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## Original article

# Association between the ultrasonographic and clinical findings in the hips of patients with juvenile idiopathic arthritis

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## ABSTRACT

**Objective:** To describe the ultrasonographic (US) findings in the hips of patients with juvenile idiopathic arthritis (JIA) and the association between these findings and the signs, symptoms, and activity of the disease.

**Materials and methods:** The present retrospective study included 92 patients with JIA. The disease subtypes, age at disease onset, length of disease progression, disease activity, and clinical manifestations of the hip pathology were assessed. US examinations were routinely performed, and the images were analysed by two ultrasonographers who were blinded to the patients' clinical conditions.

**Results:** Of the 92 patients included in the study, 69.6% were girls, and the average age was  $12.4 \pm 5.1$  years. Thirty-three (35.9%) participants exhibited the persistent oligoarticular subtype, and 30 (32.6%) exhibited the rheumatoid factor (RF)-negative polyarticular subtype. Forty-four participants exhibited signs and/or symptoms of hip pathology. Twenty-nine (31.5%) participants exhibited abnormal US findings, and 34.4% exhibited subclinical synovitis. The US alterations exhibited an association with subclinical synovitis in 34.4% of the cases. The US alterations bore a correlation with the presence of hip-related signs and/or symptoms ( $P = 0.021$ ), particularly joint limitations ( $P = 0.006$ ), but were not correlated with the disease activity ( $P = 0.948$ ) or subtype ( $P = 0.108$ ). Clinical synovitis was associated with polyarticular involvement ( $P = 0.002$ ) and disease activity ( $P = 0.017$ ). Subclinical synovitis was not correlated with the investigated variables.

**Conclusion:** Clinical affection of the hip in JIA, particularly joint limitation, is associated with synovitis (revealed by US assessment) independently of the activity and subtype of the disease. Therefore, healthcare professionals should consider the possible occurrence of silent disease and subclinical synovitis, which might contribute to hip deterioration.

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## Associação entre achados ultrassonográficos e clínicos do quadril de pacientes com artrite idiopática juvenil

### R E S U M O

#### Palavras-chave:

Ultrassonografia

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Artrite idiopática juvenil

Sinovite subclínica

**Objetivo:** Descrever os achados ultrassonográficos do quadril em pacientes com artrite idiopática juvenil (AIJ) e sua associação com sinais, sintomas e atividade da doença.

**Materiais e métodos:** Estudo retrospectivo com 92 pacientes com AIJ. Foram avaliados os subtipos da doença, a idade de início, o tempo de evolução, a atividade da doença e as manifestações clínicas do envolvimento do quadril. A avaliação ultrassonográfica foi realizada na rotina dos pacientes, e as imagens foram analisadas por dois ultrassonografistas cegos em relação às condições clínicas dos pacientes.

**Resultados:** Do total de 92 pacientes, 69,6% eram meninas, com média de idade de  $12,4 \pm 5,1$  anos. Trinta e três (35,9%) apresentaram subtipo oligoarticular persistente e trinta (32,6%) poliarticular com fator reumatoide negativo. Quarenta e quatro (47,8%) apresentaram sinal e/ou sintoma relacionado ao quadril. Vinte e nove (31,5%) apresentaram alterações ultrassonográficas, com sinovite subclínica em 34,4%. As alterações ultrassonográficas se associaram com presença de sinais e/ou sintomas do quadril ( $P = 0,021$ ), especialmente limitação articular ( $P = 0,006$ ), mas não com atividade ( $P = 0,948$ ) ou subtipo de doença ( $P = 0,108$ ). Sinovite clínica se associou com comprometimento poliarticular ( $P = 0,002$ ) e atividade de doença ( $P = 0,017$ ). Não houve associação entre sinovite subclínica e as variáveis estudadas.

**Conclusão:** O acometimento clínico do quadril na AIJ, especialmente a limitação articular, está associado à sinovite na avaliação por US, independente do subtipo e da atividade da doença. Os profissionais de saúde devem estar atentos à possibilidade de doença silenciosa com sinovite subclínica, que pode contribuir para a deterioração da articulação do quadril.

