

The Prevalence of the Coxitis in Patients with Spondyloarthritis and its Relation with the Disease Features: RBSMR Study

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ABSTRACT

Background: The coxitis is a common complication of spondyloarthritis representing a major prognostic factor of severe disability with an important impact on the patients' socioeconomic quality of life, which needs replacement surgery in the end-stage hip disease.

Objective: This study aims to investigate the prevalence of coxitis in patients with spondyloarthritis (SpA) included in the Moroccan registry of biological therapies in rheumatic diseases RBSMR (Registro des Biothérapies de la Société Marocaine de Rhumatologie) and to assess the relationship between coxitis and disease features.

Methods: We performed a multicenter cross-sectional study using the RBSMR database that recruited 194 patients with SpA. The patients were categorized into two groups: SpA with coxitis (radiographic and/or ultrasound coxitis in its unilateral and bilateral forms) and SpA without coxitis. We compared the patients' demographic characteristics and the disease features using descriptive statistics. Univariate and multivariate analysis using the logistic regression models were applied to identify the factors related to coxitis during the disease.

Results: Among 194 patients with SpA, the coxitis was present in 80 patients (41.2%). The patients having coxitis were significantly younger with a mean age of 33.4 versus 44.9 years and had male gender predominance (82.5%) ($p < 0.001$). In both groups, no significant differences have been noted in the disease features which are disease duration, HLA B27, the family history of SpA, the type of SpA, the extra-articular manifestations (uveitis, psoriasis, inflammatory bowel disease), syndesmophytes, visual analogue scale for fatigue, the disease activity parameters (erythrocyte sedimentation rate, C-reactive protein), the disease activity (BASDAI, ASDAS-CRP) and functional (BASFI) scores. The radiographic sacroiliitis grade 4 was significantly more frequent in patients with coxitis ($p = 0.001$). In multivariate analysis, after adjustment for confounding factors, the factors related to coxitis were age, male gender and radiographic sacroiliitis grade 4.

Conclusion: Our study reports that the prevalence of coxitis in patients with SpA included in the RBSMR registry was 41.2% and suggests that the factors associated to coxitis were the age, the male gender and the radiographic sacroiliitis grade 4. No relationship was found between coxitis and disease activity parameters, disease activity and functional scores.

Keywords: Coxitis, Spondyloarthritis, Prevalence, RBSMR Registry

Abbreviations: SpA: Spondyloarthritis; RBSMR: Registro des Biothérapies de la Société Marocaine de Rhumatologie; HLA B27: Human leukocyte antigen B27; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score-CRP; BASFI: Bath Ankylosing Spondylitis Disease Functional Index; AS: Ankylosing spondylitis; ASAS: Assessment of Spondyloarthritis International Society; MRI: Magnetic resonance imaging; RA: Rheumatoid arthritis; SPSS: Statistical Package for the Social Sciences; VAS-F: Visual analogue scale for fatigue; ESR: Erythrocyte sedimentation rate; CRP: C-Reactive Protein; TNF: Tumor Necrosis Factor; RESPONDIA: Ibero-American Spondyloarthropathies Registry; REGISPONDER: Registro Español de Espondiloartritis de la Sociedad Española de Reumatología.

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BACKGROUND

The spondyloarthritis is an interrelated group of chronic rheumatic diseases involving spine, sacroiliac and peripheral joints sharing in common several characteristics [1,2]. Ankylosing spondylitis (AS) is the prototype disease of this group that includes other clinical entities, enteropathic spondylitis, psoriatic arthritis, reactive arthritis and undifferentiated spondyloarthritis [3]. They are manifested by inflammation and progressive structural damage of spine and joints [1,2]. The AS affects particularly young men and has a strong genetic association with human leukocyte antigen B27 (HLA B27). The 2009 ASAS (Assessment of SpondyloArthritis International Society) classification criteria have helped to provide the early diagnosis of SpA using the magnetic resonance imaging (MRI) and the HLA B27 determination [4]. Hip is one of the frequently afflicted joints making the patient disabled due to pain and deformity. The hip joint involvement occurs in about one-third of patients with SpA, reflecting more active and severe disease [5].

