Clinical Rheumatology (2021) 40:3401–3410
https://doi.org/10.1007/s10067-021-05630-w

REVIEW ARTICLE

Spondyloarthritis in North Africa: an update

Samy Slimani[1] · Wafa Hamdi[2] · Kawtar Nassar[3] · Asgar Ali Kalla[4]

Received: 14 July 2020 / Revised: 6 December 2020 / Accepted: 2 February 2021 / Published online: 9 February 2021

Abstract

Spondyloarthritis (SpA) has been less well studied than rheumatoid arthritis in North Africa, due to a belief that it is rare and benign in certain populations. The main genetic trait of SpA is its association with human leukocyte antigen (HLA)-B27. The distribution of this allele largely explains the prevalence and severity of SpA. The prevalence of HLA-B27 in the general population of North Africa is estimated at about 4%, and rises to about 60% among people affected with SpA. Coxitis is one of the main features of North African SpA, but the response to treatment is comparable to the literature from the West. The major challenge in North Africa remains accessibility to specialized care and means of early diagnosis. Prevalent infections in North Africa do not seem to be a major obstacle to optimal treatment strategies.

Keywords Epidemiology · HLA-B27 · North Africa · Spondyloarthritis

Introduction

Spondyloarthritis (SpA) is a very common inflammatory condition in most of the world, but until recently, SpA was less well studied in North Africa than rheumatoid arthritis, owing to the belief that it is rare and benign in certain populations. The first description of SpA in North Africa came from a series of 78 cases of reactive arthritis during the Algerian War [1]. However, it is well known that ankylosing spondylitis (AS) existed in ancient Egypt [2]. The main genetic characteristic of SpA in Western populations is its association with human leukocyte antigen (HLA)-B27 [3]. The large distribution of this allele explains the prevalence and severity of SpA in these populations.

SpA data from North Africa are more limited than those from Europe and North America, despite the high frequency and severity of the disease in this area. Thus, the management of SpA in North Africa under these circumstances is a challenging task. In fact, a scarcity of human resources in terms of rheumatologists and allied health workers and limited access to modern imaging and biological treatments lead to delays in diagnosis and treatment, which are detrimental to patients. Nevertheless, in recent decades, several North African publications have emerged, which have improved our understanding of the epidemiology and specific features of SpA in the North African population. This review highlights the pecularities of SpA in terms of its epidemiology, diagnosis, and treatment in North African countries and attempts to identify the challenges and the areas that should be developed to improve patient care.

This article is part of the Topical Collection on *Rheumatology in Africa*

✉ Samy Slimani
slimani@dr.com

[1] Atlas Clinic, Batna, Algeria

[2] Service de rhumatologie institut M. T Kassab. UR17SP04 Faculté de médecine de Tunis, Université Tunis el Manar, Tunis, Tunisia

[3] Service de rhumatologie, Centre Hospitalier Universitaire Ibn Rochd, Faculté de médecine et de pharmacie, Université Hassan II, Casablanca, Morocco

[4] Department of Medicine, University of Cape Town, Cape Town, South Africa

Genetic particularities of North African spondyloarthritis

HLA-B27

The North African population is a mixture of Berber, Arab, Jewish, Roman, European, Mediterranean, and African people. Despite the lack of epidemiologic studies estimating the incidence of the disease in this area, SpA is commonly considered a public health concern, owing to its apparent frequency and especially its severity. Although HLA-B27 is the strongest genetic risk factor associated with SpA, its association to

the disease seems to be less strong in North African populations. In fact, most of the available data suggest that the prevalence of HLA-B27 among both healthy individuals and SpA patients is much lower in North African populations than in Western populations (Table 1) [4–13]. In Caucasian populations, most patients with AS express HLA-B27 (90%), and the frequency of this gene in the general population is approximately 8% [14, 15], whereas the majority of studies in North African populations estimate the frequency of HLA-B27 to be between 50 and 60% among SpA patients and between 3 and 4% among healthy individuals [4–14].

Variations in the frequency of the HLA-B27 allele within the same country, which is particularly observed in Morocco, could be explained by the diverse ethnicities of the studied populations. For example, a cohort from Marrakech [13] had a higher proportion of Sahrawi and Berbers, while cohorts from Rabat [12] had higher proportions of Arabs and Caucasians. The lower frequency of HLA-B27 in North African countries could suggest the involvement of other HLA genes or even genes beyond the major histocompatibility complex (MHC) system. Epigenetic and environmental factors specific to these countries should also be investigated to better understand the predisposition to SpA in this area.

Data on North African patients with non-radiographic SpA are scarce [16]. This lack of information is also noted around the world and constitutes a new research direction in the coming years [14].

Several studies have suggested that HLA-B27 influences the phenotype of SpA [16]. Numerous studies in different populations have confirmed that HLA-B27 is more frequently associated with the male sex, a family history of SpA, and an earlier disease onset [17–20]. These data have also been confirmed in North African populations [6, 12, 15, 16, 20]. A Tunisian study found that HLA-B27-positive patients had an earlier disease onset, more frequent uveitis, more frequent bilateral and destructive hip arthritis, and a higher modified Stoke Ankylosing Spondylitis Spinal score (mSASSS) than HLA-B27-negative patients [19]. A Moroccan study reported similar findings, with an earlier onset, more frequent uveitis, and a higher likelihood of a family history of SpA in HLA-B27-positive patients than in HLA-B27-negative patients [12].

Khan [21] reported in 2017 more than 160 subtypes of *HLA-B27* have been identified and found to be encoded by 213 allelic variants, and at the latest update on EBI search database, 231 subtypes of *HLA-B27* have been identified and encoded by 328 allelic variants [22]. Their worldwide distribution is influenced mainly by ethnicity. The most common subtypes in the North African population are B*2705 and B*2702 [7, 8, 12, 15]. This distribution is valid for both SpA patients and healthy individuals and matches the Mediterranean genotype. B*2702 follows a West-to-East gradient, and is the predominant allele in more Eastern populations, such as the Greek [23], Greek Cypriot [23], Lebanese, Turkish, and Jewish populations [24–27]. In contrast, B*2705 follows a North-South distribution and is commonly found in the French [28], Croatian, and Spanish populations [29–31]. However, these alleles do not seem to influence the SpA phenotype in the North African population [7, 8, 12]. This is

Table 1 Prevalence of *HLA-B27* and subtypes in North African patients with spondyloarthritis

Country	Study	HLA-B27 among SpA patients		HLA-B27 among healthy individuals		
		%	No. of patients	B27 subtypes	%	No. of individuals
Egypt	Tayel MY [1] Registry	58.5%	75 [ESSG]	N/A	N/A	
Tunisia	Sakly N [2] Case control	42.9%	365 SpA and/or BD*	N/A	3.2%	124
	Mahfoudh N [3]	62.3%	64 [ESSG]	N/A	3%	100
	Kchir MM [4] Case control	62%	100 [NY m]	B*27 02: 32% B*27 05: 24%	3%	100
	Ben Radhia [5] Case control		121[NY m]	B*27 02: 47% B*27 05: 47%	B*27 02: 41% B*27 05: 41%	39
	Siala M [6]		42	B*27 02: 42% B*27 05: 57%		100
Algeria	Dahmani C.A [7] Case Control	52%	81	N/A	5%	116
	Amroun H [8] Case control	69%	129 SpA (ESSG and NYm)		4%	76
Morocco	El Mouraghi I [9] Case control	64%	75	*B*2705:* 43.7% *B*2702:* 20.8%	6%	100
	Akassou A [10] Case control	45.3%	53 [AMOR and ESSG]		4.7%	128

*Behcet disease

contrary to the findings reported for Asian populations, for whom HLA-B27 polymorphisms may affect disease phenotype, particularly B*2704 and B*27015, which are associated with earlier disease onset and more frequent uveitis than B*2705 among Asian patients [15, 32–39]. It is important to note, however, that the small sample sizes in many of the North African studies preclude a definitive conclusion about the influence of HLA-B27 subtypes on the phenotype of SpA in this population.