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## Introduction

Juvenile idiopathic arthritis (JIA) is a chronic rheumatic disease most common in childhood. JIA is defined by the presence of arthritis for 6 or more weeks in children and adolescents up to 16 years of age and is a diagnosis of exclusion.<sup>1</sup> JIA exhibits a wide clinical scope currently classified by the International League of Association for Rheumatology (ILAR) under seven subtypes as a function of the patient's characteristics at the disease onset, with the latter progression occurring 6 months thereafter.<sup>1</sup>

The hips are affected in 30-50% of JIA cases, and this pathology is more common among young patients who are within the first 10 years since the disease onset, who have the polyarticular and systemic subtypes, or who exhibit persistent active disease.<sup>2-4</sup> The presence of hip arthritis is a factor of poor prognosis due to the relevance of this joint for gait and body-weight support, whereby this condition might lead to functional disability.<sup>3,5,6</sup> Consequently, hip involvement indicates a requirement for more aggressive treatments using disease-modifying anti-rheumatic drugs and biological agents.<sup>4,7</sup>

The clinical identification of hip-joint effusions is difficult without the use of diagnostic imaging methods due to the deep localisation and the difficulties of palpation.<sup>2,5</sup> Symptoms such as pain, radiating pain, claudication, and limitation may be associated with hip affection; nonetheless, many patients are asymptomatic.<sup>3,5</sup>

Hip ultrasonography (US) is useful for detecting joint effusions and synovitis and enables clinicians to identify changes

earlier and with greater sensitivity compared with radiography. In addition, hip US is a non-invasive, rapid, and low-cost method; however, it is both examiner-dependent and device-dependent.<sup>2,5,8-10</sup> Friedman and Gruber employed US to demonstrate a significant increase in the articular space in patients with seronegative juvenile rheumatoid arthritis compared with healthy controls ( $0.6 \times 0.43$  cm.  $P < 0.001$ ).<sup>2</sup> US also detects subclinical synovitis, which is defined as the presence of joint effusions or synovial thickening in asymptomatic patients who have been rated as normal upon clinical examination.<sup>8,10,11</sup>

The aim of the present study was to describe US findings in the hips of patients with JIA, and the association between these findings and the signs, symptoms, and activity of the disease.

## Patients and methods

The present investigation was a retrospective study that included 92 individuals who met the ILAR<sup>1</sup> diagnostic criteria for JIA, who were within a minimum of 6 months after the disease onset, and who were treated at the paediatric-rheumatology outpatient clinic.

The demographic and clinical data of the participants were collected from their clinical records and included the JIA subtype, the age at onset, and the elapsed time since the disease onset. Regarding the clinical manifestations of hip affection, the following parameters were considered: pain, radiating pain, movement limitation, and claudication. The disease activity was assessed according to the criteria formulated by Wallace et al.<sup>12</sup>

The assessment included US examinations of the patients at the institutional radiology unit from 2008 to 2010. US was part of the participants' annual follow-up routine, independently from the presence of symptoms, and was performed when the physical examinations yielded doubtful results. US was performed using the Siemens Sonoline Antares and Philips Envisor devices, with a linear transducer at 8-12 MHz of frequency placed parallel to the femoral neck (longitudinal plane). The images were stored immediately after their acquisition, and those with a quality satisfactory for assessment were analysed jointly by two radiologists who were experienced in musculoskeletal US and blinded as to the participants' clinical conditions.

Joint effusion and synovitis were defined as the presence of joint effusions and/or synovial hypertrophy and were classified according to the modified criteria of Szkudlarek et al.<sup>13</sup> In addition, the anterior hip recess (AHR) was measured based on the distance between the femoral neck and the joint capsule<sup>3</sup> (Fig. 1).

Grade 0 (normal): the synovial capsule follows the femoral cortical bone curvature.

Grade 1 (mild): the synovial capsule does not follow the femoral cortical bone curvature, but is concave or straight.

Grade 2 (moderate/severe): bulging synovial capsule, i.e., its curvature is inverted relative to the femoral cortical bone curvature.

Abnormal US findings were rated as Grade 2. The cases with abnormal US findings but lacking clinical signs and/or symptoms were classified as subclinical synovitis, whereas the cases with abnormal US findings and the presence of clinical signs and/or symptoms were classified as clinical synovitis.

