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RESEARCH ARTICLE

Active Sacroiliitis on MRI, Inflammation Biomarkers, and Clinical Disease Activity: What Relationship Does Link Between the Three, in Non-Radiographic Axial Spondyloarthritis?

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ABSTRACT

Introduction: Magnetic resonance imaging of sacroiliac joints (MRI SI) is the gold standard imaging tool for axial spondyloarthritis (ax SpA) diagnosis, when the pelvic radiograph is normal or non-conclusive. In fact, subchondral bone marrow edema (BME) is the primary MRI feature of early ax SpA. The associated factors with active sacroiliitis on MRI are still not properly elucidate. The main objective of this study is to identify the relationship between active sacroiliitis on MRI, biomarkers of inflammation and Disease Activity Scores.

Materials and methods: Our work could be categorized as a cross sectional study that enrolls all patients with non-radiographic axial spondyloarthritis (nr axSpA), meeting each; the assessment of SpondyloArthritis international Society axSpA criteria (ASAS 2009), and who were admitted in our Rheumatology Department, in the university hospital Hassan II of Fez (Morocco), all along the period laying between January 2012 and March 2018. The relationship between MRI-SI, Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), C reactive protein and erythrocyte sedimentation rate was investigated.

Results: 105 patients were involved in the study. The average age was [44years ± 13.5]. The Sex ratio was about [1.4]. 29 % of patients were smokers. 76% of cases had active sacroiliitis on MRI, while only 28% had inactive sacroiliitis. The average CRP serum level was roughly [23.5 ± 36mg / l]. On the other side, the ESR blood level was almost [25.9±24mm/h]. 94.2% of patients used non-steroidal antiinflammatory drugs (NSAIDs). The average ASDAS value was about [2.3 ± 1]. Whereas the BASDAI one was [4.2± 1], and the BASFI one was about [4± 1.5]. Actually, No significant relationship was found between active sacroiliitis and inflammation's biomarkers. Indeed, men had 5.6 times more active sacroiliitis, of which smokers had even 3 times more the risk to develop active sacroiliitis, while treatment with NSAIDs was proved to be a protective factor.

Conclusion: Biomarkers of inflammation cannot be used as a marker of objective inflammation of sacroiliac joints on MRI; hence, the necessity of MRI screening, and more additional studies with larger number of patients, should be conducted, to identify this association even better.

KEYSWORDS: Axial Spondyloarthritis, Biomarkers of Inflammation, Active Sacroiliitis, MRI of Sacroiliac Joints.

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INTRODUCTION

Spondylarthritis might be defined as a group of chronic inflammatory rheumatic diseases, characterized by a predominant damage of the spine and sacroiliac joints. Enthesitis is also a common feature, with a tendency to enthesophytes formation. It is actually the second most frequent chronic inflammatory rheumatic disease after rheumatoid arthritis. The diagnostic value of sacroiliac joints MRI (MRI-SI) in non-radiographic axial spondyloarthritis (nr axSpA) is nowadays clearly established [1]. The contribution of MRI to our understanding of spondyloarthritis including ankylosing spondylitis (AS) is indisputable. In fact, MRI can be used to detect inflammatory lesions of the spine and sacroiliac joints. Furthermore, spinal MRI is currently considered as being a powerful tool to bring out the treatment efficacy by detecting improvement, persistence or new onset of spinal inflammation in AS [2].

The associated factors with active sacroiliitis are yet poorly understood. This study aims to investigate the relationship existing between active sacroiliitis, CRP blood level, and clinical activity scores of non-radiographic axial spondyloarthritis.

MATERIALS AND METHODS :

The concerned population: It is a question of a cross sectional study, that enrolls the whole patients with axial spondyloarthritis admitted in the Rheumatology Department of University hospital Hassan II of Fez, in Morocco , throughout the period laying between January 2012 and March 2018.

All the Patients who met the Assessment of SpondyloArthritis international Society (ASAS) criteria for axSpA, were involved [3].

The data collected from each patient's register, are the following:

• Age, gender, address, education level, career, and tobacco consumption.

• Clinical disease activity measures:

☐ The disease activity was assessed by the mean of ankylosing Spondylitis disease Activity Score with C reactive protein (ASDAS-CRP), and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). The disease was considered active when BASDAI ≥4 and ASDAS ≥2,1.

• Biological markers: Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). CRP was considered to be negative when it is less than 6 mg/l, and positive if it is over >6 mg/l.

• The functional effect of axSpA was evaluated by mean of BASFI: Bath Ankylosing Spondylitis Functional Index in a validated Moroccan version [4].

• The use or not of NSAIDs.

MRI of sacroiliac joints:

Definition of active sacroiliitis on MRI:

The ASAS group concluded that the presence of inflammation (defined as Bone Marrow Oedema – BMO) is the principal observation required by the current definition and no additional findings are necessary.