Other MHC genes

Many studies have analyzed the HLA-A, HLA-B, HLA-C, HLA-DRB1, and HLA-DQB1 genes in North African patients with SpA [6, 11, 12, 16, 40–42]. El Mouraghi et al. [12] found a significant increase in the prevalence of *HLA-Cw*02* and *HLA-DRB*15* in Moroccan SpA patients.

In a Tunisian study of 100 SpA patients and 100 healthy controls, Kchir et al. [11] found a significant increase in the frequencies of DRB1*11 and DQB1*03 in the SpA group and a negative association of these two alleles with DRB1*13. Multivariate logistic regression analysis revealed that DRB1*11 and DQB1*03 had no direct links with the disease, but were dependent on the presence of HLA-B27. Moreover, B*07 and B*51 seemed to have an independent negative correlation with SpA, but DRB1*13 seemed to depend on B*51 [11]. Mahfoudh et al. [6] found that HLA-DRB1*15 and HLA-A3 were increased in 68 Tunisian SpA patients, but analysis of the HLA-B27-negative subgroup showed that both HLA-DRB1*15 and HLA-A3 expressions were dependent on the presence of HLA-B27. On the other hand, it is important to note that HLA-DRB1*15 has been independently and negatively associated with SpA but positively associated with uveitis in patients with SpA in large studies of European and North American population [43–45].

Some studies have reported an increased incidence of B7-CREG antigens (B7, B22, and B40) in HLA-B27-negative Caucasian and Black American SpA patients, but these results could not be confirmed in other racial groups, particularly in North Africa [40]. Otherwise, recent studies have found a significantly diminished frequency of HLA-B7 with even a protective effect of the subtype HLA-B*07:02 (OR: 0.82) in European descendent patients but increased frequency of HLA-B40 with increased risk with the subtype HLA-B*40:01 (OR: 1.22) [43]. These data were also confirmed in Whites, Blacks, and Han Chinese patients with SpA confirming that other HLA class I and II alleles than HLA-B*27 to be operative in SpA predisposition [44]. More studies controlling the dominant effect of HLA-B27 were needed to demonstrate the role of HLA B40 [43–47].

Moreover, numerous studies have revealed that the gene-gene interaction between HLA-B60 and HLA-B27 increases the risk of SpA susceptibility [15, 41, 42]. However, these data have not been found in the North African population, highlighting the genotypic singularity of this population.

The JAK-STAT pathway and gene-to-gene interactions have been assessed in Algerian and Han Chinese SpA cohorts [48]. This study revealed a difference in the allelic frequency of rs321222 in the interleukin (IL)-12β gene between SpA patients and controls in both the Han Chinese and Algerian cohorts. Two other associations were reported with JAK2 rs7857730 in the Han Chinese allelic p cohort and STAT3 rs2293152 in the Algerian cohort [49]. Moreover, logistic regression analyses showed several significant combinations within the Algerian and Han Chinese populations, and the gene-gene epistasis effects in SpA were confirmed in both cohorts [48].

In an Algerian study, Amroun et al. [10] assessed polymorphisms of MHC class I chain–related A (MICA) molecules and their relationship to SpA susceptibility in a cohort of 129 SpA patients and 76 healthy controls. The authors demonstrated an association between the MICA-129 met/met genotype and juvenile-onset SpA, independently of *HLA-B27* status [10].

Along with gene polymorphism, functional abnormalities such as the transmitted copy number variation seem to play a role in SpA susceptibility [50]. Some studies have shown that the copy number variations of some genes, particularly FCGR3A, FCGR3B, and CCL3L1, were associated with several autoimmune disorders [51–55]. Only two studies, including an Algerian study, have assessed these genes in SpA patients [50, 56]. Dahmani et al. [57] revealed that the *CTLA4* gene *Polymorphism* (SNP) *CT60**G allele increased susceptibility to SpA in *HLA-B27*-negative individuals. These studies suggest that some genes such as FCGR*3A* and the *CTLA4* gene *Polymorphism* (SNP) *CT60**G allele may be involved in the susceptibility to SpA in the Algerian population, independent of the *HLA-B27* status [56, 57]. In fact, the FCGR3A association seen in Algerian SpA patients was particularly interesting, as it is located very near FCGR2A, which has been found to be associated with SpA in well powered genome wide association studies in European and North American white populations [58]. Additional studies in North African populations are required to confirm these findings.

Clinical features

In North Africa and the Middle East, the disease measures used for the diagnosis and management of patients with SpA include the various physical components of the disease, such as morning stiffness (duration of spinal stiffness in the past week), lumbar flexion (Schober test), chest expansion, lateral spinal flexion, occiput-to-wall distance, and tragus-to-wall distance [59]. Regional experts from North Africa and the Middle East have reported that conventional scoring methods are regularly used for patient visits, including the Ankylosing

Spondylitis Disease Activity Score, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), Visual Analog Scale (VAS) to evaluate spinal pain, and Ankylosing Spondylitis Quality of Life Questionnaire to measure the health-related quality of life [59].

Axial and peripheral articular and enthesis manifestations

In Algeria, a prospective study was carried out on a cohort of 400 SpA patients to highlight patient characteristics [60]. The study included 295 (73.75%) male patients and 105 (26.25%) female patients, with an average age of 39.41 ± 11.70 years. The mean age at disease onset was 23.68 ± 9.73 years, and 106 (26.5%) patients had a juvenile onset (≤16 years). A family history of SpA was found in 86 (21.5%) patients. The average BASMI was 5.05 ± 2.33. Axial involvement was present in 305 (76.25%) patients, including 118 (29.5%) patients with fixed kyphosis. In another Algerian observational prospective study, 325 SpA patients were included [61]. Axial involvement was found in 223 (68.5%) patients, including 197 (61.2%) patients with spinal stiffness. The disease was active in 183 (56.8%) patients, with an average BASDAI of 5.6 ± 1.8. Sacroiliitis was found in 291 (72.75%) patients.

