

## Evaluation of the Impact of Smoking on Spondyloarthritis: Data from the Moroccan Biotherapy Register (RBSMR)

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### Abstract

**Objective:** The aim of our study was to determine the prevalence of smoking and its impact on the various parameters of spondyloarthritis based on collected data from the Moroccan biotherapy register. **Materials and methods:** This is a multicenter study based on data from the Moroccan biotherapy register related to patients suffering from spondyloarthritis. An analysis of the socio-demographic parameters as well as an evaluation of the variables associated with the disease were performed. Univariate and multivariate logistic regressions were conducted to assess what the impact of smoking is on the various spondyloarthritis parameters.  $p < 0.05$  was set to be the significant threshold. **Results:** The study is based on data collected from 194 patients (21 smokers and 173 non-smokers) suffering from AS included in the Moroccan biotherapy register. The prevalence of smoking was 10.8%. Male gender was associated with smoking (63% of men in non-smoking group versus 90% of men in the smoking group) ( $p = 0.006$ ). In addition, a higher CRP: 8 [2-17] was observed in the smoking group compared to 5.5 [2-28] in the non-smoking group ( $p = 0.048$ ). No significant difference between the 2 groups was statistically noted in terms of the disease activity evaluated by the BASDAI and ASDAS CRP score which were respectively  $2.77 \pm 1.82$  and  $2.25 \pm 1.66$  in the smoking group and  $3.24 \pm 2.15$  and  $2.09 \pm 1.7$  in the non-smoking one. Furthermore, our results did not reveal a significant correlation between smoking and the functional impact of spondyloarthritis. No correlation was established between smoking and the structural progression of the disease. **Conclusion:** Our study suggests that male gender and a higher CRP are statistically associated with tobacco consumption. Larger scale studies are needed to support these results.

**Keywords:** Tobacco, spondyloarthritis, prevalence.

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### INTRODUCTION

Spondyloarthritis is a chronic inflammatory disease which affects the sacroiliac joints, the spine and all peripheral joints causing chronic pain and progressive stiffness [1]. The global prevalence is around 1.5% and can be the cause of a major functional handicap. While genetic predisposition plays a major

role in the risk of developing spondyloarthritis, other elements such as environmental factors are necessary to trigger or even maintain the disease [3].

Smoking is known to be an important environmental risk factor for the development of rheumatoid arthritis [2, 11]. For the past ten years, some concordant studies have shown its harmful effect on the

activity of spondyloarthritis [4, 5], on its functional repercussions [5, 6, 8] and its influence on the radiographic progression of the disease [3, 4, 7]. However, these studies are limited. Smoking interferes with the disease, the underlying mechanism being unknown. It can be noted that smoking deeply modifies the respiratory microbiota and host-bacteria interactions in the airways [10]. During spondyloarthritis, smoking has a direct pro-inflammatory effect [9], worsens the already existing inflammation and may play a role in the emergence and the evolution of the disease.

Tobacco is a factor that can be adjusted. It is therefore a target we can act on to control the disease. Thus, we have an important role to play in helping patients suffering from spondyloarthritis quit smoking. The objectives of our study are to assess the prevalence of smoking in patients with spondyloarthritis included in the Moroccan register of biotherapy (RBSMR) and to assess its impact on the various clinical, biological and structural parameters of the disease (activity, functional repercussions, and severity of the disease).

## PATIENTS AND METHODS

This is a multicenter cross-sectional study (10 university hospital / rheumatology departments) using inclusion data from the Moroccan register of biotherapy (RBSMR) collected between May 2017 and December 2018. One hundred ninety four patients with spondyloarthritis were included 21 of them actively smoking. The different socio-demographic parameters of the smoking / non-smoking groups were analyzed (age, gender, smoking status) as well as the variables related to the disease (BASDAI, ASDAS, BASFI, ESR, CRP, HLA B27, syndesmophytes, coxitis, radiographic sacroiliitis or MRI). The comparison tests between the two groups were performed using Student's T test for quantitative variables with normal distribution, Mann Witheney « U » test for non parametric variables with asymmetric distribution and Chi2 for qualitative variables. A univariate and multivariate logistic regression were conducted to investigate the impact of

smoking on the various parameters of spondyloarthritis. SPSS v20 software was the main tool for the statistical analysis and a  $p < 0.05$  was considered statistically significant.