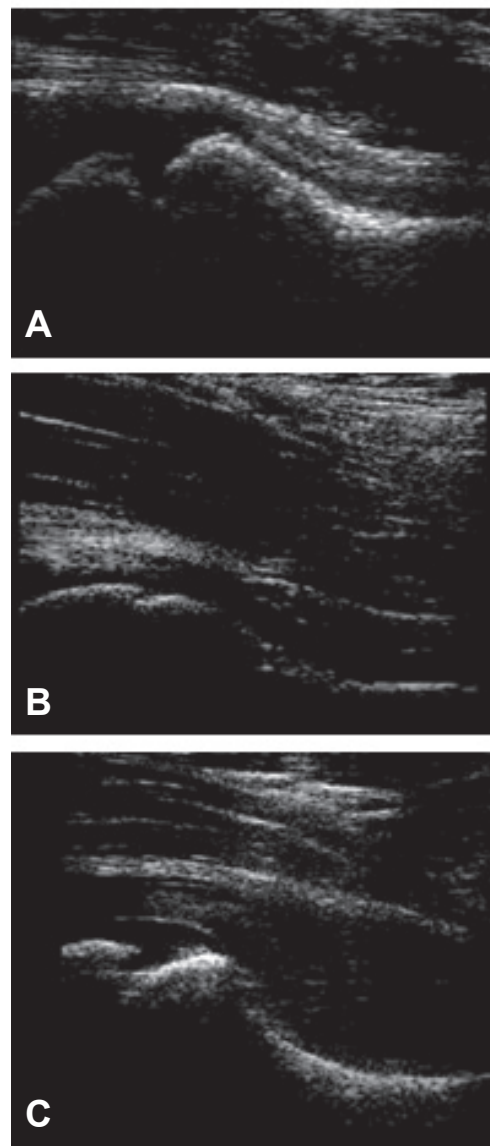
The present study was approved by the institutional research ethics committee. The descriptive analysis of the study population was expressed as absolute and relative frequencies and as means and standard deviations according to the distribution of each variable. To assess the correlation between the clinical data and the US alterations, Fisher's exact test and Pearson's chi-square test were applied to the categorical variables, Student's t-test was applied to the parametric continuous variables, and the Mann-Whitney test was applied to the non-parametric continuous variables. The significance level was established as a P value < 0.05.

## Results

Of the 92 participants in the sample, 69.6% were girls, and the average age at assessment was  $12.4 \pm 5.1$  years. Thirty-three (35.9%) participants exhibited the persistent oligoarticular subtype of JIA, and 30 (32.6%) presented the negative-rheumatoid factor (RF) polyarticular subtype. The demographic and clinical data of the sample are described in Table 1.

Forty-four (47.8%) participants displayed signs and/or symptoms of hip affection, of whom 38 (86.4%) exhibited joint limitation, 13 (29.5%) exhibited pain, six exhibited (13.6%) radiating pain, and six (13.6%) exhibited claudication.

Upon US assessment, 15 (16.3%) participants were classified as Grade 0, 48 (52.2%) were classified as Grade 1, and 29 (31.5%) were classified as Grade 2. Of the 29 participants with



**Fig. 1 – AHR grading. (a) Grade 0 (normal): the synovial capsule follows the femoral cortical bone curvature; (b) Grade 1 (mild): the synovial capsule does not follow the femoral cortical bone curvature, but is concave or straight; (c) Grade 2 (moderate/severe): bulging synovial capsule, i.e., its curvature is inverted relative to the femoral cortical bone curvature.**

abnormal US findings (Grade 2), 10 (34.5%) had subclinical synovitis, and 19 (65.5%) had clinical synovitis.

In total, 184 (right and left) AHRs were assessed. The AHR could be measured in 137 recesses, being  $5.9 \pm 2.5$  mm on average. Of these 137 cases, 98 AHRs measured  $\leq 6$  mm, and 39 AHRs measured  $> 6$  mm. The difference between the right and left recesses was 2 mm or greater in 18 assessed recesses.

The US alterations were associated with the presence of signs and/or symptoms ( $P = 0.021$ ) of hip affection, particularly joint limitation ( $P = 0.006$ ), but not with the activity ( $P = 0.948$ ) or subtype ( $P = 0.108$ ) of the disease. The US alterations did not exhibit differences relative to the age at disease onset ( $P = 0.072$ ) or the duration of disease progression ( $P = 0.260$ ) (Table 2).