A Moroccan study focused on cervical spine involvement in AS [62] with the aim of evaluating correlations between disease symptoms and structural severity. Among the 61 enrolled patients, there were 38 (62.3%) males and 23 (37.7%) females, with a mean age of 35.1 years (range, 17–66 years) and a mean disease duration of 10.6 years (range, 0.5–30 years). In all, 43 (70.4%) patients had a history of inflammatory neck pain with limitation of range of motion on at least one of the tests used in the clinical examination. Furthermore, a cross-sectional study investigated spinal mobility and its impact in Moroccan patients with AS [63]. Spinal mobility was assessed using metrological scores. Impaired spinal mobility (higher BASMI scores) was significantly correlated with prolonged disease duration, severe functional disability (BASFI), and deterioration of most domains of the Short Form (SF)-36 ($p < 0.001$).

In Tunisia, a study was conducted to assess the clinical, radiographic, and biologic particulars of AS according to *HLA-B27* and its subtypes. Among the 100 included patients (85 males/15 females; mean age, 38.4 ± 12.6 years), 62 were positive for *HLA-B27*. A comparison of the *HLA-B27*-positive and *HLA-B27*-negative patients revealed that *HLA-B27* was correlated with age, male sex, family history of spondylarthropathies, age at disease onset, acute onset, spinal involvement at presentation, uveitis, bilateral and destructive hip arthritis, and high mSASSS [19].

Foot involvement in AS has been the subject of several studies. A review of 26 Moroccan patients with psoriatic arthritis and foot involvement was published [64]. Time from symptom onset to diagnosis of 4.5 ± 3.3 years (range, 0.5–9 years). Of the 26 patients, 14 patients reported inflammatory heel pain, 7 patients had forefoot involvement, and 2 patients presented with sausage toe. None of the patients had Bauer toe (combined arthritis and psoriatic skin and/or nail changes) or psoriatic onychopachydermoperiostitis of the great toe. A cross-sectional study of 60 Tunisian patients with SpA [65] showed that foot involvement was present in 31 (52%) patients. It was symptomatic in 35% of patients and present since disease onset in 42% of patients. The most frequent site was the hindfoot (22 patients), and forefoot involvement was found in 18 patients. Forefoot deformities were found in 9 patients,

A 2012 study of AS in Moroccan patients and its relationships with disease parameters [66] evaluated enthesitis using the Mander enthesis index and the Maastricht Ankylosing Spondylitis Enthesitis Score. Among the 76 included patients, the most frequent sites of enthesitis were the costochondral joints, calcaneal insertions, and Achilles tendons, and less frequently involved sites were the thoracic spinous process and ischial tuberosities.

Extra-articular features and comorbidities

According to one review, the extra-articular manifestations of AS include anterior uveitis (20–30%), inflammatory bowel disease (5–10%), histological inflammation of the gut (50–60%), lung abnormalities on high-resolution computed tomography (HRCT; 52%), heart conduction disturbances (3–33%), aortic insufficiency (6–10%), psoriasis (10–25%), renal abnormalities (10–35%), osteoporosis (11–18%), and vertebral fractures (10–18%) [66]. The international cross-sectional ASAS-COMOSPA study, which included North African countries, investigated the prevalence of comorbidities and their evaluation during the screening of SpA [67]. The most frequent comorbidities were osteoporosis (13%) and gastroduodenal ulcer (11%), and the most frequent risk factors or comorbidities were hypertension (34%), smoking (29%), and hypercholesterolemia (27%).

A study of 80 Moroccan patients with AS [68] found that 25% of patients had osteoporosis, and 18.8% of patients had grade 2 or 3 vertebral fractures. Factors associated with osteoporosis were low weight and body mass index, longer disease duration, and higher erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), BASFI, and BASDAI. Vertebral fractures were associated with advanced age, longer disease duration, higher BASFI, Bath Ankylosing Spondylitis Radiology Index (BASRI), and mSASSS, reduced bone mineral density and T-score of the hip, and presence of osteoporosis at any site. Another study explored the relationships

among pre-sarcopenia, sarcopenia, cachexia, and osteoporosis in 67 AS patients as compared to healthy controls [69]. The prevalence rates of pre-sarcopenia, sarcopenia, cachexia, and osteoporosis were 50.4%, 34.3%, 11.9%, and 16.0%, respectively.

In a study of pulmonary involvement in AS, 44 consecutive Moroccan AS patients without respiratory symptoms underwent pulmonary function tests, posteroanterior chest radiography, and HRCT of the thorax [70]. Plain radiography was abnormal in only 2 patients, but 24 (55%) patients showed abnormalities on HRCT. Twenty (45%) patients had mild non-specific interstitial abnormalities of insufficient severity or extent, labelled as interstitial lung disease. Pulmonary function tests showed a restrictive pattern in 8 patients: 3 of these patients had a normal chest on HRCT, 3 had interstitial lung disease, and 2 patients had non-specific interstitial abnormalities (blebs, pleural thickening, and parenchymal bands). Two patients had obstructive lung disease; one of these patients had a normal chest HRCT, and the other patient had emphysema and apical fibrosis. In an Algerian study, respiratory involvement was present in 46% of patients, and uveitis was present in 20% of patients [60].

Psychological impact and quality of life

A Moroccan study evaluated the psychological status of patients with ankylosing spondylitis and its relationship with disease parameters and quality of life [71]. Depression was found in 55.5% and anxiety in 60% of the 110 patients included in the study. The subscales of the Hospital Anxiety and Depression Scale were significantly correlated with clinical parameters and with worsening in all domains of the SF-36. Another study examined fatigue in patients with AS [72]. A study that assessed the health-related quality of life in AS patients [73] reported deterioration (low scores) in all domains of the SF-36. The most affected SF-36 subgroups were role limitation (18.8 ± 28.1), role emotional (19.4 ± 35), general health (44.9 ± 20.3), and vitality (38.0 ± 18.2). Lower scores on the SF-36 were highly correlated with altered functional status (BASFI), worse general well-being (Bath Ankylosing Spondylitis General Index), altered metrology (BASMI); and moderately correlated with high disease activity (BASDAI), important radiological damage (BASRI), restricted chest expansion, and prolonged morning stiffness ($p < 0.001$).

A Tunisian study looking at the prevalence of depression and anxiety in SpA found that 31% of the included patients were depressed and 39% had anxiety [74]. The risk factors for depression and anxiety among SpA patients were a VAS score for fatigue > 50, morning stiffness > 15 minutes, BASDAI > 4, BASFI > 4, Bath Ankylosing Spondylitis Patient Global Score > 50, and a high Functional Assessment of Chronic Illness Therapy-Fatigue scale score.

Imaging in spondyloarthritis in North Africa: challenges and unmet needs

Data regarding the use of modern imaging tools in the diagnosis and management of patients with SpA in North Africa are scarce and focused mainly on ultrasonography. The use of magnetic resonance imaging (MRI), in particular, for the diagnosis of non-radiographic SpA, is less common than in European or North American countries. Although MRI facilities are widely available in North African hospitals, access to these facilities remains limited mainly due to the costs generated by these facilities.