The description for sacroiliac joint BMO consistent with active SpA is :

1. Bone marrow oedema (BMO) on a T2-weighted sequence sensitive free water (such as short tau inversion recovery (STIR) or T2FS) or bone marrow contrast enhancement on a T1-weighted sequence (such as T1FS post-Gd).
2. Inflammation must be clearly present and located in a typical anatomical area (subchondral bone).
3. MRI appearance must be highly suggestive of SpA. [5]

Statistical analysis : Statistical analysis was performed using the EPI INFO software 3.5.4 version. Statistical comparison was carried out between patients who do have an active sacroiliitis and the ones who do not. A multivariate logistic regression analysis was performed to calculate the odds ratio (OR) of various clinical parameters. P value was considered significant if it was less than 0.05.

Results : 105 patients were included in our study. The average age of patients was 44 years+/- 13.5 [15, 80] with a sex ratio Female/Male of 1.4 (62 women and 43 men). MRI of sacroiliac joint's showed that 76% of patients had active sacroiliitis (figure 1) whereas 28% of them had inactive sacroiliitis (figure 2). Moreover, 29% of cases were smokers, and 94.2% took NSAIDs.

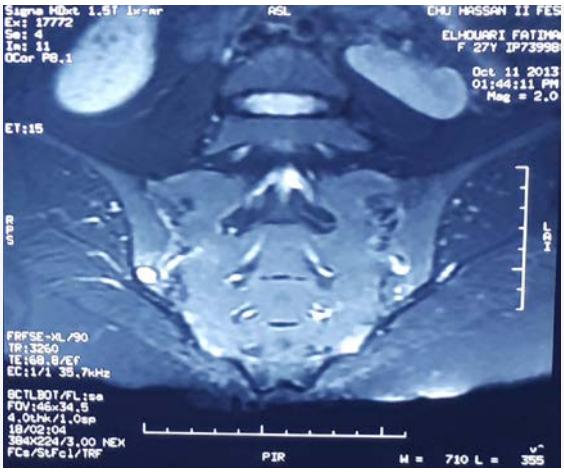
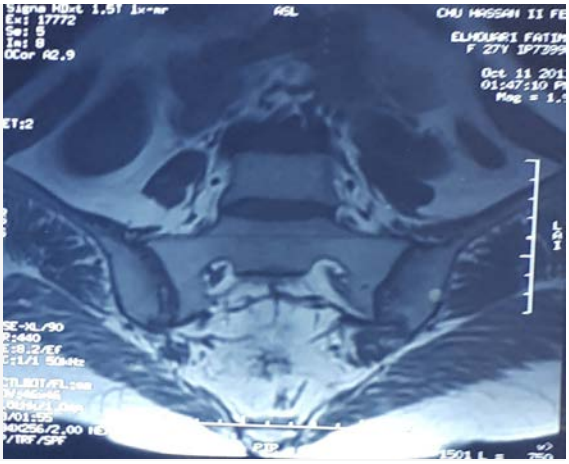


Figure 1 : Active sacroiliitis



Picture 2 : Inactive sacroiliitis

As far as biomarkers are concerned; the average blood level of ESR was 25.9 mm H1± 24 and the one of CRP was 23.5 mg/l ± 36. Regarding the axSpA activity and functional effect, the mean value of BASDAI, ASDAS and BASFI were 4.2 ± 1 [1,8], 2.3 ± 1 [1, 5] and 4 ± 1.5 [0.5, 7] respectively.

The univariate analysis figures in Table1, the associated factors with active sacroiliitis were male gender, tobacco consumption, BASDAI, BASFI and use of NSAIDs.

86.9% of women and 53,5% of men had active sacroiliitis, while13.1% of women and 46.5% of men had inactive sacroiliitis (p=0,01).48.3% of the smokers had active sacroiliitis, whereas 51.7% had inactive sacroiliitis (P=0,03). BASDAI and BASFI were higher in case of active sacroiliitis, the p value was (p=0,01) and (p=0,000), respectively.

Concerning the use of NSAIDs, 75.5% of patients had active sacroiliitis while 24.5% of them had inactive sacroiliitis (p=0, 04). (Table 1)

Table 1: Characteristics of patients with axial spondyloarthritis included in this study: bivariate analysis

	Active sacroliitis 76 (73,1%)	**Inactive sacroiliitis** 28 (26,9%)	**p-value**
Age	44,8	39,2	P=0,3
Gender			
• Women	86,9%	13,1%	P=0,01
• Men	53,5%	46,5%	
Tabacco consumption :			
• **Yes**	48,3%	51,7%	P=0,03
• **No**	82,7%	17,3%	
NSAIDs	75,5%	24,5%	P=0,04
VS	23,7	31,9	p=0,69
CRP	19,7	36,4	P=0,27
ASDAS	2,5	2	P=0,86
BASDAI	4,2	4	P=0,01
BASFI	4,2	3,5	P=0,000

Total : N=104 ; Males N= 43 (41,3 %) ; Females N=61 (58,7 %)

After multiple logistic regression analysis, the factors associated with active sacroiliitis were male gender, tobacco consumption and NSAIDs use.

