


## ORIGINAL ARTICLES

# Factors associated with hip involvement in spondyloarthritis: a retrospective study

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## ABSTRACT

**Background:** Hip involvement is a life-changing event during spondyloarthritis (SpA) since it's responsible for significant disability and functional impairment. This study aimed to determine the factors associated with hip involvement in patients with SpA.

**Methods:** This was a retrospective study, including patients with axial and/or peripheral SpA divided into two groups: patients without and with hip involvement. Hip involvement was defined as pain or abnormality on clinical examination of the hip and/or on imaging. We collected clinical and laboratory data, activity and functional scores, and radiographic parameters. We conducted a multivariate analysis to identify the associated factors of hip involvement.

**Results:** We included 165 patients with a mean age of  $46.13 \pm 13.07$  years, 121 patients were male. The mean duration of disease was  $10.91 \pm 6.94$  years. Hip involvement, defined as SpA-related hip pain, joint limitation, and dysfunction and/or imaging involvement (X-ray/MRI), was noted in 60 cases (36.4%). Multivariate analysis indicated that disease duration over 10 years (OR=3.8, 95% confidence interval (CI95%)[1.3-11.2],  $p=0.013$ ), radiographic sacroiliitis (OR=8.9, CI95%[1.3-63.5],  $p=0.028$ ), very high disease activity (Ankylosing Spondylitis Disease Activity Score: ASDASCRP $\geq 3.5$ ) (OR=9.4, CI95%[2.6-34.4],  $p=0.001$ ), higher Bath Ankylosing Spondylitis Functional Index (BASFI) (OR=1.4, CI95%[1.1-1.9],  $p=0.004$ ) and higher Bath Ankylosing Spondylitis Metrology Index (BASMI) (OR=1.3, CI95%[1.1-1.6],  $p=0.011$ ) were independently associated with hip involvement in these patients. Regarding extra-articular features, we found that pulmonary involvement and osteoporosis were significantly more frequent in patients with hip involvement, but neither retained significance in multivariate analysis.

**Conclusion:** Disease duration over 10 years, radiographic sacroiliitis, very high disease activity, functional impairment, and limited spine mobility were potential associated factors with hip involvement. Patients with these factors should be closely monitored to detect hip involvement at an early stage.

Keywords: Hip involvement; Spondyloarthritis; Risk factors; Quality of life; Disability.

## INTRODUCTION

Spondyloarthritis (SpA) is a chronic, progressive, and disabling inflammatory disease in young adults. It mainly affects the spine, sacroiliac, and peripheral joints<sup>1</sup>.

Hip involvement is frequent in SpA, occurring in around 20-40%<sup>2</sup>. It varies between different countries, re-

flecting a high impact of ethnicity. Up to 25% of SpA patients have hip damage after 20 years of disease duration<sup>3</sup>.

Hip involvement is predictive of a severe form of SpA with a sensitivity of 50%<sup>4</sup>. It can be responsible for pain, limited range of motion, and joint dysfunction due to inflammatory signs and structural damage. Its diagnosis is based on clinical examination and imaging findings<sup>5</sup>.

The Bath Ankylosing Spondylitis Radiology Index (BASRI-Hip) assesses the severity and progression of hip damage in SpA. Radiographic hip involvement is defined as a BASRI-Hip greater than one<sup>6</sup>.

Magnetic resonance imaging and ultrasonography can be helpful in the diagnosis of hip involvement in patients with hip pain without radiographic abnormalities (BASRI-Hip $\leq 1$ ). The diagnosis of hip involvement should be made earlier since advanced stages are responsible for disability and functional impairment<sup>7</sup>.

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Data regarding factors associated with hip involvement are scarce. Awareness of these factors is necessary to identify SpA patients with a high risk of hip involvement to ensure closer monitoring of these patients to make an early diagnosis<sup>8</sup>. Modification of these factors can prevent hip damage. Only a few data concerning this subject are available.

This study aims to determine the associated factors of hip involvement in patients with SpA.

## PATIENTS AND METHODS

### Study design

We conducted a retrospective study, including patients with axial and/or peripheral SpA, followed in the rheumatology outpatient department in the military hospital, between August 2017 and June 2021.

### Patients

We included patients who fulfilled the Assessment of Spondyloarthritis International Society classification criteria for axial and peripheral SpA<sup>9,10</sup>. We divided the patients into two groups:

- G0: SpA patients without hip involvement
- G1: SpA patients with hip involvement

Non-inclusion criteria were history of hip dysplasia, primary osteoarthritis, or avascular necrosis. We also excluded patients who reported symptoms of hip pain without imaging confirmation of hip involvement.

Demographic and clinical data including age, gender, ethnicity, age at onset, diagnostic delay, and disease duration were collected. Body mass index was calculated based on the formula weight/height<sup>2</sup>.<sup>11</sup> Therapeutic management was assessed.

