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Research Article

Correlation between Ultrasonography and Clinical Indices of Disease Activity in Juvenile Idiopathic Arthritis Patients

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Abstract

Objectives: To correlate between Ultrasonography and clinical indices of disease activity regarding the severity of joint affection in Juvenile Idiopathic Arthritis (JIA).

Methods: 30 children having Juvenile Idiopathic Arthritis as well as 20 controls were studied. Demographic and disease related data were collected. Laboratory investigations including Erythrocyte Sedimentation Rate (ESR), C Reactive Protein (CRP), Rheumatoid Factor (RF) and were performed. Clinical examination, including routine joint examination was carried. Disease activity was assessed with a parental questionnaire and physical examination by the physician; over all JIA activity and disability was assessed with patient (or parent) and physician's Visual Analogue Scales (VAS) and with Childhood Health Assessment Questionnaire (CHAQ). Ultrasonographic examination of the involved joints by high frequency transducer (7.5-10) MHz was carried out with evaluation of synovial thickness, joint effusion, cartilage erosion and possible joint space changes.

Results: Demographic data were comparable in patients *vs*. control. The mean disease duration was 2.38±2.61. The polyarticular subtype constituted the majority of the patients (76.6%). The polyarticular subtype had the highest mean CHAQ (2.06±0.63) and VAS 46.52±29.02. There was significant correlation between US and clinical examination in detection of inflammatory changes, with US presenting earlier detection in some cases. Cartilage changes were detected earlier by US.

Conclusion: Musculoskeletal Ultrasonography was more accurate than clinical examination in detection of early joint changes in JIA patients. It allows the visualization of subtle effusion and early cartilage changes. Musculoskeletal US are a rapid, safe, accurate and reproducible method for evaluating and monitoring joint changes in JIA.

Keywords: Ultrasonography; Juvenile idiopathic arthritis; Rheumatoid factor; Childhood health assessment questionnaire

Introduction

Juvenile Idiopathic Arthritis (JIA) is a broad term describing a clinically heterogeneous group of arthritis, that begin before the age of sixteen and persist for more than six weeks and is considered the main cause of chronic arthritis in children [1]. This chronicity of joint involvement in JIA distinguishes this group of disorders from many short term causes of joint pain and swelling [1]. The term encompasses several disease categories, each of which has distinct presentation, clinical symptoms, signs and in some cases genetic background [1]. Classification of JIA is still not fully defined as it has often depended on the clinical features that show variations between patients [2]. Different classification schemes have been suggested for understanding the immuno-pathology of the disease [3-5]. Assessment of disease activity and joint changes in children represents a relative difficulty when compared to adults. Over the last decade Ultrasonography has emerged as a reliable and powerful tool for evaluating soft tissue in rheumatic diseases [6]. The main advantages of Ultrasonography include absence of radiation, good visualization of tendons and joint spaces, multiplanner imaging capability; it can be rapidly performed at the bedside, it is readily accepted by the patient's parents [7-10].

Aim of the Study

To correlate between Ultrasonography and clinical indices of disease activity regarding the severity of joint affection in Juvenile Idiopathic Arthritis (JIA).

Subjects

Thirty patients diagnosed as JIA according to the ACR criteria (1977) [11], from those attending the Outpatient Clinic of Physical Medicine, Rheumatology, and Rehabilitation Department , Faculty of Medicine, Alexandria University were enrolled in the study, after taking an informed consent from their parents.

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Table 1: Demographic characteristics of the studied groups.

Variable	Patients	Control	Significance
Age(mean &range)	8.8(3-16)	7.56(5-11)	T=1.25
Gender n (%)			
Male	14(46.7%)	11(55%)	X^2=1.65
Female	16(53.3%)	9(45%)	P=0.251

Table 2: Disease duration and pattern of disease onset of the studied patients.

Disease duration	-
Range (mean)	1-3(2.38±2.61)
Disease onset	-
Polyarticular	23(76.6%)
Oligoarticular	5(16.6%)
Systemic	2(6.6%)

Table 3: Comparison between the different studied groups according to CHAQ and VAS.