## RESULTS

194 patients with AS were included in this study: 21 were actively smoking and 173 were non-smokers the prevalence of smoking being 10.8%.

The mean age of patients was similar in the 2 groups (40.3 +/- 13.6 years in the smoking group and 40.2 +/- 13.7 in the non-smoking one).

Male gender was associated with smoking: 63% of men in the non-smoking group versus 90% in the smoking group ( $p = 0.006$ ). HLA b27 status was positive for 6 smokers (86%) and 29 non-smokers (63%). No significant difference between the 2 groups was statistically noted in terms of the disease activity as evaluated by the BASDAI score (Bath Ankylosing Spondylitis Disease Activity Index) and the ASDAS CRP score which were respectively 2.77 +/- 1.82 and 2.25 ± 1.66 in the smoking group and 3.24 +/- 2.15 and 2.09 ± 1.7 in the other one. A correlation between smoking and a biological inflammatory syndrome was found: a higher CRP of 8 [2-17] was reported in the smoking group compared to 5.5 [2 -28] in the non-smoking group ( $p = 0.048$ ).

In addition, our results did not reveal a significant correlation between smoking and the functional impact of spondyloarthritis as evaluated by the BASFI (Bath Ankylosing Spondylitis Functional Index): 3.34 ± 2.91 for the smoking group versus 3.35 ± 2.38 for the non smoking group (Table-1). Smoking is not associated with the structural progression of the disease identified by radiographic sacroiliitis (20 (95%) smokers, 150 (87%) non-smokers), the presence of syndesmophytes (10 (47.6%) smokers, 61 ( 35.3%) non-smokers) and the presence of ultrasound coxitis (4 (31%) smokers, 17 (18%) non-smokers) (Table-2).

**Table-1: Characteristics of included patients**

Age <sup>1</sup> (years)	40.3±13.6	40.2±13.7	0.995
Male sex <sup>2</sup>	19 (90)	109 (63)	0.006
BASDAI <sup>1</sup>	2.77 ± 1.82	3.24 ± 2.15	0.378
BASFI <sup>1</sup>	3.34 ± 2.91	3.35 ± 2.38	0.985
ASDAS CRP <sup>1</sup>	2.25 ± 1.66	2.09 ± 1.7	0.707
ESR <sup>3</sup> (mm/h)	14 [6.5 – 48]	20 [8 – 35]	0.450
CRP <sup>3</sup> (mg/L)	6 [2 – 17]	5.5 [2 – 28]	0.048
HLA B27 <sup>2</sup>	6 (86)	29 (63)	0.400

1: Mean and standard deviation, 2: Number and percentage, 3: Median and interquartiles

**Table-2: Smoking and radiographic progression**

Radiographic Sacroiliitis <sup>2</sup>	20 (95)	150 (87)	0.47
Syndesmophytis <sup>2</sup>	10 (47.6)	61 (35.3)	0.34
Ultrasound Coxitis <sup>2</sup>	4 (31)	17 (18)	0.28

1: Mean and standard deviation, 2: Number and percentage, 3: Median and interquartiles

## DISCUSSION

Our study suggests that tobacco consumption is associated with the male gender and a more elevated CRP. The prevalence of smoking in patients with spondylarthritis from our series was 10.8%. It varies between 37.2% and 76% depending on the different studies reported in the literature [11-13]. This could be explained by the difference in socio-demographic parameters of the studied populations and their life habits. Male gender is significantly associated with tobacco consumption in our study corroborating with the results reported in the literature. The highest percentage was reported by Zhang and al. (348 male patients out of 425 patients included in the study, ie 81.9%) [13]. This difference can be explained by the fact that Moroccan women consider smoking as a taboo topic and do not always say the truth about their smoking habits. In our study, we found a strong correlation between biological inflammatory syndrome, essentially CRP and tobacco. This link is explained by the fact that smoking acts on the inflammation parameters through various mechanisms [14, 15] and promotes low-grade systemic inflammation [16]. Several studies have identified smoking as a factor that worsens inflammation in axial spondylarthritis [17, 20-22] and this inflammation depends on the cumulative dose of tobacco [24]. Chen and al's study of 75 AS patients (35 smokers among them) mentioned that the biological inflammatory syndrome was more significant for the smoking group with AS compared to the non smoking one [17, 23].