We also reported extra-articular manifestations including psoriasis, inflammatory bowel disease, pulmonary involvement, and osteoporosis. Pulmonary involvement related to SpA was diagnosed based on chest radiographs and confirmed by chest computed tomography (CT) scan in patients with respiratory symptoms, decreased chest expansion, or abnormalities on plain chest radiographs, after excluding other causes of pulmonary diseases (infections, autoimmune disorders, etc.).

Osteoporosis was assessed by measuring bone mineral density by dual-energy X-ray absorptiometry and was defined as a T-score  $\leq -2.5$  standard deviation<sup>12</sup>.

### Spondyloarthritis evaluation

Clinical and radiological assessments were performed independently by two board-certified trained rheumatologists.

For G1, we also collected these data from the medical records of these patients at the timepoint of diagnosis of hip involvement.

### SpA clinical assessment

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)<sup>13</sup> and Ankylosing Spondylitis Disease Activity Score using C-reactive protein (CRP) (ASDASCRP)<sup>14</sup> were used to assess disease activity.

BASDAI score higher than 4 refers to active disease. Using the ASDASCRP, we defined four states: inactive disease ( $<1.3$ ), moderate disease activity [ $1.3; 2.1[$ , high disease activity [ $2.1; 3.5[$  and very high disease activity ( $>3.5$ ).

Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI) were used to assess the functional impact of spondyloarthritis and the spine mobility, respectively<sup>15</sup>.

### Radiological assessment

The radiographic spine damage was assessed using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS)<sup>16</sup> and the BASRI-Spine (BASRI-S)<sup>17</sup>. These scores were evaluated from the radiographs performed in the past follow-up year.

For G1, we also evaluated these scores using radiographs performed at the diagnosis of hip involvement.

The BASRI-S was calculated by adding the average score for the sacroiliac joints to the scores for the lumbar (BASRI-L) and cervical spine (BASRI-C).

The total BASRI score (BASRI-T) included the BASRI-Hip (range 0-4) and BASRI-S (range 2-12).

The mSASSS score varies from 0 to 72. The sacroiliac joints were scored according to the modified New York criteria<sup>18</sup>. The final score corresponded to the sum of each side of the sacroiliitis grade.

### Biological assessment

We retrieved erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) results for all patients at the time of the study, and those corresponding to the time of diagnosis of hip involvement for patients with hip involvement.

We also obtained from the medical records, the result of the HLA-B27 typing.

### Hip involvement

Radiographic hip involvement was defined as a score higher than one using BASRI-Hip<sup>6</sup>.

The diagnosis of non-radiographic hip involvement was made based MRI abnormalities in patients with pain and restricted hip mobility with discreet or absent radiographic involvement (BASRI-Hip  $\leq 1$ ).

We specified the delay between hip involvement and the onset of SpA, the presence of pain, and the estimation of this pain by the visual analogue scale (VAS).

### Statistical analysis

We performed statistical analysis using the Statistical

Package for Social Sciences, version 26.

We calculated frequencies for qualitative variables and means  $\pm$  standard deviation for quantitative variables.

We compared means of independent series using the independent samples Student T test for normally distributed variables.

The Chi-square test was performed to assess the association between two categorical variables.

The prevalence ratio (PR) was used to quantify the link between categorical independent variables and hip involvement<sup>19</sup>.

We performed a stepwise backward binary logistic regression to identify risk factors independently associated with hip involvement.

For this study, we included parameters that were associated ( $p < 0.05$ ) within the univariate analysis and those having a  $p < 0.20$ .

All statistical tests were two-sided, and the level of statistical significance was set up at ( $p < 0.05$ ).

## RESULTS

### Patient characteristics

We included 165 patients in the study. All of them were Tunisians. There were 121 men (73.3%) with a male to a female sex ratio of 2.7.

Hip involvement was noted in 60 patients (36.4%). It was bilateral in 45 patients (75%). The number of the involved hip was 105. It occurred during the disease course in 45 cases with an average delay of  $47.84 \pm 60$  months. For the 15 other cases, it was simultaneously diagnosed with SpA.

The diagnosis of hip involvement was made in 8 asymptomatic patients (number of affected hips=11, (10.48%)). Eight symptomatic patients (11 hips) had non-radiographic hip involvement.

NSAIDs, methotrexate (MTX), and sulfasalazine (SLZ) were prescribed in 145 (87.9%), 44 (26.7%), and 53 (32.1%) of patients respectively. Piroxicam was the most prescribed first line NSAID. Among these patients, 60 took NSAIDs continuously. A rotation of 3 classes of NSAIDs was noted in 11 patients. An association of SLZ with MTX was noted in 15 cases.

Tumor Necrosis Factor inhibitors (TNFi) were prescribed in 53 patients (32.1%) for an average duration of  $66.40 \pm 47.90$  months [3 - 168]. Switches between the different TNFi were noted in 18 cases.

## DISEASE ASSESSMENT

### Clinical evaluation

As shown in Table I, 54.4% of patients ( $n=89$ ) had an active disease according to BASDAI. Using the ASDAS-

CRP, 5.9% ( $n=10$ ) of patients had an inactive disease, 17.8% ( $n=29$ ) had moderate activity, 41.6% ( $n=69$ ) high activity, and 34.7% ( $n=57$ ) had very high disease activity. The mean BASFI and BASMI scores were  $4.7 \pm 2.4$  and  $2.42 \pm 2.34$  respectively.