	PoJIA (n=23)	oJIA (n=5)	SoJI (n=2)
CHAQ			
Range	1-3	1-3.88	1-1.37
Mean± SD	2.06±0.63	1.78±1.25	1.19±0.26
VAS			
Range	10.00–90.00	10.0–70.00	40.00–40.00
Mean±SD	46.52±29.02	30.00±25.50	40.00±0.00

CHAQ: Childhood Health Assessment Questionnaire
VAS: Visual Analogue Scale
PoJIA: Polyarticular Onset Juvenile Idiopathic Arthritis
OJIA: Oligoarticular Onset Juvenile Idiopathic Arthritis
SoJIA: Systemic Onset Juvenile Idiopathic Arthritis

Exclusion criteria were: Age of onset more than 16 year old, Patient presenting with arthralgia only without any signs of arthritis, Disease duration less than 6 weeks, and presence of any other cause that may raise arthritis in this age.

A control group of twenty apparently healthy children with age and sex match were also enrolled to determine the normal values of the following: Rheumatoid Factor (RF) subtype IgA, RF subtypes IgM and Ultrasonographic findings of knees, ankles, and wrists concerning; joint effusion, synovial thickening, articular cartilage surface, joint space.

Methods

Each child was subjected to demographic data collection, clinical data include; present history focusing on detailed history of joint pain and swelling. Past history of any previous illness or trauma that may cause joint inflammation. Thorough clinical examination including general examination and detailed musculoskeletal examination were carried out for all the included children [12].

Disease activity was assessed with a parental questionnaire and physical examination by the physician; over all JIA activity and disability was assessed with patient (or parent) and physician's Visual Analogue Scales (VAS) and with Childhood Health Assessment Questionnaire (CHAQ) [13,14].

Laboratory investigations including Erythrocyte Sedimentation Rate (ESR), C - Reactive Protein (CRP), and RF were performed. Quantitative measurement of IgA & Ig M rheumatoid factor in the serum of patients and control were done using immunometric enzyme linked immunoassay ELISA.

All subjects were examined by high resolution ultrasound using general electric apparatus, utilizing high resolution multi frequency probe 7.5-10MHz [15]. The points examined were knees, ankles and wrists. For each joint examined; joint effusion, synovial thickening, cartilage erosion, joint space and soft tissue involvement were recorded [15].

Statistical Analysis

Data were analyzed using SPSS software package version 15.0 (SPSS, Chicago, IL, USA). Quantitative data was expressed using Range, mean and standard deviation while Qualitative data was expressed in frequency and percent. Quantitative data was analyzed using student t-test to compare between two categories while F-test (ANOVA) was used to compare more than two categories. Spearman coefficient was used to analyze correlation between different parameters. Significance was considered at $p \leq 0.05$.

Results

Demographic data were comparable in patients versus control (Table 1). The mean disease duration of the patients was 2.38±2.61. Polyarticular subtype constituted the majority, 23 patients (76.6%) (Table 2).

Functional and global assessment of the disease activity using CHAQ and VAS in the different patients is represented in (Table 3). The polyarticular subtype showed the highest mean CHAQ (2.06±0.63) and mean VAS (46.5±29.02) in comparison to other subtypes.

Findings in the studied patients related to ultrasound effusion in (Figure1). Distribution of clinical effusion represented in (Table 4).

For the purpose of statistical analysis and due to, the uneven distribution among different onset subtypes, the whole patients were considered as one group and compared to the control group as regard the Ultrasonographic findings in correlation with clinical findings (Table 5).

Correlation between clinical effusion and stiffness in knees, wrists

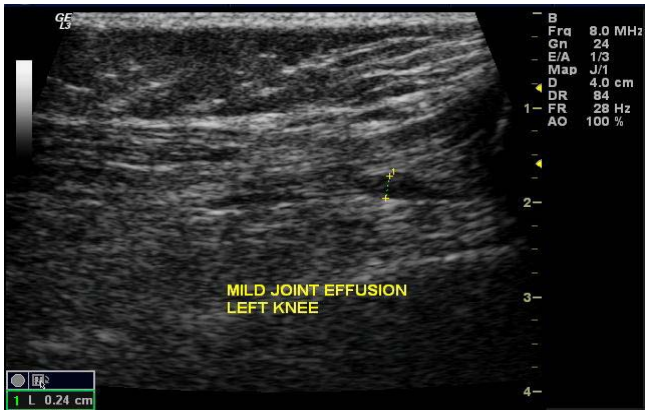

Figure 1: US mild Joint effusion of left knee.

Table 4: Distribution of clinical effusion among studied patients.