**Table 1 – Demographic and clinical data of the juvenile idiopathic arthritis patients (n = 92).**

Mean current age (in years) ± SD	12,4 ± 5,1
Mean age at onset (in years) ± SD	6,2 ± 3,8
Mean length of the disease progression (in years) ± SD	6,2 ± 4,1
Female, n (%)	64 (69,6)
JIA subtypes, n (%)	
Persistent oligoarticular	33 (35,9)
Extended oligoarticular	7 (7,6)
RF-positive polyarticular	7 (7,6)
RF-negative polyarticular	30 (32,6)
Systemic	6 (6,5)
Enthesitis-related arthritis	9 (9,8)
Disease activity, n (%)	
Active	49 (53,3)
Inactive with medication	32 (34,8)
Inactive without medication	11 (12)

JIA, juvenile idiopathic arthritis; SD, standard deviation; RF, rheumatoid factor.

For the participants with abnormal US findings, we found an association between clinical synovitis and polyarticular involvement (which included RF-positive and RF-negative polyarticular involvement and the extended oligoarticular subtypes) ( $P = 0.002$ ), as well as active disease ( $P = 0.017$ ) (Table 3).

**Table 2 – Abnormal ultrasonography hip findings and clinical data of the juvenile idiopathic arthritis patients (n = 92).**

	Alterations on the hip US (n = 29)	No alterations on the hip US (n = 63)	P
Mean age at onset (yrs.) ± SD	7.3 ± 4.3	5.7 ± 3.5	0.072 <sup>a</sup>
Mean length of the disease progression (yrs.) ± SD	7 ± 4	5.9 ± 4.1	0.260 <sup>a</sup>
JIA subtype			0.108 <sup>b</sup>
Persistent oligoarticular	6	27	
RF-negative or positive polyarticular/extended oligoarticular	16	28	
Enthesitis-related arthritis	5	4	
Systemic	2	4	
Disease activity			0.948 <sup>b</sup>
Active	15	34	
Inactive with medication	11	21	
Inactive without medication	3	8	
Hip-related clinical signs and/or symptoms	19	25	0.021 <sup>c</sup>
Pain	7	6	0.103 <sup>b</sup>
Radiating pain	2	4	1 <sup>b</sup>
Claudication	3	3	0.375 <sup>b</sup>
Limitation	18	20	0.006 <sup>c</sup>

US, ultrasonography; JIA, juvenile idiopathic arthritis; SD, standard deviation; RF, rheumatoid factor.

<sup>a</sup>Student's t test.

<sup>b</sup>Fisher's exact test.

<sup>c</sup>Pearson's chi-square test.

## Discussion

The hip is frequently affected in JIA and deserves special attention because it plays a crucial role in the disease prognosis and may indicate a requirement for more aggressive treatments. Almost one-half of the participants exhibited clinical manifestations of hip affection, and joint limitation was the most frequent sign and/or symptom found. One-third of the participants did not exhibit any clinical manifestations, but US disclosed the presence of synovitis, which was thus classified as subclinical.

According to the literature, the hip is affected in 20-50% of JIA cases.<sup>4,7,14,15</sup> Batthish et al. found hip involvement in 51% of the cases after 24 months of follow-up.<sup>14</sup> Rostom et al. found bilateral, clinical hip affection in 85% of the cases, which was more frequent in the polyarticular subtypes and in enthesitis-related arthritis.<sup>4</sup> In our study, 47.8% of the participants exhibited clinical hip involvement, which confirms the reports in the literature (38-63%).<sup>3</sup> We further found that 41.3% of the hip-affection cases were bilateral, which also agrees with the literature (25-85%).<sup>2,4</sup> We found that hip pathology was more frequent in the polyarticular and extended oligoarticular JIA subtypes. Although the hip is more frequently affected in cases where the disease starts at an early age and in patients with longer disease duration, this phenomenon did not occur in our case series.<sup>3</sup>

Joint limitation was the most frequent clinical manifestation in the present study. Hip arthritis causes a progressive reduction of the articular space, with consequent joint limitation, and eventually causes complete ankylosis in certain cas-

**Table 3 – Characteristics of the juvenile idiopathic arthritis patients relative to the subclinical and clinical synovitis detected on hip ultrasonography (n = 29).**

	Subclinical synovitis (n = 10)	Clinical synovitis (n = 19)	P
Average age at onset (yrs.) ± SD	6.9 ± 4.7	7.5 ± 4.2	0.701 <sup>a</sup>
Mean length of disease progression (yrs.) ± SD	6 ± 3.6	7.4 ± 4.2	0.403 <sup>a</sup>
JIA subtype			0.003 <sup>b</sup>
Persistent oligoarticular	5	1	
RF-negative or positive polyarticular/extended oligoarticular	2	14	
Enthesitis-related arthritis	3	2	
Systemic	0	2	
Disease activity			0.018 <sup>b</sup>
Active	2	13	
Inactive with medication	7	4	
Inactive without medication	1	2	

JIA, juvenile idiopathic arthritis; SD, standard deviation; RF, rheumatoid factor.