Thus, limited information is available on the prevalence of non-radiographic axial SpA among patients with inflammatory back pain in North African countries. Indeed, only one study on non-radiographic axial SpA in North African patients has been reported to date. This study consisted of a post hoc subset analysis of a global study focused on estimating the prevalence of non-radiographic axial SpA among patients with inflammatory back pain from Morocco and Algeria [16]. The study found that of the 168 patients with inflammatory back pain from Northwest Africa, 26 (15.5%) were diagnosed with non-radiographic axial SpA [17], while in the global cohort of patients with inflammatory back pain, 29.10% of patients met the criteria for non-radiographic axial SpA. Moreover, the prevalence of non-radiographic axial SpA varied significantly by region, with the highest prevalence being reported in Asia (36.46%) and the lowest being reported in Africa (16.02%); in Latin America and Europe, the prevalence was 19.2% and 29.5%, respectively [75].

Unlike MRI, ultrasonography is a much more widely available tool, and its use is more widespread in North African countries. This is particularly due to the availability of low-cost ultrasound equipment and the training of many rheumatologists in ultrasound examination. Entheseal involvement in SpA has been particularly assessed. A prospective Tunisian study of 60 patients who met the modified New York criteria for SpA compared the clinical, radiographic, and ultrasonographic assessments of 5 peripheral entheses (patellar insertion of the quadriceps tendon, proximal and distal insertions of the patellar tendon, and calcaneal insertions of the Achilles tendon and superficial plantar fascia) [76]. The authors found a good correlation between the clinical and ultrasonographic scores for enthesitis, whereas the radiographic score seemed to correlate with the general parameters of SpA rather than with the clinical scores of enthesitis. The authors also found that ultrasonography had excellent sensitivity but weak specificity, as compared with radiography, for the detection of erosion, swelling, and new bone formation. Hence, ultrasonography seems to be a useful instrument in detecting the signs of chronic enthesitis, particularly when radiography is normal [77].

Ali Ou Alla et al. [78] assessed the ultrasound features of shoulder involvement in Moroccan patients with SpA in a

case control study. They found that shoulder enthesitis on ultrasonography was significantly more common in patients with SpA than in control subjects (56.6% versus 10.5%). Involvement of the rotator cuff tendons was significantly more common in SpA patients than in controls; however, involvement of the gleno-humeral and acromio-clavicular joints was infrequent in both groups [78]. Further studies are necessary to evaluate the frequency and specificities of enthesis involvement in patients with SpA in North Africa and to determine the role of ultrasonography in the management of these patients.

Diagnosis

The cultural and genetic differences between North Africa and the Middle East are likely to affect screening strategies, which will need to be validated or developed locally [59]. The typical profile of a patient with non-radiographic axial SpA in North Africa and the Middle East is a young patient with inflammatory low back pain, poor response to analgesics, normal X-rays, asymmetrical arthritis, and unexplained ankle swelling with Achilles tendinitis [59]. In most studies performed in North Africa, the diagnosis of SpA relies on the modified New York criteria for AS [79]. For the diagnosis of non-radiographic axial SpA, the majority of experts practicing in this region use the ASAS classification criteria [61]. MRI is a key component in the diagnosis of this specific pattern, and although it is widely available in hospitals, there are issues restricting its use; there may be a long waiting list for MRI in some of the hospitals in the region, which may lead to a delay in diagnosis [59].

A Moroccan study aimed to determine the relationship between diagnostic delay and disease features in 100 patients with AS [80]. The average age at disease onset among the included patients was 28.56 ± 10.9 years, and juvenile-onset AS was present in 16% of the patients. The average disease duration was 9.5 ± 6.8 years, and the average diagnostic delay was 4.12 ± 3.99 years. There were no differences in diagnostic delay according to the age at onset, educational level, or the presence of extra-articular involvement. Patients with late diagnosis (>5 years) had significantly higher structural damage (BASRI) and severely limited spinal mobility. There was no correlation between diagnostic delay and disease activity. In an Algerian study, the average diagnostic delay was 6.11 years ± 6.7 [60].

Several studies have aimed to identify local normative values, define cutoff points, and develop novel indexes. In a study from Morocco, values of the BASFI in the general population as compared with AS patients were used to evaluate the discriminating power of the BASFI and determine its best cutoff score [81]. The median BASFI of the healthy subjects and AS patients were 0.2 and 4.5 ($p < 0.001$), respectively. Overall, the best cutoff of the BASFI was 1.5 (sensitivity, 86%; specificity, 90%), while the best cutoffs in the age groups of 18–29 years, 30–50 years, and over 50 years were 0.9 (sensitivity, 93%; specificity, 94%), 1.5 (sensitivity, 84%; specificity, 88%), and 2.5 (sensitivity, 84%; specificity, 97%), respectively. Another study compared the BASDAI and an alternative index, the mini-BASDAI, for the assessment of disease activity in patients with AS [82]. The aim was to determine whether the mini-BASDAI [(Question (Q) 1 fatigue + Q2 spinal pain) + mean of (Q5 strength morning stiffness + Q6 duration morning stiffness)]/3] accurately measures disease activity in the subgroup of AS patients without peripheral manifestations. Like the original BASDAI, the mini-BASDAI showed good correlation with the patient global and physician disease activity scores, the BASFI, ESR, and CRP in AS patients without peripheral involvement.

Management

The objectives of treatment in SpA are to control inflammatory flares of the disease, reduce pain and stiffening, and maintain functional capacity. Pharmacological treatment is based on the use of analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) [83]. In case of insufficient efficacy of these drugs, the use of a disease-modifying antirheumatic drug (DMARDs) may be considered. DMARDs are part of a global management strategy, including rehabilitation and patient education as well as local treatments and rarely surgery.

Non-pharmacological treatment

There are many non-pharmacological treatments for SpA, including self-exercises and group exercises. They have been demonstrated to improve activity indices (BASDAI) and functional indices (BASFI), and are generally inexpensive, making their application possible in low- and middle-income countries [83, 84].

Pharmacological treatments

NSAIDs are the most commonly used drugs to treat SpA patients. More than 80% of SpA patients take NSAIDs continuously or intermittently [85]. Their symptomatic and structural effectiveness has long been known, but they result in moderate tolerance when taken over the long term and in high doses.

A 2010 Tunisian study reviewed the treatments administered to patients with axial SpA [86]. Of the 50 patients included in this study, 44 had predominant axial impairment. The average age of the patients was 39 years. The main DMARDs were sulfasalazine (23 patients), methotrexate (2 patients), and infliximab (2 patients). Corticosteroid injections

were administered to 16 patients. Rehabilitative care was reported in 33 patients, consisting essentially of self-rehabilitation exercises and thermal cures. Six patients underwent surgery, mainly prosthetic hip replacement.

A multicenter Egyptian registry detailed the prescriptions of 75 SpA patients. NSAIDs were taken by more than 95% of patients, while oral corticosteroids were taken by 6% of patients. Sulfasalazine and methotrexate were taken by 52% and 51% of patients, respectively, and 14% of patients were administered bDMARDs, mainly infliximab [4].