Men had almost 5.6 times more the risk of developing an active sacroiliitis [CI: 1.8-17.5], while smokers had 3 times more the risk of having an active sacroiliitis [CI: 1.00-8.7]. However, NSAIDs are considered as a protective factor against active sacroiliitis 0Ra= 0.16; [CI: 0.45-0.96]. (Table 2)

Table 2: Characteristics of patients with axial spondyloarthritis included in this study: multivariate analysis

		Adjusted Odd Ratio	**Confidence Interval (CI)**	**P-value**
Gender	Female	1	CI : 1,8-17,5	0.003
	Male	5,6		
Tabacco consumption	No	1	CI : 1,00-8,7	0.05
	Yes	2,9		
NSAIDs	No	1	CI : 0,45-0,96	0,03
	Yes	0,16		

Relationship between biomarkers of inflammation and active sacroiliitis on MRI:

There was a significant correlation between BASDAI, BASFI and inflammation of sacroiliac joint's on the MRI (p=0,01), (p=0,000),respectively.

No other significant association was denoted, neither between inflammation biomarkers (CRP and ESR) and active sacroilitis on MRI, nor with disease activity assessed by ASDAS CRP measurement; (p=0,27), (p=0,69), (p=0,86), respectively.

DISCUSSION

This study shows that inflammation of SI joint's on MRI, is not correlated to CRP serum levels. However, the literature reviews report inconsistent results. In fact, several studies proved an association between CRP blood level and the SI inflammation on the MRI, [6, 7, 8, 9, 10]. While many others [11, 12, 13, 14] didn't bring out any similar association, as it is the case in our study. These contradictory findings may reflect differences between the studies in terms of the baseline status of their cohorts. In addition, a recent study showed that only CRP serum level is linked to MRI SI joints inflammation in patients with short disease duration versus patients with long-standing disease [15]. This observation indicates also that the relationship between inflammation of SI joints on MRI and biomarkers may change in the course of the disease. This may be a bias in our study, since the duration of the disease's evolution wasn't analyzed. We focused on the analysis of the CRP levels at the moment of active sacroiliitis.

This study shows that active sacroiliitis is more common in the male gender. An observational cohort study (The GLAS cohort) who has included 466 patients with axial SpA, demonstrated that patient-reported measures of disease activity, physical function and quality of life are significantly worse in females [16]. However,other studies confirm our results [17,18].

Our results prove that Tabacco consumption is considered as the closest factor, related to MRI SI joints inflammation, since it was significantly associated with active sacroiliitis in our study, and it has always been known as a factor of severity of the disease. Many studies had acctualy proven this finding [17, 18]. A cross-sectional analysis of a cohort (DESIR cohort) reported that smoking was associated with an increased axial inflammation of SI joints on MRI (p=0.02) [19].

Among the investigated scores, BASDAI and BASFI were significantly related to MRI-SI inflammatory lesions, but only in the univariate analysis [P=0,014, P=0,000]. This may be explained by the fact that BASDAI and BASFI do not reflect the real extension of inflammation. ASDAS was not significantly associated with active sacroiliitis in our study but this activity score is correlated to active sacroiliitis in other studies, especially in non radographic axial spondyloarthritis [6].

Our study showed that NSAIDs are a protective factor against active sacroiliitis. This can be explained physiopathologically by their anti-inflammatory action. Our findings are consistent with those of a cohort study conducted in a single-center where a total of 117 patients with clinically suspected axial SpA were screened. A positive MRI of the SI joints, as defined by the Assessment of SpondyloArthritis international Society (ASAS) criteria, was performed after 6 weeks of an optimal dose of NSAIDs. In this cohort of consecutive patients, they found out a significant and distinct decrease in intensity of SI joints' lesions, after 6 weeks of full NSAIDs therapy, in newly presenting patients with axial Spondyloarthritis. They concluded that reduced bone marrow edema signal intensity may be indicative of NSAIDs intake and therefore affects interpretation of SI joint MRI in early stages of the disease. [19]. Many other studies proved this protective effect of NSAIDs against

active sacroiliitis [20,21]. On the other hand, some studies reported no changes were observed, in objective signs of inflammation on MRI and CRP levels, after taking NSAIDs [22].

Limitations of our study: The few number of the enrolled patients limits our cross-sectional study. Indeed, several other parameters were not analyzed as well. Thus, our perspective is to lead prospective studies on larger groups of patients, in order to identify the real relationship between active sacroiliitis on MRI and CRP blood level, in a better way.

CONCLUSION

Our data suggest that there is no correlation between biomarkers of inflammation, disease activity scores and inflammation of SI joint's on MRI, in patients with axial spondyloarthritis, hence the necessity of MRI screening .Further studies are needed to elucidate the predictor factors of this association.

AUTHORS' CONTRIBUTIONS

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors. Indeed, all the authors have actively participated in the redaction, the revision of the manuscript and provided approval for this final revised version.

COMPETING INTERESTS

The authors declare no competing interests.

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