<sup>a</sup>Mann-Whitney test.

<sup>b</sup>Fisher's exact test.



es. Whereas a physical examination might easily detect joint limitation, this clinical assessment is unable to establish the presence of joint effusions due to the deep localisation of the hip, which hinders their detection. Moreover, radiographs are not useful in these cases because the radiological alterations, including erosions and articular space reductions, appear late in the disease progression, and the images do not supply satisfactory information about the presence of joint effusions and synovitis.<sup>3</sup> US allows for overcoming these problems, and thus it is routinely included in the patients' annual assessment in our service. US is easy to perform, its cost is low, and it allows for detecting hip alterations before damage occurs. It is well-established that serial US supplements the clinical assessment of the disease activity and the response to treatment, especially in patients with hip involvement.<sup>7,16</sup>

In our study, the abnormal US findings were associated with the presence of signs and/or symptoms of hip affection, particularly with joint limitation. Approximately 31.5% of the participants did not exhibit any clinical manifestations, but US disclosed the presence of synovitis, which was thus classified as subclinical. The frequency of subclinical synovitis reported in the literature is 19.8%;<sup>3</sup> however, certain studies assessed only the knees, ankles, wrists, and small joints.<sup>11,17,18</sup> The concordance between the results from clinical examinations and US studies might be lower as a function of the joints selected for assessment. For instance, the small joints of the hands and feet have been associated with a greater discrepancy.<sup>17</sup>

Clinical synovitis was associated with the polyarticular subtypes and the active disease, whereas subclinical synovitis bore no correlation with the disease activity. Furthermore, Frosch et al. found a correlation between subclinical synovitis and the disease activity.<sup>8</sup> These findings suggest that patients with polyarticular subtypes and signs and/or symptoms of hip involvement should be carefully assessed because the presence of clinical manifestations is associated with US alterations rather than with the disease sequelae only. In addition, subclinical synovitis might occur in cases with either active or inactive disease, which justifies the performance of periodic hip assessments via imaging methods in all patients, independent of the JIA-activity status.

A failure to detect synovitis by US in JIA patients might result in delayed diagnosis and treatment or in the undertreatment of cases with low levels of disease activity. Subclinical synovitis might be responsible for the structural deterioration exhibited by JIA patients who are considered to be in clinical and laboratory remission, which is a well-established fact in rheumatoid arthritis.<sup>11,19,20</sup> Subclinical synovitis might also interfere with the classification of JIA patients, whereby individuals with polyarticular subtypes (which require more aggressive treatments) are misdiagnosed as oligoarticular cases.<sup>11,17</sup>

The measurement of AHR is a relevant part of the US assessment. According to the literature, the normal AHR value is less than 6 mm.<sup>3,8</sup> In our study, the global average AHR value was 5.9 mm  $\pm$  2.5 mm, while 29% of the measurements were greater than 6 mm. Friedman and Gruber reported a positive correlation between the measurement of the anechoic space and hip-movement limitations.<sup>2</sup> Fedrizzi et al. assessed 53 JIA patients and 10 controls and found that almost 50% of the patients exhibited hip alterations characterised by joint capsule

distension (convex shape), increased echogenicity, and AHRs greater than 6 mm.<sup>3</sup>

Our investigation had certain limitations. First, it was a retrospective study based on the analysis of clinical records, whereas the inter- and intra-examiner concordance between the radiologists was not tested. In addition, power Doppler (PD) US, which assesses the synovial blood flow, was not performed. Recent studies have demonstrated that a positive flow determined by PD might be associated with activity and progression of the joint disease in patients with rheumatoid arthritis and JIA, although the classification scores have not yet been validated.<sup>19-23</sup>

Finally, it is noteworthy that hip affection in JIA causes psychosocial problems, and the physical limitations and chronic pain affect the patients' quality of life.<sup>24</sup> Therefore, healthcare professionals should consider the possible occurrence of silent disease and subclinical synovitis, which might contribute to hip deterioration.

Prospective studies with a larger number of participants, in addition to the use of PD US and magnetic resonance imaging might enable greater precision in the prognosis of patients with hip involvement.

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