For G1, restricted range of motion on examination of hips was noted in all cases. The mean value of the VAS at the time of diagnosis of hip disease was  $3.46 \pm 3.70$ .

### Radiological assessment

Radiographic sacroiliitis was noted in 77.6% ( $n=128$ ) of patients. It was bilateral in 90.6% of cases ( $n=116$ ). Among the 231 sacroiliac joints fulfilling the mNew-York criteria, 29.9% ( $n=69$ ) had grade 4 and 42.4% ( $n=98$ ) grade 3. The mean mSASSS was  $10.51 \pm 15.51$ . The mean BASRI-C, BASRI-L, BASRI-S and BASRI-T were  $1.92 \pm 1.62$ ,  $1.71 \pm 1.43$ ,  $4.13 \pm 3.05$  and  $4.5 \pm 3.94$  respectively at the time of the study.

For G1, the mean BASRI-Hip at the time of diagnosis of hip disease was  $2.59 \pm 1.02$ .

MRI of the hips was performed in 8 symptomatic patients with  $BASRI \leq 1$  (11 hips) and revealed synovitis, joint space narrowing, and periarticular bone edema in all cases and intra-articular effusion in a single affected hip.

### Biological assessment

The mean ESR and CRP values of all patients at the time of the study were  $37.49 \pm 28.1$  mm and  $30.14 \pm 43.55$  mg/L, respectively. High inflammatory biomarkers were noted in 86.1% of cases ( $n=142$ ).

HLA typing was performed in 62 patients. The HLA-B27 allele was present in 40 (64.5%) cases.

### Factors associated with hip involvement

As shown in Table II, we found an association between hip involvement and these parameters: age  $\geq 40$  years ( $p=0.030$ , PR=1.7,  $CI_{95\%}$  [1.0-2.6]), symptoms duration  $\geq 10$  years ( $p=0.015$ , PR=1.7,  $CI_{95\%}$  [1.1-2.5]), very high disease activity ( $p=0.041$ , PR=1.7,  $CI_{95\%}$  [1.0-2.6]), and radiographic sacroiliitis ( $p=0.023$ , PR=2.8,  $CI_{95\%}$  [0.9-8.1]).

Patients in G1 had more functional impairment (BASFI:  $5.48 \pm 2.06$  vs  $4.12 \pm 2.49$ ,  $p=0.002$ ) and more limited spine mobility (BASMI:  $3.71 \pm 2.46$  vs  $1.65 \pm 1.90$ ,  $p < 0.001$ ).

Pulmonary involvement and osteoporosis were also significantly more frequent in these patients, respectively ( $p=0.023$ , PR=1.7,  $CI_{95\%}$  [1.1-2.6]) and ( $p=0.034$ , PR=1.7,  $CI_{95\%}$  [1.1-2.7]). Besides, these patients had more structural damage in the spine (mSASSS:  $16.24 \pm 19.28$  vs  $5.80 \pm 9.41$ ,  $p=0.001$ ; BASRI-C or BASRI-L  $\geq 3$ :  $p=0.032$ , PR=2.2,  $CI_{95\%}$  [1.0-3.2]).

Peripheral joint involvement was significantly less

**TABLE I. Patients and disease characteristics at the time of the study**

<b>Age</b> , mean $\pm$ SD years		46.13 $\pm$ 13.07
<b>Age<math>\geq</math>40 years</b> (n (%))		104 (63)
<b>Sex ratio</b> (male/female)		121/44
<b>Smoking</b> (n (%))		74 (46.5)
<b>Body mass index</b> , mean $\pm$ SD kg/m <sup>2</sup>		25.10 $\pm$ 16.67
<b>BMI<math>\geq</math>25 kg/m<sup>2</sup></b> (n (%))		77 (46.7)
<b>Age at diagnosis</b> , mean $\pm$ SD years		38.37 $\pm$ 13.22
<b>Diagnostic delay</b> , mean $\pm$ SD (months)		37,54 $\pm$ 50,51
<b>Symptom duration</b> , mean $\pm$ SD (months)		130.96 $\pm$ 83.26
<b>Symptoms duration<math>\geq</math> 10 years</b> (n (%))		78 (47.3)
<b>HLA-B27</b> (n (%))		40 (64.5)
<b>Radiographic sacroiliitis</b> (n (%))		144 (87.3)
<b>Peripheral joint damage</b> (n (%))		21 (12.7)
<b>Extra-articular involvement</b> (n (%))		113 (68.5)
<b>Uveitis</b> (n (%))		33 (20.0)
<b>IBD</b> (n (%))		16 (9.7)
<b>Psoriasis</b> (n (%))		37 (22.4)
<b>Pulmonary involvement</b> (n (%))		27 (16.4)
<b>Osteoporosis</b> (n (%))		21 (12.7)
<b>Biological parameters</b>	<b>ESR</b> , mean $\pm$ SD mm	37.49 $\pm$ 28.1
	<b>CRP</b> , mean $\pm$ SD mg/dL	30.14 $\pm$ 43.55
<b>Clinical assessment</b>	<b>BASDAI</b> , mean $\pm$ SD	4 $\pm$ 1.8
	<b>ASDAS<sub>CRP</sub></b> , mean $\pm$ SD	3.09 $\pm$ 1.13
	<b>BASFI</b> , mean $\pm$ SD	4.7 $\pm$ 2.4
	<b>BASMI</b> , mean $\pm$ SD	2.42 $\pm$ 2.34
Radiographic assessment	<b>mSASSS</b> , mean $\pm$ SD	10,51 $\pm$ 15,51
	<b>BASRI-T</b> , mean $\pm$ SD	4.50 $\pm$ 3.93
<b>Treatment</b>	<b>NSAIDs</b> (n (%))	145 (87.9)
	<b>Methotrexate</b> (n (%))	44 (26.7)
	<b>Sulfasalazine</b> (n (%))	53 (32.1)
	<b>TNF inhibitor</b> (n (%))	53 (32.1)