In North Africa, anti-TNF-α agents seem to have the same efficacy as in Western populations. The percentage of SpA patients on anti-TNF-α agents was estimated at 12% of all patients in an Algerian study [54]. Another Algerian study of 30 SpA patients with coxitis evaluated the effectiveness of anti-TNF-α agents and found an improvement in the Harris score (a score specific to clinical involvement of the hip), in addition to improvements in the BASDAI, BASFI, and CRP [87]. In addition, these agents were well tolerated, with no serious adverse events.

Overall, the patient tolerance to bDMARDs is good, apart from a risk of infections, which justifies a preliminary search for latent tuberculosis and standardized screening and management of the various clinical situations with which the patient is likely to be confronted. In North Africa, in addition to the risk of tuberculosis, there is an average-to-high prevalence of hepatitis B and C in certain regions, which should not be overlooked. In an Algerian study of 152 SpA patients on anti-TNF-α agents (90 on etanercept, 66 on adalimumab, and 8 on infliximab), representing a follow-up of 279 patient-years, the rate of severe infections was 2.9/100 patient-years, and 2 patients developed tuberculosis during anti-TNF-α treatment [88].

One of the major obstacles to the prescription of bDMARDs in North African countries is their accessibility, which is limited by their high cost. In Algeria, anti-TNF-α agents are available only in hospitals and are provided free of charge, but waiting times can sometimes be long. In Tunisia, Morocco, and Egypt, subcutaneous bDMARDs are available in pharmacies, but social security coverage is available to a small part of the population. Anti-IL-17 and JAK inhibitors will be available soon in Tunisia and Algeria, whereas anti-IL-17 treatment is already available in Morocco.

Recommendations

Global recommendations for the therapeutic management of SpA have been published and are regularly updated by the ACR, EULAR, and ASAS. These reports generally recommend the use of non-pharmacological means in all cases, and the use of NSAIDs first, followed by bDMARDs in the case of ineffectiveness or failure of NSAIDs.

In North Africa, the Moroccan Rheumatology Society (SMR) published national recommendations for the therapeutic management of AS in 2017 [89]. These recommendations advise the use of at least 3 NSAIDs at maximum dosage for 2 weeks each, before considering DMARD treatment. Anti-TNF-α agents are recommended as the first line of bDMARDs, and for the second line of treatment, the SMR recommends a choice between a second anti-TNF-α agent and secukinumab.

Local recommendations for the management for patients with SpA in Tunisia were communicated during the Maghrebian Congress of Rheumatology held in Hammamet, on the 19 and 20 April 2019, and are currently submitted to an authority for approval and will be published soon.

Conclusion

In recent decades, knowledge about the epidemiology and specificity of SpA in North Africa has increased considerably. We now know that SpA in North Africa is frequent, partially dependent on *HLA-B27*, and more severe than SpA in Western countries due to a very high prevalence of coxitis. The response to treatment is comparable to Western countries. The major challenges in North Africa remain accessibility to specialized care and means of early diagnosis. Prevalent infections, particularly tuberculosis, in North Africa do not seem to be a major obstacle to optimal treatment strategies which include biologics.

Declarations

Disclosures None.

References

1. Pernod J, Bruneaux J (1960) Bull Mem Soc Med Hop Paris 76: 351–356
2. Feldtkeller E, Lemmel EM, Russell AS (2003) Ankylosing spondylitis in the pharaohs of ancient Egypt. Rheumatol Int 23(1):1–5. https://doi.org/10.1007/s00296-002-0242-7
3. Braun J, Sieper J (2007) Ankylosing spondylitis. Lancet 369:1379–1390
4. Tayel MY, Soliman E, El Baz WF, El Labaan A, Hamaad Y, Ahmed MH (2012) Registry of the clinical characteristics of spondyloarthritis in a cohort of Egyptian population. Rheumatol Int 32(9):2837–2842. https://doi.org/10.1007/s00296-011-2068-7
5. Sakly N, Boumiza R, Zrour-Hassen S, Hamzaoui A, Ben Yahia S, Amara H, Khairallah M, Mahjoub S, Bergaoui N, Ghedira I (2009) HLA-B27 and HLA-B51 Determination in Tunisian healthy subjects and patients with suspected ankylosing spondylitis and Behcet's disease Ann. N.Y. Acad Sci 1173:564–569. https://doi.org/10.1111/j.1749-6632.2009.04756.x
6. Mahfoudh N, Siala M, Rihl M, Kammoun A, Frikha F, Younes M, Gdoura R, Gaddour L, Hakim F, Bahloul Z, Baklouti S, Bargaoui N, Sellami S, Hammami A, Makni H (2011) Association and