In addition, a few studies have reported a significant correlation between smoking and AS activity (BASDAI, ASDAS CRP) [26] as well as between smoking and functional impairment (BASFI). This association was not retrieved in our test population and this may be due, among other factors, to the small size of our sample compared to the ones studied in the literature, to the subjective nature of the BASDAI and BASFI questionnaires as well as the high illiteracy rate of our patients. In the French multicenter prospective cohort of recent undifferentiated spondylarthropathy DESIR (it included patients with recent inflammatory rachialgia of less than 3 years suggestive of spondylarthritis) [19], 37.2% of the 647 patients were smokers (old or active). Smoking was associated in multivariate analysis with a higher disease activity, assessed by BASDAI and ASAS-CRP (regardless of B27 status). In the Swiss cohort SCQM (Swiss Clinical Quality Management in Rheumatic Diseases) including 1129 patients receiving treatment for axial SA, the

smoking rate was 37%. The activity of the disease, evaluated by BASDAI, was again significantly higher in the smoking group but only in the HLA B27 positive subgroup. This was not the case in the HLA B27 negative subgroup [27]. This interaction between tobacco and HLA B27 was not found in the DESIR cohort given the much higher proportion of HLA B27 positive subjects in the Swiss cohort (84% compared to 65% in DESIR). A higher BASDAI and ASDAS were also found in the smoking group of patients with spondylarthritis in the baseline of the Swiss SCQM cohort [18].

In our series, we did not find a significant correlation between smoking and the radiographic progression of the disease (coxitis, syndesmophytes, sacroiliitis). The causal relationship between smoking and the progression of SpA is still not well established in the literature [25]. The GERman SPondylarthritis Inception Cohort (GESPIC cohort) included 210 patients with axial spondylarthritis and tried to assess the factors associated with radiographic progression (defined by an increase of the mSASSS score greater than 2 points over 2 years) [29]. In multivariate analysis, smoking appeared to be an independent factor associated with radiological progression (OR = 2.10; 95% CI: 1.03–4.30). In addition, the importance of the radiographic progression was proportional to the smoking frequency: the progression of the mSASSS score was on average  $2.20 \pm 4.62$  in heavy smokers (> 10 cigarettes per day) against  $0.48 \pm 1.48$  in light smokers ( $\leq 10$  cigarettes per day) [25, 28]. The DESIR cohort also showed that smoking was correlated with more frequent inflammatory lesions of the sacroiliac and spine on MRI.

Our work has some limitations, namely the small size of the sample and given the nature of the register, some data is missing such as the duration and the cumulative dose of smoking. These parameters are necessary when looking for a dose dependency effect on the severity of the disease as well as the search for cardiovascular comorbidities in tobacco consumers suffering from SA. In addition, we have presented the descriptive results of the inclusion data from the multicenter study of the first Moroccan and African registry of biotherapies that will monitor these patients over a period of 3 years. This will allow us to assess the impact of smoking on the outcome and the evolution of the disease.

## CONCLUSION

Our study suggests that male gender and a biological inflammatory syndrome (more elevated CRP) are significantly associated with smoking, while the latter is not linked to the functional and structural activity of the disease and its impacts. Given the relatively young age of most of our spondyloarthritis patients, it is justified to act in order to prevent smoking, or at least advise and help patients limit their tobacco consumption to reduce the additional cardiovascular risk and potentially improve their long-term prognosis.

## DECLARATIONS

**Ethics 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: Ethics committee for biomedical research Mohammed V university-RABAT. Faculty of medicine and pharmacy of RABAT. The committee's reference number: 117/17

**Consent to publish:** This project has been reviewed and accepted by the scientific committee of the RBSMR study. Moreover, this committee has reviewed this current manuscript and has agreed upon its submission to your journal.

**Availability of data and materials:** All data generated or analyzed during this study are included in this published article.

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**Competing interests:** No competing interests.

**Authors' Contributions:** We declare that we participated to the study as following: SB performed the statistical analysis and interpretation and prepared the manuscript. SR participated in the article writing and critical review of the manuscript. IH reviewed and interpreted the statistical analysis. RB participated in the critical review of the manuscript. All authors read and approved the final manuscript.

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