SD: standard deviation, BMI: Body mass index, HLA: Human Leukocyte Antigen, IBD: inflammatory bowel disease, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, ASDAS: Ankylosing Spondylitis Disease Activity Score, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, mSASSS: Modified stoke ankylosing spondylitis spinal score, BASRI: Bath Ankylosing Spondylitis Radiology Index, NSAIDs: Non-steroidal anti-inflammatory drugs, TNF: Tumor Necrosis Factor

frequent in the presence of hip involvement ( $p=0.023$ ,  $PR=0.7$ ,  $CI_{95\%}[0.6-0.9]$ ).

In multivariable analysis, we found an association between hip involvement and these variables: disease duration over 10 years ( $OR=3.8$ ,  $CI_{95\%}[1.3-11.2]$ ,  $p=0.013$ ), radiographic sacroiliitis ( $OR=8.9$ ,  $CI_{95\%}[1.3-63.5]$ ,  $p=0.028$ ), very high disease activity ( $ASDAS-$

$CRP\geq 3,5$ ) ( $OR=9.4$ ,  $CI_{95\%}[2.6-34.4]$ ,  $p=0.001$ ), higher BASFI ( $OR=1.4$ ,  $CI_{95\%}[1.1-1.9]$ ,  $p=0.004$ ), and higher BASMI ( $OR=1.3$ ,  $CI_{95\%}[1.1-1.6]$ ,  $p=0.011$ ) (Table III).

## DISCUSSION

In our study, we attempted to determine the frequency

**TABLE II. Factors associated with hip involvement: univariate study**

	G0 (n=105)	G1* (n=60)	P	PR [CI <sub>95%</sub> ]
Age, mean ± SD (years)	44.82 ± 13.68	48.38 ± 11.72	0.093	
Age ≥ 40 years (n (%))	58 (56.3)	44 (73.3)	0.030	1.7 [1.0-2.6]
Sex ratio (male/female)	78/27	43/17	0.714	0.9 [0.6-1.4]
Smoking (n (%))	41 (41.4)	33 (55)	0.096	1.5 [0.94-2.1]
BMI, mean ± SD (kg/m <sup>2</sup> )	24.84 ± 3.75	25.54 ± 5.16	0.338	
BMI ≥ 25 kg/m <sup>2</sup> (n (%))	48 (45.7)	29 (48.3)	0.754	1.1 [0.7-1.6]
Age at onset, mean ± SD (years)	35.15 ± 13.42	34.78 ± 11.02	0.859	
Age at onset < 40 years (n (%))	70 (66.7)	42 (70.0)	0.659	1.1 [0.7-1.7]
Diagnostic delay, mean ± SD (months)	33.00 ± 41.23	45.27 ± 62.91	0.136	
Age at diagnosis, mean ± SD (years)	38.17 ± 14.08	38.72 ± 11.73	0.798	
Disease duration, mean ± SD (months)	114.82 ± 75.49	158.40 ± 89.14	0.002	
Disease duration ≥ 10 years (n (%))	42 (40.2)	36 (60)	0.015	1.7 [1.2-2.5]
HLA-B27 (n (%))	30 (71.4)	10 (50)	0.099	0.5 [0.3-1.2]
Radiographic sacroiliitis (n (%))	87 (82.7)	57 (95)	0.023	2.7 [1.0-8.1]
Peripheral joint damage (n (%))	18 (17.3)	3 (5)	0.023	0.7 [0.6-0.9]
Extra-articular involvement (n (%))	65 (62.1)	48 (80.0)	0.018	2.4 [1.1-3.1]
Uveitis (n (%))	19 (18.1)	14 (23.3)	0.418	1.2 [0.8-1.9]
IBD (n (%))	9 (8.6)	9 (15.0)	0.203	1.4 [0.9-2.4]
Psoriasis (n (%))	27 (25.7)	10 (16.7)	0.180	0.7 [0.4-1.2]
Pulmonary involvement (n (%))	12 (11.4)	15 (25.0)	0.023	1.7 [1.1-2.6]
Osteoporosis (n (%))	9 (8.6)	12 (20)	0.034	1.7 [1.1-2.7]
ESR > 20 mm (n (%))	70 (66.7)	44 (73.3)	0.385	1.2 [0.8-2.0]
CRP > 8 mg/L (n (%))	77 (73.3)	53 (88.3)	0.036	2.0 [0.9-3.8]
BASDAI, mean ± SD	3.98 ± 1.71	4.03 ± 1.93	0.881	
BASDAI ≥ 4 (n (%))	58 (55.2)	32 (53.3)	0.786	0.9 [0.6-1.4]
ASDAS <sub>CRP</sub> , mean ± SD	2.89 ± 1.10	3.38 ± 1.12	0.033	
ASDAS <sub>CRP</sub> ≥ 3,5 (n (%))	28 (26.7)	28 (46.7)	0.041	1.7 [1.0-2.6]
BASFI, mean ± SD	4.12 ± 2.49	5.48 ± 2.06	0.002	
BASMI, mean ± SD	1.65 ± 1.90	3.71 ± 2.46	<0.001	
mSASSS, mean ± SD	5.80 ± 9.41	16.24 ± 19.28	0.001	
BASRI-L, mean ± SD	1.30 ± 1.36	2.07 ± 1.41	0.058	
BASRI-C, mean ± SD	1.35 ± 1.43	2.42 ± 1.63	0.018	
BASRI-C or BASRI-L ≥ 3 (n (%))	37 (35.2)	39 (65)	0.032	2.2 [1.0-3.2]
BASRI-S, mean ± SD	2.91 ± 2.20	5.97 ± 3.24	<0.001	
BASRI-T, mean ± SD	2.61 ± 2.45	7.74 ± 3.88	<0.001	
NSAIDs (n (%))	91 (86.7)	54 (90.0)	0.528	1.2 [0.6-2.5]
Methotrexate (n (%))	28 (26.7)	16 (26.7)	1.000	1.0 [0.6-1.3]
Sulfasalazine (n (%))	30 (28.6)	23 (38.3)	0.196	1.3 [0.9-2.0]
TNF inhibitor (n (%))	20 (19.0)	33 (55.0)	<0.001	2.6 [1.7-3.8]