frequency of HLA-A, B and HLA-DR genes in south Tunisian patients with spondyloarthritis (SpA). Clin Rheumatol 30:1069–1073. https://doi.org/10.1007/s10067-011-1705-6
7. Ben Radhia K, Ayed-Jendoubi S, Sfar I, Ben Romdhane T, Makhlouf M, Gorgi Y, Ayed K (2008) Distribution of HLA-B*27 subtypes in Tunisians and their association with ankylosing spondylitis. Joint Bone Spine 75:172–175. https://doi.org/10.1016/j.jbspin.2007.05.020
8. Siala M, Mahfoudh N, Gdoura R, Younes M, Fourati H, Kammoun A, Cheour I, Meddeb N, Gaddour L, Hakim F, Baklouti S, Bargaoui N, Sellami S, Hammami A, Makni H (2009) Distribution of HLA-B27 and its alleles in patients with reactive arthritis and with ankylosing spondylitis in Tunisia. Rheumatol Int 29:1193–1196. https://doi.org/10.1007/s00296-009-0840-8
9. Dahmani CA, Benzaoui A, Amroun H, Mecabih F, Sediki FZ, Zemani-Fodil F, Fodil M, Boughrara W, Mecheti B, Attal N, Mehtar N, Petit-Teixeira E, Boudjema A (2018) Association of the HLA-B27 antigen and the CTLA4 Gene CT60/rs3087243 polymorphism with ankylosing spondylitis in algerian population: a case-control study. Int J Immunogenet 45(3):109–117
10. Amroun H, Djoudi H, Busson M, Allat R, El Sherbini SM, Sloma I et al (2005) Early onset ankylosing spondylitis is associated with a functional MICA polymorphism. Hum Immunol 66:1057–1061
11. Kchir MM, Hamdi W, Laadhar L, Kochbati S, Kaffel D, Saadellaoui K, Lahmar H, Ghannouchi MM, Azzouz D, Daoud L, Ben Hamida A, Zouari B, Zitouni M, Makni S (2010) HLA-B, DR and DQ antigens polymorphism in Tunisian patients with ankylosing spondylitis (a case–control study). Rheumatol Int 30:933–939. https://doi.org/10.1007/s00296-009-1079-0
12. El Mouraghi I, Ouarour A, Ghozlani I, Collantes E, Solana R, El Maghraoui A (2015) Polymorphisms of HLA-A, -B, -Cw and DRB1 antigens in Moroccan patients with ankylosing spondylitis and a comparison of clinical features with frequencies of HLA-B*27. Tissue Antigens 85:108–116
13. Akassou A, Yacoubi H, Jamil A, Dakka N, Amzazi S, Sadki K, Niamane R, Elhassani S, Bakri Y (2015) Prevalence of HLA-B27 in Moroccan healthy subjects and patients with ankylosing spondylitis and mapping construction of several factors influencing AS diagnosis by using multiple correspondence analysis. Rheumatol Int 35(11):1889–1894
14. Bohn R, Cooney M, Deodhar A, Curtis JR, Golembesky A (2018) Incidence and prevalence of axial spondyloarthritis: methodologic challenges and gaps in the literature. Clin Exp Rheumatol 36:263–274
15. Akassou A, Bakri Y (2018) Does HLA-B27 Status influence ankylosing spondylitis phenotype? Clin Med Insights Arthritis Musculoskelet Disord 8(11):1179544117751627. https://doi.org/10.1177/1179544117751627
16. Shirazy K, Hajjaj-Hassouni N, Hammond C, Jones H, Ladjouze Rezig A, Pedersen R, Vlahos B (2018) The prevalence of non-radiographic axial spondyloarthritis among patients with inflammatory back pain from Northwest and South Africa: data from a noninterventional, cross-sectional study. Rheumatol Ther 5:437–445
17. Ziadé N (2017) HLA B27 antigen in Middle Eastern and Arab countries: systematic review of the strength of association with axial spondyloarthritis and methodological gaps. BMC Musculoskelet Disord 18:280. https://doi.org/10.1186/s12891-017-1639-5
18. Chung HY, Machado P, van der Heijde D, D'Agostino MA, Dougados M (2011) HLA-B27 positive patients differ from HLA-B27 negative patients in clinical presentation and imaging: results from the DESIR cohort of patients with recent onset axial spondyloarthritis. Ann Rheum Dis 70(11):1930–1936. https://doi.org/10.1136/ard.2011.152975
19. Hamdi W, Kaffel D, Ghannouchi MM, Laadhar L, Makni S, Kchir MM (2012) Clinical, radiographic and biologic particularities of ankylosing spondylitis in Tunisian patients according to the presence or the absence of the HLA B27 and its sub-types. Rev Med Liege 67(7-8):430–436
20. Claudepierre P, Gueguen A, Ladjouze A, Hajjaj-Hassouni N, Sellami S, Amor B, Dougados M (1995) Predictive factors of severity of spondyloarthropathy in North Africa. Br J Rheumatol 34(12):1139–1145. https://doi.org/10.1093/rheumatology/34.12.1139
21. Khan MA (2017) An update on the genetic polymorphism of HLA-B*27 with 213 alleles encompassing 160 subtypes (and still counting). Curr Rheumatol Rep 19:9. https://doi.org/10.1007/s11926-017-0640-1
22. Allele search Tool. https://www.ebi.ac.uk/cgi-bin/ipd/imgt/hla/allele.cgi. Accessed 02 December 2020
23. Varnavidou-Nicolaidou A, Karpasitou K, Georgiou D et al (2004) HLA B27 in the Greek Cypriot population distribution of subtypes in patients with ankylosing spondylitis and other HLA B27 related diseases. The possible protective rôle of B*2707. Hum Immunol 65:1451–1454. https://doi.org/10.1016/j.humimm.2004.08.177
24. Scordaki Z, Spyropoulou-Vlachou M, Vrani V et al (2003) Polymorphism of HLA-B27 alleles in association with HLA-B27 related diseases in Greek population. Hum Immunol 1:S144#195
25. Khan MA (1997) Prevalence of HLA B27 in world populations. In: Lopez-Larrea C (ed) HLA B27 in the development of spondyloarthropathies. Landes Spinger, Austin, pp 1–16
26. Tamouza R, Awada H, Marzais F (1997) HLA B27 in the Lebanese population: subtypes analysis and association with ankylosing spondylitis. In: Charron D et al (eds) Genetic diversity of HLA: functional and medical implications. EDK, Paris, p 649
27. Gonzalez-Roces S, Brautbar C, Pena M et al (1994) Molecular analysis of HLA B27 haplotypes in Caucasoids. frequencies of B27-Cw in Jewish and Spanish populations. Hum Immunol 41:127–134. https://doi.org/10.1016/0198-8859(94)90005-1
28. Oguz FS, Ocal L, Diler AS et al (2004) HLAB27 subtypes in Turkish patients with spondyloarthropathy and healthy controls. Dis Markers 20:309–312
29. Marsh SGE, Albert ED, Bodmer WF et al (2005) WHO nomenclature committee for nomenclature factors of the HLA system 2004. Tissue Antigens 65:301. https://doi.org/10.1111/j.1399-0039.2005.00379.x
30. Fernandez-Sueiro JL, Alonso C, Blanco FJ et al (2004) Prevalence of HLA B27 and subtypes of HLAB27 associated with ankylosing spondylitis in Galicia, Spain. Clin Exp Rheumatol 122:465–468
31. Grublic Z, Kerhin-Brkljacic V, Peric P et al (2001) Variation in HLA B27 gene subtypes and susceptibility of ankylosing spondylitis in the Croatian population. Reumatizam 48:7–11
32. Fraile A, Martin J, Lopez-Nevot MA et al (1998) HLA B27 subtyping by PCR RFLP in Spanish patients with ankylosing spondylitis. Tissue Antigens 52:492–496
33. Wu Z, Lin Z, Wei Q, Gu J (2009) Clinical features of ankylosing spondylitis may correlate with HLA-B27 polymorphism. Rheumatol Int 29:389–392
34. Fallahi S, Mahmoudi M, Nicknam MH et al (2013) Effect of HLA-B*27 and its subtypes on clinical manifestations and severity of ankylosing spondylitis in Iranian patients. Iran J Allergy Asthma Immunol 12:321–330
35. Mou Y, Zhang P, Li Q et al (2015) Clinical features in juvenile-onset ankylosing spondylitis patients carrying different B27 subtypes. Biomed Res Int 2015:594878
36. Qi J, Li Q, Lin Z et al (2013) Higher risk of uveitis and dactylitis and older age of onset among ankylosing spondylitis patients with HLA-B*2705 than patients with HLA-B*2704 in the Chinese population. Tissue Antigens 82:380–386