The coxitis is associated with significant functional impairment, which increases the burden of the disease and impacts negatively not only on physical status but also on psychosocial status and the quality of life [1,6]. The data on effective therapeutic strategies that can prevent hip involvement are deficient. The standard treatment option in patients with end-stage hip disease is the total hip arthroplasty, which will allow to relieve pain and improve hip functions [1,7,8]. These prostheses have a limited life span and can expose the patients to the risk of surgery [5,7,8]. Therefore, conservative management strategies are expected and new therapeutic options should be explored to prevent hip damage during the SpA evolution [1,5].

We report in this article the outcomes of our study, which is the first study in Morocco with the main purpose to investigate the prevalence of coxitis and to identify the factors associated to coxitis in patients with SpA included in the RBSMR registry.

METHODS

The RBSMR registry

The RBSMR (Registre des Biothérapies de la Société Marocaine de Rhumatologie) is a registry of biological

therapies in rheumatic diseases of the Moroccan Society of Rheumatology. It is a historical, prospective and multicenter registry, which includes 10 departments of rheumatology in university medical centers. The patients recruited in the registry, had an age over than 18 years. They were diagnosed for rheumatoid arthritis (RA) or spondyloarthritis (SpA) and treated by biotherapy (initiation or ongoing biotherapy) in different university medical centers in Morocco. The inclusion period was from May 2017 to January 2019 and the follow-up was 3 years. The number of the included patients was 440 patients, which 419 patients were validated (225 RA/194 SpA). The primary objective of the RBSMR registry was to assess the tolerability of the patients with RA or SpA treated by biotherapy in rheumatology. The secondary objectives were to identify the most common side effects in daily practice, to evaluate the effectiveness of biotherapies in rheumatology and to evaluate the impact of biotherapies on the patients' quality of life. The details of the data collected have been published previously [9].

The study

In this cross-sectional and multicenter study using the RBSMR registry database, which included 194 patients with SpA who fulfilled the 2009 ASAS criteria, we have divided the patients in two groups: SpA with radiographic and/or ultrasound coxitis in its unilateral and bilateral forms versus SpA without coxitis. The objectives of the present study are to investigate the prevalence of coxitis, to assess its relationship with the disease activity parameters, the disease activity and functional scores and to determine the factors associated to coxitis in patients with SpA included in the registry.

The statistical analysis

The statistical study was conducted according to the database frozen in January 2019.

The statistical analysis was performed using SPSS software, version 13.0. Data for patients were presented as means, standard deviations, medians and interquartile ranges for continuous variables and as numbers and percentages for categorical variables.

The comparisons between the two groups -SpA with coxitis versus SpA without coxitis-were examined using the Student's *t*-test for continuous variables with a normal distribution while the Mann-Whitney test for continuous variables with non-normal distribution and using the Chi-squared test or Fischer's exact test for categorical variables. We completed the analysis with logistic regression models (Univariate followed by multivariate logistic regressions) to assess the relationship between coxitis and the disease activity parameters, the disease activity and functional scores and to identify the associated factors to coxitis. P values less than 0.05 were considered statistically significant.

RESULTS

The prevalence of coxitis in our study population was 41.2%. The coxitis was manifested by radiological coxitis in 59 patients (73.7%), radiological and ultrasound coxitis in 20 patients (25%) and ultrasound coxitis without radiological involvement in one patient (1.3%) at the time of inclusion. We noted 135 coxitis including 72 left coxitis and 63 right coxitis with bilateral coxitis in 59 patients (73.7%). The comparison of the demographic characteristics between the two groups, SpA with coxitis (*n* = 80) versus SpA without coxitis (*n* = 114), showed that the patients having coxitis were significantly younger with a mean age of 33.4 versus 44.9 years (*p* < 0.001) and had male predominance 82.5% versus 50% (*p* < 0.001)(**Table 1**). We did not find significant differences between the two groups in the disease features, which are the disease duration, the HLA B27, the family history of SpA, the type of SpA (axial, peripheral and enthesal), the extra-articular manifestations (uveitis, psoriasis, inflammatory bowel disease), the syndesmophytes and the visual analogue scale for fatigue (VAS-F). We noted that the radiographic sacroiliitis grade 4 according to the modified New York criteria was significantly frequent in patients with coxitis (*p* = 0.001) (**Table 1**).

There were no significant differences between the two groups in the disease activity parameters (ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive protein) and the disease activity (BASDAI: Bath Ankylosing Spondylitis Disease Activity Index and ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score-CRP) and functional (BASFI: Bath Ankylosing Spondylitis Disease Functional Index) scores (**Table 2**).