Note: We have bolded the significant values.

\*: For G1, we used data collected at the timepoint of diagnosis of hip involvement.

PR: prevalence ratio, CI: confidence interval, p: significance level, SD: standard deviation, BMI: Body mass index, HLA: Human Leukocyte Antigen, IBD: inflammatory bowel disease, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, ASDAS: Ankylosing Spondylitis Disease Activity Score, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, mSASSS: Modified stoke ankylosing spondylitis spinal score, BASRI: Bath Ankylosing Spondylitis Radiology Index, NSAIDs: Non-steroidal anti-inflammatory drugs, TNF: Tumor Necrosis Factor



**TABLE III. Factors associated with hip involvement in spondyloarthritis: multivariable analysis**

	p	OR [CI <sub>95%</sub> ]
Disease duration ≥ 10 years	0.013	3.85 [1.3-11.2]
Radiographic sacroiliitis	0.028	8.95 [1.3-63.5]
ASDAS <sub>CRP</sub> ≥ 3.5	0.001	9.4 [2.5-34.3]
BASFI	0.004	1.4 [1.1-1.8]
BASMI	0.011	1.3 [1.1-1.6]

OR: odds ratio, CI: confidence interval, p: significance level, ASDAS: Ankylosing Spondylitis Disease Activity Score, CRP: C-reactive protein, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index

of hip involvement among patients with spondyloarthritis, and to assess factors associated with this disorder. We found that hip involvement was frequent in SpA patients, occurring in 60 patients (36.4%). Factors associated with hip involvement were disease duration over 10 years, radiographic sacroiliitis, very high disease activity (ASDAS-CRP ≥ 3.5), more functional impairment (higher BASFI) and more limited spine mobility (higher BASMI).

Several studies showed that the prevalence of hip involvement ranged from 24% to 36% in SpA patients<sup>2</sup> and seemed to be more common than in patients with rheumatoid arthritis (RA) as hip disease affected only 5% to 17% of RA patients<sup>20,21</sup>.

In North Africa, SpA patients have a higher risk of hip involvement compared to Europeans. This risk is estimated at 40% after a 10-year disease duration<sup>22</sup>. Poor socioeconomic conditions leading to diagnosis and therapeutic delays explain mainly this finding. Genetic factors and ethnicity may also contribute to this high prevalence<sup>22</sup>.

Unlike RA, hip involvement is often simultaneously diagnosed with SpA or occurs early in the disease course<sup>23</sup>.

Previous studies showed that early age of onset of SpA<sup>24,25</sup> and long course of more than 10 years<sup>25</sup> were associated with the risk of hip involvement. Our study was in line with these studies.