37. Chavan H, Samant R, Deshpande A, Mankeshwar R (2011) Correlation of HLA B27 subtypes with clinical features of ankylosing spondylitis. Int J Rheum Dis 14:369–374
38. Mou Y, Wu Z, Gu J et al (2010) HLA-B27 polymorphism in patients with juvenile and adult-onset ankylosing spondylitis in Southern China. Tissue Antigens 75:56–60
39. Lee SH, Choi IA, Lee YA et al (2008) Human leukocyte antigen-B*2705 is the predominant subtype in the Korean population with ankylosing spondylitis, unlike in other Asians. Rheumatol Int 29: 43–46
40. Khan MA (1983) B7-CREG and ankylosing spondylitis. Br J Rheumatol 22(4 Suppl 2):129–133
41. Van Gaalen FA, Verduijn W, Roelen DL, Böhringer S, Huizinga TWJ, van der Heijde D, Toes RE (2013) Epistasis between two HLA antigens defines a subset of individuals at a very high risk for ankylosing spondylitis. Ann Rheum Dis 72:974–978. https://doi.org/10.1136/annrheumdis-2012-201774
42. Wei JC, Sung-Ching HW, Hsu YW, Wen YF, Wang WC, Wong RH, Lu HF, van Gaalen F, Chang WCH (2015) Interaction between HLA-B60 and HLA-B27 as a better predictor of ankylosing spondylitis in a Taiwanese population. PLoS One 10:e0137189
43. Cortes A, Pulit SL, Leo PJ, Pointon JJ, Robinson PC, Weisman MH (2015) Major histocompatibility complex associations of ankylosing spondylitis are complex and involve further epistasis with ERAP1. Nat Commun 21(6):7146. https://doi.org/10.1038/ncomms8146
44. Reveille JD, Zhou X, Lee M, Michael H, Weisman MH, Yi L, Lianne S, Gensler LS, Zou H (2019) HLA class I and II alleles in susceptibility to ankylosing spondylitis. Ann Rheum Dis 78(1):66–73. https://doi.org/10.1136/annrheumdis-2018-213779
45. Huang XF, Li Z, De Guzman E, Robinson P, Gensler L, Ward MM et al (2020) Genomewide association study of acute anterior uveitis identifies new susceptibility loci. Invest Ophthalmol Vis Sci 61(6): 3. https://doi.org/10.1167/iovs.61.6.3
46. Payami H, Joe S, Farid NR, Stenszky V, Chan SH, Yeo PP, Cheah JS, Thomson G (1989) Relative predispositional effects (RPEs) of marker alleles with disease: HLA-DR alleles and Graves disease. Am J Hum Genet 45(4):541–546
47. Díaz-Peña R, Vidal-Castiñeira JR, López-Vázquez A, López-Larrea C (2016) HLA-B*40:01 Is Associated with ankylosing spondylitis in HLA-B27-positive populations. J Rheumatol 43(6): 1255–1256. https://doi.org/10.3899/jrheum.151096
48. Saadi A, Dang J, Shan S, Ladjouze-Rezig A, Lefkir-Tafiani S, Gong Y, Liu Q, Benhassine T (2019) Ankylosing spondylitis: analysis of gene-gene interactions between IL-12β, JAK2, and STAT3 in Han Chinese and Algerian cohorts. Centr Eur J Immunol 44(1): 65–74
49. Khan MA, Kushner I, Braun WE, Zachary AA, Steinberg AG (1978) HLA-B27 homozygosity in ankylosing spondylitis: relationship to risk and severity. Tissue Antigens 11:434–438
50. Wang LI, Yang X, Cai G, Xin L, Xia Q, Zhang XU, Li X, Wang M, Wang K, Xia G, Xu S, Xu J, Zou Y, Pan F (2016) Association study of copy number variants in FCGR3A and FCGR3B gene with risk of ankylosing spondylitis in a Chinese population. Rheumatol Int 36(3):437–442. https://doi.org/10.1007/s00296-015-3384-0
51. Chen JY, Wang CM, Chang SW, Cheng CH, Wu YJ, Lin JC, Yang B, Ho HH, Wu J (2014) Association of FCGR3A and FCGR3B copy number variations with systemic lupus erythematosus and rheumatoid arthritis in Taiwanese patients. Arthritis Rheum 66(11):3113–3121. https://doi.org/10.1002/art.38813
52. Willcocks LC, Lyons PA, Clatworthy MR, Robinson JI, Yang W, Newland SA, Smith KG (2008) Copy number of FCGR3B, which is associated with systemic lupus erythematosus, correlates with protein expression and immune complex uptake. J Exp Med 205(7):1573–1582. https://doi.org/10.1084/jem.20072413
53. Graf SW, Lester S, Nossent JC, Hill CL, Proudman SM, Lee A, Rischmueller M (2012) Low copy number of the FCGR3B gene and rheumatoid arthritis: a case-control study and meta-analysis. Arthritis Res Ther 14(1):R28
54. McKinney C, Fanciulli M, Merriman ME, Phipps-Green A, Alizadeh BZ, Koeleman BP, Merriman TR (2010) Association of variation in Fcgamma receptor 3B gene copy number with rheumatoid arthritis in Caucasian samples. Ann Rheum Dis 69(9): 1711–1716. https://doi.org/10.1136/ard.2009.123588
55. Wu J, Li Y, Guan W, Viken K, Perlman DM, Bhargava M (2016) FCGR3A and FCGR3B copy number variations are risk factors for sarcoidosis. Hum Genet 135(7):715–725. https://doi.org/10.1007/s00439-016-1669-3
56. Dahmani CA, Benzaoui A, Amroun H, Zemani-Fodil F, Petit-Teixeira E, Boudjema A (2019) Association study of copy number variants in CCL3L1, FCGR3A and FCGR3B genes with risk of ankylosing spondylitis in a West Algerian population. Int J Immunogenet 00:1–7. https://doi.org/10.1111/iji.12454
57. Dahmani CA, Benzaoui A, Amroun H, Mecabih F, Sediki FZ, Zemani-Fodil F, Fodil M, Boughrara W, Mecheti B, Attal N, Mehtar N, Petit- Teixeira E, Boudjema A (2018) Association of the HLA-B27antigen and the CTLA4 gene CT60/rs3087243 polymorphism with ankylosing spondylitis in Algerian population: A case–control study. Int J Immunogenet 45(3):109–117. https://doi.org/10.1111/iji.12369
58. Ellinghaus D, Jostins L, Spain SL, Cortes A, Bethune J, Han B, Park UR (2016) Analysis of five chronic inflammatory diseases identifies 27 new associations and highlights disease-specific patterns at shared loci. Nat Genet 48(5):510–518. https://doi.org/10.1038/ng.3528
59. Hammoudeh M, Abdulaziz S, Alosaimi H, Al-Rayes H, Aldeen Sarakbi H, Baamer M et al (2016) Challenges of diagnosis and management of axial spondyloarthritis in North Africa and the Middle East: an expert consensus. J Int Med Res 44(2):216–230
60. Allat R (2015) Particularités des spondyloarthrites algériennes. Rev Rhum 82S:A363
61. Haid S, Rahal S, Teniou A, Gasmi A, Megateli I, Abdessemed A et al (2015) Les Coxites dans la spondyloarthrite. Rev Rhum 82S: A358
62. Maghraoui AE, Bensabbah R, Bahiri R, Bezza A, Guedira N, Hajjaj-Hassouni N (2003) Cervical spine involvement in ankylosing spondylitis. Clin Rheumatol 22(2):94–98
63. Ibn Yacoub Y, Amine B, Laatiris A, Abouqal R, Hajjaj-Hassouni N (2011) Spinal mobility and its impact in Moroccan patients with ankylosing spondylitis. Clin Rheumatol 30(2):239–243
64. Bezza A, Niamane R, Amine B, El Maghraoui A, Bensabbah R, Hajjaj-Hassouni N (2004) Involvement of the foot in patients with psoriatic arthritis. A review of 26 cases. Joint Bone Spine 71(6): 546–549
65. Sahli H, Bachali A, Tekaya R, Mahmoud I, Sedki Y, Saidane O et al (2019) Involvement of foot in patients with spondyloarthritis: prevalence and clinical features. Foot Ankle Surg 25(2):226–230
66. Laatiris A, Amine B, Ibn Yacoub Y, Hajjaj-Hassouni N (2012) Enthesitis and its relationships with disease parameters in Moroccan patients with ankylosing spondylitis. Rheumatol Int 32(3):723–727
67. Moltó A, Etcheto A, van der Heijde D, Landewé R, van den Bosch F, Bautista Molano W et al (2016) Prevalence of comorbidities and evaluation of their screening in spondyloarthritis: results of the international cross-sectional ASAS-COMOSPA study. Ann Rheum Dis 75(6):1016–1023
68. Ghozlani I, Ghazi M, Nouijai A, Mounach A, Rezqi A, Achemlal L et al (2009) Prevalence and risk factors of osteoporosis and vertebral fractures in patients with ankylosing spondylitis. Bone 44(5): 772–776

