Egypt where families prioritize seeking medical care for males.

In terms of JIA subtypes, oligoarticular JIA was the most common (58.3%), followed by RF-negative polyarticular JIA (23.3%) and RF-positive polyarticular JIA (13.3%). Systemic JIA and enthesitis-related arthritis were rare, affecting 3.3% and 1.7% of patients, respectively. These results align with findings from El-Banna et al.,[14] and other study, which similarly reported that oligoarticular JIA is the most prevalent subtype.[15]

MSUS can effectively detect changes in JIA, such as synovial thickening, effusion, and vascularity. Increased fluid, expansion of the synovial membrane, and/or increased vascularity may be interpreted as an indication of disease

activity.[16] The study found that severe synovial thickening was more common in oligoarticular JIA (28.3%) than polyarticular JIA (12.5%), while moderate thickening was more frequent in polyarticular JIA (35.9%) compared to oligoarticular JIA (25.0%). There were no significant differences in effusion grades, and joint erosion was rare in both groups, with only 5 joints affected in the polyarticular group. However, Doppler activity showed more positive results in oligoarticular JIA, suggesting more active inflammation, though the degree of activity was milder compared to polyarticular JIA.

The study found a significant positive correlation between MSUS features—such as synovial thickening, effusion, and Doppler activity—and ESR levels, suggesting Doppler ultrasound could be a valuable tool for monitoring JIA disease activity. Doppler ultrasound detects blood flow in inflamed synovial tissue, indicating active inflammation. These results align with findings by Mosa et al.[12] and El-Banna et al.,[13] who also reported positive correlations between MSUS scores and CRP levels. ESR was chosen as the inflammatory marker in the study because it was consistently recorded as part of the JADAS score, which was used as the primary method for assessing disease activity in our patients.

We also demonstrated strong agreement between MSUS findings and clinical diagnoses, particularly for oligoarticular JIA, where 33 patients were accurately diagnosed. Good agreement was also observed for polyarticular JIA (18 patients) and enthesitis-related arthritis, highlighting the diagnostic accuracy of MSUS in JIA.

In our study, MSUS identified polyarticular involvement in 2 out of 35 oligoarticular JIA patients. Clinically, these patients were diagnosed with oligoarticular JIA based on arthritis in the knees and wrists, but MSUS revealed significant synovial proliferation with positive Doppler signals in the small joints of hands as PIP joints (middle 3 fingers in both sides), which were not detected during clinical exams. Conversely, MSUS found reduced joint involvement in 4 of 22 polyarticular JIA patients, these patients were following up and presented in activity. Mostly there is change in disease pattern in current state of the study versus on the time of diagnosis, possibly due to treatment effects or a change in disease pattern, suggesting these patients may not be fully controlled on their current medications. This aligns with Suhaib's study,[17] where ultrasound detected subclinical synovitis in 8.8% of clinically normal joints, leading to the reclassification of three patients from oligoarticular to polyarticular JIA. MSUS' ability to uncover subclinical disease highlights its value in accurately classifying and monitoring JIA.[17] Similarly to the findings of Zou et al.,[18] where MSUS revealed synovitis in clinically normal joints of 32 children with JIA, they found subclinical synovitis more frequently in the wrist, PIP, subtalar, and foot joints than in the larger joints like the glenohumeral, elbow, wrist, and knee. A notable mismatch between clinical and MSUS examinations was observed, especially in oligoarticular JIA patients, where synovitis in small joints of the hands and feet went undetected clinically. This suggests that using MSUS in JIA can help detect joint synovitis earlier and identify arthritis progression in clinically normal joints, making it a more effective diagnostic tool than clinical examination alone.[18]

Thus, combining clinical examination with MSUS findings for the same joint may provide more comprehensive information, helping to prevent under- or overtreatment in JIA patients. It may be beneficial to develop and validate a grading system that integrates clinical, MSUS, and Doppler assessments for JIA.[19]

Obviously, this study has several limitations. First, a larger sample size is needed to confirm the predictive value of MSUS in JIA subtypes. Second, variations in MSUS parameters and findings across different age groups and the lack of specific MSUS definitions for each pediatric age group suggest that studies should be conducted for each group. Lastly, a group of the enrolled patients in the study were already receiving treatment, which could have influenced the number of affected joints detected by MSUS compared to the initial diagnosis.

In conclusion, MSUS is a valuable tool for the diagnosis of synovitis in children and adolescents with JIA. Its non-invasive, safe, and cost-effective nature, combined with its high sensitivity and specificity, make it a valuable addition to the diagnostic modalities in pediatric rheumatology. However, further studies are needed to validate its use in different settings and to determine its long-term impact on joint outcomes in this population.

CONFLICTS OF INTEREST

The authors declare they have no conflict of interest in relation to this work.

AUTHORS' CONTRIBUTIONS

N.S.O: Collection of data, history taking, clinical evaluation and diagnosis of the cases, identifying JIS subtypes and JADAS score for patients, writing, editing and submitting the manuscript, **AM.E:** Performing MSUS for patients (under supervision), data collection and entry, writing the manuscript, **AA.K:** Selection of the study idea and revision of the manuscript, **H.M.I**: Performing MSUS for patients, writing the methods section, **S.M.A.:** Selection of idea of research, writing method section, editing the manuscript, revision of references

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