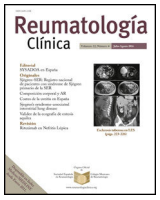
Reumatol Clin. 20 (2024) 547–554

Sociedad Española de Reumatología - Colegio Mexicano de Reumatología

Reumatología Clínica

www.reumatologiaclinica.org



Original Article

Do patients with axial spondyloarthritis with active disease suffer from greater disease burden and work impairment? Results from the International Map of Axial Spondyloarthritis (IMAS)

Marco Garrido-Cumbrera[a,b,*], Denis Poddubnyy[c,d], Fernando Sommerfleck[e], Christine Bundy[f], Souzi Makri[g], José Correa-Fernández[a], Shashank Akerkar[h], Jo Lowe[i], Elie Karam[j], Victoria Navarro-Compán[k]

[a] *Health & Territory Research (HTR), Universidad de Sevilla, Seville, Spain*
[b] *Spanish Federation of Spondyloarthritis Patient Associations (CEADE), Madrid, Spain*
[c] *Charité-Universitätsmedizin Berlin, Berlin, Germany*
[d] *German Rheumatism Research Centre, Berlin, Germany*
[e] *Sanatorio Julio Mendez, Buenos Aires, Argentina*
[f] *Cardiff University, Cardiff, UK*
[g] *Cyprus League of People with Rheumatism (CYLPER), Nicosia, Cyprus*
[h] *Mumbai Arthritis Clinic, Mumbai, India*
[i] *Axial Spondyloarthritis International Federation (ASIF), London, UK*
[j] *Canadian Spondylitis Association (CSA), Toronto, Canada*
[k] *IdiPaz, Hospital Universitario La Paz, Madrid, Spain*

ARTICLE INFO

Article history:
Received 28 June 2024
Accepted 3 October 2024

Keywords:
Axial spondyloarthritis
Disease activity
Employment
Worldwide

ABSTRACT

Background: To assess the prevalence of clinically active disease in axial spondyloarthritis (axSpA) and its associated factors in a large global sample of patients from the International Map of Axial Spondyloarthritis (IMAS) study.

Methods: IMAS is a cross-sectional online survey (2017–2022) of 5557 axSpA patients. Patients were divided between those with active disease (BASDAI ≥4) and without active disease (BASDAI <4). The factors evaluated were sociodemographic, lifestyle, patient-reported outcomes, employment, disease characteristics, extra-musculoskeletal manifestations, and treatment. Logistic regression analysis stratified by gender were used to evaluate the relationship between investigated factors and active disease.

Results: In the present study, 5295 patients who had responded to the BASDAI scale were included in the present study: 3231 were from Europe, 770 from North America, 600 from Asia, 548 from Latin America, and 146 from Africa. The mean age was 43.8 ± 12.9 years and 55.4% were females. Patients reported a mean BASDAI of 5.4 (±2.1) with 75% having active disease (BASDAI ≥4). In South Africa, 87.0% of patients reported having active disease, compared to 68.5% in Asia. Multivariable logistic regression showed an association of active disease with higher functional limitation, greater spinal stiffness, difficulty finding a job due to axSpA and worse mental health in both genders. For males, younger age and shorter diagnostic delay, and for females, no physical activity and presence of inflammatory bowel disease were associated with active disease.

Conclusions: Three quarters of patients with axSpA reported clinically active disease, with higher proportion of patients with active disease in South Africa and lower proportion in Asia. Our results underline the complexity of the clinical disease activity concept in axSpA and the need for a holistic approach in the patient management, care and treatment.