In our study, the radiographic hip involvement was systematically assessed which allowed the diagnosis of hip involvement in asymptomatic patients (10.48% of the involved hips). Previous studies reported that patients may experience only mild symptoms or none even in the presence of inflammatory ultrasound lesions<sup>26</sup>.

Previous studies have reported an association between radiographic sacroiliitis and hip damage<sup>25</sup> and the severity of hip involvement<sup>27</sup>. Our study also concluded a strong association between radiographic sacroiliitis and hip involvement. Furthermore, Kim *et al.* reported that hip disease at the onset of SpA is a reliable predictor of structural sacroiliac joint damage<sup>28</sup>. All these findings suggest that hip and sacroiliac joint damages may be mutually related.

In line with previous studies<sup>2,25,29</sup>, we concluded that BASRI-S and mSASSS were higher in patients with hip involvement. Besides, patients in G1 had higher BASMI suggesting an association between a limited spinal mobility and hip involvement.

Furthermore, our study showed that the frequency of isolated peripheral joint involvement was significantly lower in the presence of hip involvement. All these findings may support the hypothesis suggesting that the hip can be considered as a “root joint” behaving more like the spine than like the peripheral joints<sup>2,30,31</sup>.

However, other studies have reported a more frequent association of hip involvement with peripheral involvement<sup>2,3</sup>. These data highlight the particularity of this joint, which may be related to both axial and peripheral manifestations of SpA.

In our study, we found that high disease activity assessed by the ASDASCRP score was also independently associated with hip involvement. This finding is consistent with previous studies<sup>2,32</sup>. However, we did not find an association between BASDAI and hip involvement.

Our study demonstrated that patient with hip involvement had higher CRP levels. Several studies found that inflammatory markers showed to be predictors of hip joint damage after a 3-year follow-up<sup>8,25,28</sup>. This could explain the discrepancy in results between BASDAI and ASDASCRP scores in our study, since CRP is one of the items used to calculate the ASDAS.

A better control of inflammation could prevent or delay the onset of hip involvement in this population.

As for the BASFI score, it was associated with hip involvement in accordance with literature data<sup>2,25,33,34</sup>.

The effect of obesity on hip osteoarthritis (OA) is well known<sup>35</sup>. However, its effect on hip involvement in SpA is unclear. OA and inflammatory involvement may also coexist.

In our current study, we did not identify an association between obesity and SpA-related hip disease. Our results were in line with the study conducted by Karmacharya *et al.*<sup>36</sup>. However, another study demonstrated an association between higher BMI and the severity of hip involvement in SpA<sup>37</sup>. Furthermore, Jeong *et al.* found that a high BMI was associated with a risk of hip joint replacement surgery in SpA patients<sup>8</sup>.

Our study also showed that the HLA-B27 allele was

more frequent in case of hip involvement. However, it was not associated with hip involvement in the multivariate study. This association is controversial<sup>2,25,34</sup>.

Regarding extra-articular involvement, we found that pulmonary lesions (all types included) were significantly more common in patients with hip involvement. Previous data demonstrated that pulmonary involvement, notably the restriction of pulmonary function, related to reduced spine mobility<sup>37,38</sup>. However, the relationship between pulmonary involvement and hip disease is less clear as information is scarce. In line with previous reports, we also found that osteoporosis was significantly more frequent in patients with hip involvement<sup>39</sup>. However, the multivariate analysis retained neither the pulmonary involvement nor osteoarthritis as factors associated with hip involvement.

Although the effectiveness of TNFi in the management of the hip disease is less clear<sup>39</sup>, hip involvement may justify the prescription TNFi<sup>40,41</sup>. The use of TNFi agents is more frequent in patients with hip arthritis<sup>8</sup>. It may be due to disease severity and the necessity of more aggressive treatment<sup>28</sup>.

Some limitations must be acknowledged notably the limited sample size and the retrospective design. Prospective cohort studies with longitudinal follow-up are needed to determine predictive factors of hip involvement and prognostic factors of radiographic progression.

Moreover, pulmonary involvement and osteoporosis can be associated with high disease activity and could therefore be confounding factors in the multivariate study.

## CONCLUSIONS

Our study showed that hip involvement is frequent in SpA patients. Disease duration over 10 years, radiographic sacroiliitis, very high disease activity, functional impairment and limited spine mobility were associated with hip involvement.

Patients having these factors required a tight control to diagnose early hip involvement and to optimize therapeutic management to avoid worsening of structural damage of hip joint. A better control of disease activity could prevent or delay the onset of hip involvement.