Univariate analysis showed the association between coxitis and the parameters: age, male gender, radiographic sacroiliitis grade 4 and CRP (**Table 3**). In multivariate analysis after adjustment for confounding factors, the related factors to coxitis in patients with SpA included in RBSMR registry were the age, the male gender and the radiographic sacroiliitis grade 4 (**Table 3**).

DISCUSSION

Hip is one of the frequently afflicted joints in SpA with worse functional outcomes [1]. Several studies have evaluated the prevalence of hip involvement in SpA varying between 19% and 36% [10,11,12,13]. The hip replacement surgery was indicated in 5% to 8% of AS patients, which was bilateral in 47% of cases, particularly in patients with longer disease duration. After 30 years of disease duration, 12% to 25% of patients underwent at least one total hip arthroplasty [10,13,14]. The wide range of the prevalence of hip involvement reported in the literature can be explained by the different used definitions in the absence of a standard definition for hip involvement as a complication of an active SpA [5,10].

In our study, among 194 patients with SpA recruited in the RBSMR registry, 80 patients had a coxitis corresponding to the prevalence of 41.2%. This rate is slightly higher compared to previous studies [10,11,12,13] but it is consistent with an older Moroccan study that had compared patients with SpA in Morocco and France and had revealed that Moroccan patients had more severe disease with high frequency of coxitis (48% versus 6%) [15,16] and also with another more recent Moroccan study that found a prevalence of 47.3% for the radiographic hip involvement in 117 patients diagnosed for AS [17]. Comparing patients' characteristics, the patients having coxitis were significantly younger with a mean age of 33.4 versus 44.9 years reflecting the younger disease onset, which is consistent with all studies having showed the association between the early age at disease onset and the hip involvement [1,5,10,18]. The patients with juvenile onset disease (age at disease onset less than 16 years) are likely to develop coxitis earlier than patients with adult-onset AS [11,18]. Consequently, they require early total hip arthroplasty and need closer monitoring [1,10,19]. The patients with coxitis had a male gender predominance, which is reported in some studies [20,21] and had relatively longer disease duration with a median of 574 weeks.

Concerning the disease features, we did not find significant difference between the two groups in the HLA B27, which is compatible with the outcomes of Hamdi W et al. [22] and contrasting with a Moroccan study that have been demonstrated an association between the HLA B27 and AS with coxitis [15]. No significant differences were found in the family history of SpA, the type of SpA (axial, peripheral and enthesal), the extra-articular manifestations (uveitis, psoriasis, and inflammatory bowel disease), the syndesmophytes and the VAS-F. We noted that radiographic sacroiliitis grade 4 was significantly frequent in SpA patients with coxitis. There were no significant differences between the two groups concerning the disease activity parameters (ESR, CRP), the disease activity (BASDAI, ASDAS-CRP) and functional (BASFI) scores. These outcomes are contrasting with previous reports that have shown worse BASFI scores in patients with hip involvement [2,5,14,19].

The relationship between coxitis and disease activity or physical function was not found in our study population with low medians BASDAI, ASDAS-CRP and BASFI scores because all patients included in the study are receiving anti-TNF α as a treatment.

Table 1. The comparison of demographic characteristics and disease features between the two groups: SpA with coxitis versus SpA without coxitis.

Parameters	SpA with coxitis (n = 80)	SpA without coxitis (n = 114)	p value
Age (years) ¹	33.4 $\pm$ 11.8	44.9 $\pm$ 12.8	<0.001
Gender (male) ²	66 (82.5)	57 (50)	<0.001
Disease duration (weeks) ³	574 [365-783]	522 [365-783]	0.408
HLA B27 positive ²	15 (78.9)	20 (58.8)	0.138
The family history of SpA ²	10 (13.5)	16 (15.2)	0.747
Uveitis ²	8 (10.7)	19 (17.1)	0.221
Psoriasis ²	2 (2.6)	11 (9.9)	0.052
Inflammatory bowel disease ²	7 (9.2)	13 (11.7)	0.587
Axial involvement ²	78 (97.5)	108 (95.6)	0.481
Peripheral involvement ²	55 (71.4)	78 (69)	0.723
Enthesal involvement ²	44 (59.5)	71 (62.8)	0.643
Radiographic sacroiliitis grade 4 ²	37 (49.3)	24 (25.3)	<0.001
Syndesmophytes ²	33 (41.2)	38 (33.6)	0.279
VAS-F ¹	6 $\pm$ 2.5	6.4 $\pm$ 2.2	0.259

HLA B27: Human leukocyte antigen B27; VAS-F: Visual analogue scale for fatigue.