	PoJIA (n=23)	oJIA(n=5)	SoJIA (n=2)
	No. (%)	No. (%)	No. (%)
Knee			
Bilateral	10(43.47%)	2(40%)	0(0%)
Unilateral	5(21.73%)	1(20%)	1(50%)
Ankles			
Bilateral	13(56.52%)	1(20%)	1(50%)
Unilateral	3(13.04%)	0(0%)	0(0%)
Wrists			
Bilateral	7(30.43%)	0(0%)	0(0%)
Unilateral	10(43.47%)	0(0%)	1(50%)

and ankles according to US effusion, US thickness, articular erosion and joint space narrowing: (Table 6)

There was significant correlation between clinical effusion and Ultrasonographic effusion, thickness and erosion in the knees. Also, there was significant correlation between knee stiffness and Ultrasonographic effusion, thickness and erosion.

As regard wrist joints, clinical effusion and joint stiffness showed significant correlation with Ultrasonographic effusion, thickness and joint space narrowing. Also writ stiffness significantly correlated with articular erosion.

In the ankle joints, there were significant correlation between clinical effusion and stiffness and Ultrasonographic effusion. Significant correlation was also detected between ankle stiffness and Ultrasonographic synovial thickness.

Discussion

The current international classification system proposed by International League of Associations for Rheumatology (ILAR) defines clinical differences between the groups. In this study, the polyarticular subgroup constituted the majority of the patients Oligoarticular subtype was the second and systemic onset subtype was the least group of patients. Similar pattern of disease onset was observed by Wong S et al. [16]. However, oligoarticular pattern represented the majority of patients in a study conducted by Solau E et al. [17]. The systemic onset subtype constituted the smallest group of patients in both studies [16,17].

In a clinical setting, the degree of joint tenderness and joint swelling are important characteristics for assessing not only the degree of disease activity but also, the response to therapeutic intervention. In our study, knee joint was the most affected joint and this finding was apparent in the three subtypes, and more over this affection was commonly bilaterally. The wrist joint was the second most affected joint, and the ankle joint was the third joint affected. These findings are in agreement with, Resende C et al., they included, 72 children with the diagnosis of JIA. The knee was the most commonly involved joint in all subtypes: The wrist was the second joint affected with a prevalence of 83.3% in the polyarticular subtype, but their findings showed a greater prevalence of wrist affection in the systemic onset subtype (50%), and (30%) in Oligoarticular subtype [18]. The knee being the most affected joint as seen in our study and other studies is may be due to that, the knee is a weight bearing joint. The second most affected joint was the wrist joint, we came and other investigators to a conclusion that the wrist joint is one of the first joints to be affected by such condition due to the fact that, the wrist joint is one of the most used joint in the activity of daily living.

Juvenile Idiopathic Arthritis (JIA) can affect a child's performance across a range of activities necessary to normal childhood development, in addition that, pain is the major descriptor and one of the valid indicator of clinical state which is used in the assessment and management of children with JIA during routine follow-up. Based on the previous facts we aimed at our study to, compare

Table 5: Correlation between clinical and Ultrasonographic findings.

		Pain	Clinical Effusion	US effusion	Synovial Thickness	Articular Erosion	Joint Space
Pain	R			0.546*	0.586	0.223	0.287
	P			0.002**	0.586	0.255	0.131
Clinical Effusion	R			0.786**	0.855**	0.615**	0.393*
	P			0.000	0.000	0.000	0.035
Joint Stiffness	R			0.410*	0.469*	0.314	0.316
	P			0.027	0.016	0.104	0.101
US Effusion	R	0.546**	0.786**		0.875**	0.485**	0.251
	P	0.002	0.000		0.000	0.008	0.190
Synovial Thickness	R	0.586**	0.855**	0.875**		0.597**	0.432*
	P	0.002	0.000	0.000		0.001	0.028
Articular Erosion	R	0.223	0.615**	0.485**	0.597**		0.637**
	P	0.255	0.000	0.008	0.001		0.000
Joint Space	R	0.287	0.393*	0.251	0.432*	0.637**	
	P	0.131	0.035	0.190	0.028	0.000	

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Table 6: Correlation between clinical effusion and stiffness in knees, wrists and ankles according to US effusion, US thickness, articular erosion and joint space narrowing.