## REFERENCES

- Poddubnyy D, Rudwaleit M. Early spondyloarthritis. *Rheum Dis Clin North Am*. 2012 May;38(2):387-403. doi: 10.1016/j.rdc.2012.04.007. Epub 2012 Jun 13. PMID: 22819091.
- Vander Cruyssen B, Munoz Gomariz E, Font P, Mulero J, De Vlam K, Boonen A, et al. Hip involvement in ankylosing spondylitis: epidemiology and risk factors associated with hip replacement surgery. *Rheumatology*. 2009;49:73-81.
- Burki V, Gossec L, Payet J, Durnez A, Elhai M, Fabreguet I, et al. Prevalence and characteristics of hip involvement in spondyloarthritis: a single-centre observational study of 275 patients. *Clin Exp Rheumatol*. 2012;30:481.
- Amor B, Santos RS, Nahal R, Lustrat V, Dougados M. Predictive factors for the longterm outcome of spondyloarthropathies. *J Rheumatol*. 1994 Oct;21(10):1883-7. PMID: 7837155.
- Vander Cruyssen B, Vastesaegeer N, Collantes-Estévez E. Hip disease in ankylosing spondylitis. *Curr Opin Rheumatol*. 2013 Jul;25(4):448-54. doi: 10.1097/BOR.0b013e3283620e04. PMID: 23689637.
- MacKay K, Brophy S, Mack C, Doran M, Calin A. The development and validation of a radiographic grading system for the hip in ankylosing spondylitis: the bath ankylosing spondylitis radiology hip index. *J Rheumatol*. 2000 Dec;27(12):2866-72. PMID: 11128678.
- Guan M, Wang J, Zhao L, Xiao J, Li Z, Shi Z. Management of hip involvement in ankylosing spondylitis. *Clin Rheumatol*. 2013 Aug;32(8):1115-20. doi: 10.1007/s10067-013-2278-3.
- Jeong H, Eun YH, Kim IY, Kim H, Lee J, Koh EM, Cha HS. Characteristics of hip involvement in patients with ankylosing spondylitis in Korea. *Korean J Intern Med*. 2017 Jan;32(1):158-164. doi: 10.3904/kjim.2015.229. Epub 2016 Mar 25. PMID: 27017388; PMCID: PMC5214726.
- Rudwaleit M, van der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009;68:777-83.
- Rudwaleit M, van der Heijde D, Landewé R, Akkoc N, Brandt J, Chou CT, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis* 2011;70:25-31.
- Khosla T, Lowe CR. Indices of obesity derived from body weight and height. *Br J Prev Soc Med* 1967;21:122-8.
- Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO study group. *Osteoporos Int*. 1994 Nov;4(6):368-81.
- Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994;21:2286-91.
- Lukas C, Landewé R, Sieper J, Dougados M, Davis J, Braun J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. *Ann Rheum Dis* 2009;68:18-24.
- Zochling J. Measures of symptoms and disease status in ankylosing spondylitis: ankylosing spondylitis disease activity score (ASDAS), ankylosing spondylitis quality of life scale (ASQoL), bath ankylosing spondylitis disease activity index (BASDAI), bath ankylosing spondylitis functional index (BASFI), bath ankylosing spondylitis global score (BAS-G), bath ankylosing spondylitis metrology index (BASMI), dougados functional index (DFI), and health assessment questionnaire for the spondyloarthropathies (HAQ-S). *Arthritis Care Res*. 2011 Nov;63 (Suppl 11):S47-S58.
- Averns HL, Oxtoby J, Taylor HG, Jones PW, Dziedzic K, Dawes PT. Radiological outcome in ankylosing spondylitis: use of the Stoke Ankylosing Spondylitis Spine Score (SASSS). *Br J Rheumatol* 1996;35:373-6.
- MacKay K, Mack C, Brophy S, Calin A. The Bath Ankylosing Spondylitis Radiology Index (BASRI): a new, validated approach to disease assessment. *Arthritis Rheum* 1998;41:2263-70.
- Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification

- of the New York criteria. *Arthritis Rheum* 1984;27:361–8.
19. Tamhane AR, Westfall AO, Burkholder GA, Cutter GR. Prevalence odds ratio versus prevalence ratio: choice comes with consequences. *Stat Med*. 2016;35:5730–5735.
  20. Eberhardt KB, Rydgren LC, Pettersson H, Wollheim FA. Early rheumatoid arthritis —onset, course, and outcome over 2 years. *Rheumatol Int* 1990;10:135–42.
  21. Lehtimäki MY, Kaarela K, Hämäläinen MMJ. Incidence of Hip Involvement and Need for Total Hip Replacement in Rheumatoid Arthritis: An Eight-year Follow-up Study. *Scand J Rheumatol* 1986;15:387–91.
  22. Claudepierre P, Gueguen A, Ladjouze A, Hajjaj-Hassouni N, Sellami S, Amor B, Dougados M. Predictive factors of severity of spondyloarthropathy in North Africa. *Br J Rheumatol*. 1995;34:1139–45.
  23. Lehtimäki MY, Kautiainen H, Hämäläinen MM, Lehto MU, Ikävalko M, Repo AB, et al. Hip involvement in seropositive rheumatoid arthritis. Survivorship analysis with a 15-year follow-up. *Scand J Rheumatol* 1998;27:406–9.
  24. Baraliakos X, Braun J. Hip involvement in ankylosing spondylitis: what is the verdict? *Rheumatology (Oxford)*. 2010 Jan;49(1):3–4. doi: 10.1093/rheumatology/kep298. Epub 2009 Sep 15. PMID: 19755506.
  25. Chen HA, Chen CH, Liao HT, Lin YJ, Chen PC, Chen WS, et al. Factors associated with radiographic spinal involvement and hip involvement in ankylosing spondylitis. *Semin Arthritis Rheum*. 2011;40:552–8.
  26. Wink F, Arends S, Maas F, Bootsma H, Griep EN, Bruyn GAW, et al. High prevalence of hip involvement and decrease in inflammatory ultrasound lesions during tumour necrosis factor- $\alpha$  blocking therapy in ankylosing spondylitis. *Rheumatology* 2019;58:1040–6.
  27. Zhao J, Zheng W, Zhang C, Li J, Liu D, Xu W. Radiographic hip involvement in ankylosing spondylitis: factors associated with severe hip diseases. *J Rheumatol* 2015;42:106–10.
  28. Kim H, Lee J, Ahn JK, Hwang J, Park E-J, Jeong H, et al. Predictive factors of radiographic progression in ankylosing spondylitis. *Korean J Intern Med* 2015;30:391.
  29. Brophy S, Mackay K, Al-Saidi A et al. The natural history of ankylosing spondylitis as defined by radiological progression. *J Rheumatol* 2002;29:1236–43.
  30. Calin A, Elswood J. The relationship between pelvic, spinal and hip involvement in ankylosing spondylitis— one disease process or several? *Br J Rheumatol*. 1988;27:393–5.
  31. Ziadé N, El Hajj J, Rassi J, Hlais S, López-Medina C, Gamal SM, Elzorkany B, Dougados M, Baraliakos X. Root joint involvement in spondyloarthritis: a post hoc analysis from the international ASAS-PerSpA study. *Rheumatology (Oxford)*. 2022 Feb 2;61(2):667–678. doi: 10.1093/rheumatology/keab380. PMID: 33905488.
  32. Man S, Zhang L, Bian T, Li H, Ma Z, Zhou Y. Assessment of hip involvement in patients with ankylosing spondylitis: reliability and validity of the Hip Inflammation MRI Scoring System. *BMC Musculoskelet Disord* 2021;22:705.
  33. Cansu DU, Çalışır C, Savaş Yavaş U, Kaşifoğlu T, Korkmaz C. Predictors of radiographic severity and functional disability in Turkish patients with ankylosing spondylitis. *Clin Rheumatol*. 2011 Apr;30(4):557–62. doi: 10.1007/s10067-010-1665-2. Epub 2011 Jan 6. PMID: 21210291.
  34. Boonen A, vander Cruyssen B, de Vlam K, Steinfeld S et al. Spinal radiographic changes in ankylosing spondylitis: association with clinical characteristics and functional outcome. *J Rheumatol* 2009;36:1249–55.
  35. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet*. 2019 Apr 27;393(10182):1745–1759. doi: 10.1016/S0140-6736(19)30417-9. PMID: 31034380.
  36. Karmacharya P, Poudel D, Shrestha P, Dhital R, Davis J. FRI0192 Predictors of severe hip involvement in ankylosing spondylitis: data from national inpatient sample. In Annual European Congress of Rheumatology, EULAR 2018, Amsterdam, 13–16 June 2018.
  37. Slouma M, Rahmouni S, Dhahri R, Cheour E, Gharsallah I, Metoui L, Louzir B. Associated factors with the severity of hip involvement in spondyloarthritis and efficacy of TNF  $\alpha$  inhibitors in these patients. *Curr Rheumatol Rev*. 2022;18:58–63.
  38. Brambila-Tapia AJ, Rocha-Muñoz AD, Gonzalez-Lopez L, Vázquez-Del-Mercado M, Salazar-Páramo M, Dávalos-Rodríguez IP, De la Cerda-Trujillo L, Diaz-Toscano ML, Hernandez-Cuervo P, Diaz-Rizo V, Sanchez-Mosco D, Vazquez-Jimenez JC, Cardona-Muñoz EG, Gamez-Nava JI. Pulmonary function in ankylosing spondylitis: association with clinical variables. *Rheumatol Int*. 2013 Sep;33(9):2351–8. doi: 10.1007/s00296-013-2723-2. Epub 2013 Mar 30. PMID: 23543327.
  39. Liu W, Song H, Man S, Li H, Dong P. Factors associated with radiological hip joint involvement in patients with ankylosing spondylitis [Internet]. ResearchSquare; 2020 [cited 2021 Jan 21]. Available from: <https://www.researchsquare.com/article/rs-61776/v1>.
  40. López-Medina C, Castro-Villegas MC, Collantes-Estévez E. Hip and Shoulder Involvement and Their Management in Axial Spondyloarthritis: a Current Review. *Curr Rheumatol Rep*. 2020 Jul 23;22(9):53. doi: 10.1007/s11926-020-00930-7. PMID: 32705356.
  41. Rocha FAC, Deodhar A. Coxitis in axial spondyloarthritis: the unmeasured, yet functionally most important, radiographic progression. *Chin Med J (Engl)*. 2021 Sep 28;134(21):2550–2552. doi: 101097/CM9.0000000000001743. PMID: 34593699; PMCID: PMC8577678