1. Means and standard deviations; 2. Numbers and percentages; 3. Medians and interquartile ranges. Results according to available data.

Table 2. The comparison of the disease activity parameters, the disease activity and functional scores between the two groups: SpA with coxitis versus SpA without coxitis.

Parameters and scores	SpA with coxitis (n = 80)	SpA without coxitis (n = 114)	p value
ESR (mm)	16 [6-34.5]	20 [10-35]	0.358
CRP (mg/l)	7.5 [1.9-27.2]	6 [2.3-13]	0.168
BASDAI	2.9 [1-4.2]	3 [1.8-4.8]	0.276
ASDAS-CRP	1.9 [0.9-3.1]	1.8 [1-3]	0.621
BASFI	3.7 [1.1-5.4]	3 [1.2-5]	0.242

ESR: Erythrocyte Sedimentation Rate; CRP: C-reactive protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score-CRP; BASFI: Bath Ankylosing Spondylitis Functional Index. Results are expressed as medians and interquartile ranges. Results according to available data.

Table 3. Univariate and multivariate analysis.

Parameters	Univariate analysis			Multivariate analysis		
	OR	IC (95%)	p value	OR	IC (95%)	p value
Age	0.92	0.90-0.95	< 0.001	0.93	0.90-0.96	< 0.001
Male gender	4.71	2.38-9.33	< 0.001	3.02	1.3-7.01	0.01
Radiographic sacroiliitis grade 4	0.34	0.18-0.66	0.001	0.34	0.15-0.73	0.006
CRP	1.01	1.001-1.028	0.035	1	0.98-1.02	0.522

CRP: C-reactive protein

We used logistic regression models to look for the factors related to coxitis in patients with SpA. After adjustment for confounding factors, the multivariate analysis reported that the age, the male gender and the radiographic sacroiliitis grade 4 were the factors associated to coxitis in the patients with SpA included in RBSMR registry.

Although, cohorts based on RESPONDIA (Ibero-American Spondyloarthropathies Registry) and REGISPONDER (Registro Español de Espondiloartritis de la Sociedad Española de Reumatología) registries with some other studies, showed that besides the younger disease onset, hip disease seems to be associated with more severe axial disease [2,14,23,24]. Hung-A Chen et al. reported a relationship between radiographic sacroiliitis, spinal fusion and hip involvement in AS patients. They showed that elevated CRP level, advanced radiographic sacroiliitis and hip involvement were the predictors for radiographic change and spinal fusion [14]. Bert Vander Cruyssen et al. reported that juvenile onset, disease duration, enthesal disease, arthritic disease and severe axial disease were the variables associated with hip replacements in AS patients [10,22].

The present study is limited by the criterion of patients receiving biotherapy, which refers to patients having severe SpA sent to tertiary centers for treatment. Expanded studies seem to be necessary to confirm these results.

CONCLUSION

Coxitis is a common disease manifestation of SpA, reflecting more severe disease with an important functional impairment. Due to the central function of hip, the evaluation of the prevalence of coxitis in our study population is interesting.

We did not find a relation between coxitis and the disease activity parameters, the disease activity and functional scores. Our study suggests the existence of a relationship between the coxitis and the age, the male gender and the radiographic sacroiliitis grade 4 in patients with SpA included in RBSMR registry.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The protocol for the original RBSMR study was reviewed and approved by local institutional review boards and the national ethic committee: Comité d’Ethique pour la Recherche Biomédicale. Université Mohammed V - Rabat. Faculté de Médecine et de Pharmacie de Rabat, Faculté de Médecine dentaire de Rabat, N/R: dossier N° 117/17.

CONSENT FOR PUBLICATION

Written informed consent for publication was obtained from the patients.

AVAILABILITY OF DATA AND MATERIAL

The datasets are available from the RBSMR registry of the Moroccan Society of Rheumatology.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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GRANT

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AUTHORS’ CONTRIBUTIONS

SB drafted this manuscript and reviewed the literature. BA, IE, IH, SR and RB reviewed critically the manuscript. The scientific committee of the RBSMR study, composed of RA, LA, FA, IE, AE, IG, HH, TH, LI, OM and RN, has reviewed and approved the final manuscript.

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