			US effusion	US thickness	Articular erosion	Joint space narrowing
Knee	Clinical effusion	Rho	0.435*	0.591*	0.594*	0.206
		P	0.016	0.001	0.001	0.274
	Stiffness	Rho	0.532*	0.770*	0.650*	0.288
		P	0.002	<0.001	<0.001	0.123
Wrists	Clinical effusion	Rho	0.427*	0.553*	0.305	0.362*
		P	0.019	0.002	0.101	0.049
	Stiffness	Rho	0.491*	0.814*	0.390*	0.374*
		P	0.006	<0.001	0.033	0.042
Ankles	Clinical effusion	Rho	0.371*	0.179	0.144	0.15
		P	0.044	0.345	0.446	0.43
	Stiffness	Rho	0.597*	0.423*	0.277	0.183
		P	<0.001	0.02	0.138	0.333

Rho (ρ): Spearman coefficient
*: Statistically significant

and validate for such measures. There was a statistically significant correlation between global assessment of disease activity measured by the Visual Analogue Scale (VAS) and functional activity measured by the Child Health Assessment Questionnaire (CHAQ). This is in agreement with a study of Tannant A et al. [19]. Where there was a strong statistical significant correlation between disease activity and function. Oen k et al. performed a cohort study to determine the disease activity and outcome using CHAQ and VAS in JIA [20]. They found strong statistical correlation between the disease activity using the CHAQ and the pain severity using the VAS. This proves that the CHAQ appears to be the current 'best buy' for measuring function in children with arthritis. These findings show that increased functional disability correlates with increase daily pain.

In this study, there was a highly statistically significant correlation between clinical and US effusion. There was no case in which a clinically assessed effusion was not demonstrated by ultrasound. Our findings are in accordance with the study conducted by Kakati P et al. That showed positive statistical significant correlation between clinical and ultrasound effusion [15]. Also, these findings are in agreement with findings of Karmayzn B et al. in a study examining children with JIA both clinically and sonographically, and there was a statistically significant correlation between Ultrasonography and physical examination score with a p value $p < 0.001$ [21].

Synovial thickening appears as irregular echoes projecting into the joint effusion. In this study, there was a highly statistical significant correlation between clinical effusion and synovial thickening with a p value 0.000. In the previously discussed study by Kakati P, they also, detected synovial thickening in 29 joints by ultrasound, also, articular cartilage erosions were detected in 15 joints. They concluded from this study that ultrasound is a feasible tool for examining multiple joints in identifying subclinical synovitis [15]. Also Shahin A et al. detected significant correlation between clinical and sonographic effusion as well as synovial thickening of the knees in JIA. They concluded from this study that sonography is a non-invasive, low-cost, and readily available tool for the evaluation of articular involvement in knees of JIA patients [22]. Roony ME et al. found sonographic effusion in 29% of swollen ankles [23].

In this study, articular cartilage erosion showed statistically significant correlation with clinical effusion of a p value 0.000. This finding match with, Karmazyn B et al. where there was a statistical significant correlation between physical examination and sonographic evaluation $p < 0.005$. In addition, Karmazyn B et al. found in addition to the previously mentioned synovial effusion, cartilage destruction in 25 joints out of the studied 64 [21]. Joint space narrowing on US examination was detected in only 6 joints, in this study. There was statistically significant correlation between clinical effusion and joint space narrowing with a p value 0.035.

Ravilli A et al. [24] stated that US variables were moderately correlated with clinical measures of joint swelling but poorly correlated with those of joint tenderness and restricted motion. Which disagrees with our findings concerning the correlation between joint stiffness on examination and ultrasound findings, as we detected in our results there was a statistical significant correlation between joint stiffness and ultrasound effusion, synovial thickening. Ravillia A et al., concluded at the end of the study that, subclinical synovitis as detected by US is common in children with JIA. They also added that, these findings may have important implications for patient classification and may affect the choice of optimal therapeutic strategy in individual patients [24].

The interpretation of our results in comparison to other studies suggests that, ultrasound is very useful in detecting the changes in JIA such as synovial effusion, thickening, articular cartilage surface erosions, and joint space narrowing.

Conclusion

Musculoskeletal Ultrasonography was more accurate than clinical examination in detection of early joint changes in JIA patients. It allows the visualization of subtle effusion and early cartilage changes. Musculoskeletal US are a rapid, safe, accurate and reproducible method for evaluating and monitoring joint changes in JIA. Increased levels of IgA and IgM are good predictors for disease activity.

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