69. El Maghraoui A, Ebo'o FB, Sadni S, Majjad A, Hamza T, Mounach A (2016) Is there a relation between pre-sarcopenia, sarcopenia, cachexia and osteoporosis in patients with ankylosing spondylitis? BMC Musculoskelet Disord 17(1):268
70. El Maghraoui A (2005) Pleuropulmonary involvement in ankylosing spondylitis. Joint Bone Spine 72(6):496–502
71. Hakkou J, Rostom S, Aissaoui N, Berrada KR, Abouqal R, Bahiri R et al (2011) Psychological status in Moroccan patients with ankylosing spondylitis and its relationships with disease parameters and quality of life. J Clin Rheumatol 17(8):424–428
72. Aissaoui N, Rostom S, Hakkou J, Berrada Ghziouel K, Bahiri R, Abouqal R et al (2012) Fatigue in patients with ankylosing spondylitis: prevalence and relationships with disease-specific variables, psychological status, and sleep disturbance. Rheumatol Int 32(7): 2117–2124
73. Ibn Yacoub Y, Amine B, Laatiris A, Abouqal R, Hajjaj-Hassouni N (2011) Health-related quality of life in Moroccan patients with ankylosing spondylitis. Clin Rheumatol 30(5):673–677
74. Ben Tekaya A, Mahmoud I, Hamdı I, Hechmı S, Saıdane O, Tekaya R, Abdelmoula L (2019) Depression and anxiety in spondyloarthritis: prevalence and relationship with clinical parameters and self-reported outcome measures. Turk Psikiyatri Derg 30(2):90–98
75. Burgos-Varga R, Wei JC, Rahman MU, Akkoc N, Atiqul Haq S, Hammoudeh M, Mahgoub E, Singh E, Llamado LJ, Shirazy K, Kotak S, Hammond S, Pedersen R, Shen Q, Vlahos B (2016) The prevalence and clinical characteristics of nonradiographic axial spondyloarthritis among patients with inflammatory back pain in rheumatology practices: a multinational, multicenter study. Arthritis Res Ther 18(1):132. https://doi.org/10.1186/s13075-016-1027-9
76. Hamdi W, Chelli-Bouaziz M, Ahmed MS, Ghannouchi MM, Kaffel D, Ladeb MF, Kchir MM (2011) Correlations among clinical, radiographic, and sonographic scores for enthesitis in ankylosing spondylitis. Joint Bone Spine 78(3):270–274. https://doi.org/10.1016/j.jbspin.2010.09.010
77. Hamdi W, Bouaziz Chelli M, Ghannouchi MM, Hawel M, Ladeb MF, Kchir MM (2013) Performance of ultrasounds compared with radiographs to detect chronic enthesitis signs in patients with ankylosing spondylitis. Rheumatol Int 33(2):497–499. https://doi.org/10.1007/s00296-011-2174-6
78. Ali Ou Alla S, Bahiri R, Amine H, El Alaoui H, Rkain H, Aktaou S, Abouqal R, Hajjaj-Hassouni N (2013) Ultrasound features of shoulder involvement in patients with ankylosing spondylitis: a case–control study. BMC Musculoskelet Disord 14:272
79. Goei The HS, Steven MM, Van Der Linden SM, Cats A (1985) Evaluation of diagnostic criteria for ankylosing spondylitis: a comparison of the rome, new york and modified new york criteria in patients with a positive clinical history screening test for ankylosing. Rheumatology 24(3):242–249
80. Ibn Yacoub Y, Amine B, Laatiris A, Bensabbah R, Hajjaj-Hassouni N (2012) Relationship between diagnosis delay and disease features in Moroccan patients with ankylosing spondylitis. Rheumatol Int 32(2):357–360
81. Wariaghli G, Allali F, Berrada K, Idrissi Z, Hmamouchi I, Abouqal R et al (2012) Normative values for the bath ankylosing spondylitis functional index in the general population compared with ankylosing spondylitis patients in Morocco. BMC Musculoskelet Disord 13(1):40
82. Hakkou J, Rostom S, Aissaoui N, Berrada Ghezioul K, Bahiri R, Abouqal R et al (2012) Comparison of the BASDAI and the miniBASDAI in assessing disease activity in patients with ankylosing spondylitis. Clin Rheumatol 31(3):441–445
83. van der Heijde D, Ramiro S, Landewé R, Baraliakos X, Van den Bosch F, Sepriano A et al (2017) 2016 update of the ASAS-EULAR mana- gement recommendations for axial spondyloarthritis. Ann Rheum Dis 76:978–991
84. van der Heijde D, Kivitz A, Schiff MH (2006) Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial. Arthritis Rheum 54:2136–2146
85. Sieper J, Listing J, Poddubnyy D (2016) Effect of continuous versus on- demand treatment of ankylosing spondylitis with diclofenac over 2 years on radiographic progression of the spine: results from a randomi- sed multicentre trial (ENRADAS). Ann Rheum Dis 75: 1438–1443
86. Younes M, Jalled A, Aydi Z et al (2010) Socioeconomic impact of ankylosing spondylitis in Tunisia. Joint Bone Spine 77(1):41–46
87. Djebbari A, Bouakkaz S, Bennedjema S et al (2018) Hip arthritis remain free from radiographic progression for 24 months following treatment of ankylosing spondyloarthritis with tnf-A inhibitors: a prospective study. Ann Rheum Dis 77(supplement Suppl):A1542. https://doi.org/10.1136/annrheumdis-2018-eular.2971
88. Haid S, Teniou D, Megateli I et al (2015) Anti-TNF et spondyloarthrite : quel risque infectieux ? Rev Rhum 82S:A357
89. Bahiri R, Ichchou L, Bezza A et al (2017) Recommandations de la société marocaine de rhumatologie (SMR) pour la prise en charge thérapeutique des malades atteints de spondylarthrite ankylosante (SpA grave). Rev Mar Rhum 39:3–18