* Corresponding author.
E-mail address: mcumbrera@us.es (M. Garrido-Cumbrera).

https://doi.org/10.1016/j.reuma.2024.10.002

¿Los pacientes con espondiloartritis axial con enfermedad activa sufren una mayor carga de la enfermedad e incapacidad laboral? Resultados del Mapa Internacional de la Espondiloartritis Axial (IMAS)

Palabras clave:
Espondiloartritis axial
Actividad de la enfermedad
Empleo
Mundial

RESUMEN

Introducción: Evaluar la prevalencia de la enfermedad clínicamente activa en la espondiloartritis axial (EspA-ax) y sus factores asociados en una gran muestra global de pacientes del estudio Mapa Internacional de la Espondiloartritis Axial (IMAS).
Métodos: IMAS es una encuesta transversal online (2017-2022) de 5557 pacientes con EspAax. Los pacientes se dividieron entre aquellos con enfermedad activa (BASDAI ≥4) y sin enfermedad activa (BASDAI <4). Los factores evaluados fueron sociodemográficos, estilo de vida, resultados comunicados por los pacientes, empleo, características de la enfermedad, manifestaciones extraesqueléticas y tratamiento. El análisis de regresión logística estratificado por sexo permitió evaluar la relación entre los factores investigados y la enfermedad activa.
Resultados: En el presente estudio se incluyeron 5.295 pacientes con EspAax que habían respondido a la escala BASDAI: 3.231 procedían de Europa, 770 de Norteamérica, 600 de Asia, 548 de Latinoamérica y 146 de África. La edad media era de 43,8 ± 12,9 años y el 55,4% eran mujeres. Los pacientes declararon un BASDAI medio de 5,4 (±2,1), y el 75% tenía la enfermedad activa (BASDAI≥4). En Sudáfrica, el 87,0% de los pacientes declararon tener la enfermedad activa, frente al 68,5% en Asia. La regresión logística multivariable mostró una asociación de la enfermedad activa con una mayor limitación funcional, mayor rigidez de la columna vertebral, dificultad para encontrar trabajo debido a la EspAax y peor salud mental en ambos sexos. En el caso de los varones, la menor edad y el menor retraso diagnóstico y en el caso de las mujeres, la ausencia de actividad física y la presencia de enfermedad inflamatoria intestinal se asociaron con la enfermedad activa.
Conclusiones: Tres cuartas partes de los pacientes con EspAax declararon enfermedad clínicamente activa, con mayor proporción de pacientes con enfermedad activa en Sudáfrica y menor proporción en Asia. Nuestros resultados subrayan la complejidad del concepto de actividad clínica de la enfermedad en la EspAax y la necesidad de un enfoque holístico en la gestión, la atención y el tratamiento de los pacientes.

Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that primarily affects the spine and sacroiliac joints.[1] The most common symptoms include chronic low back pain, stiffness and fatigue, which are especially more intense in the morning and improves with movement.[2,3] In this sense, defining and measuring the disease activity experienced by patients is essential and challenging.

In this context, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) has traditionally been the most widely used scale in clinical practice to assess disease activity,[4] to guide medical therapy and monitor treatment response to improve the quality of axSpA care.[5] However, the recommended instrument to assess disease activity nowadays is the Ankylosing Spondylitis Disease Activity Score (ASDAS), which in addition to patient-reported questionnaire also includes an objective assessment of inflammation such as C-reactive protein or erythrosedimentation rate.[6]

Disease activity can be heterogeneous, both at initial presentation and over time.[7,8] Although some studies have shown that – even in countries with wide access to biologics – axSpA remains a disease in which more than one third of patients could remain with moderate to high disease activity for several years.[9]

Some individual characteristics are strongly associated with stable trajectories of low and improving disease activity, such as being male or having a higher degree of education.[9] Females also experience higher disease activity reported by BASDAI scale,[10,11] although variation depends on the geographic location of the patients.[12] However, when using the ASDAS, the influence of gender was not found.[13]

Some studies have demonstrated an association between elevated disease activity and progression of structural damage in the spine in patients with axSpA.[14,15] Therefore, disease inactivity would also result in controlling of radiographic progression of the spine in axSpA.[16] AxSpA is a chronic condition that may require long-term management by a specialized medical team, which should include rheumatologists, physiotherapists and other healthcare professionals to provide comprehensive treatment and improve the patient's quality of life. Hence, for an adequate management of patients it is crucial to assess the patients' disease activity and what factors might be associated with such activity. We aimed to assess the prevalence of clinically active disease in axSpA and its associated factors in a large sample of patients from the International Map of Axial Spondyloarthritis (IMAS).

Methods

Survey design and development

The IMAS initiative – involving a total of 27 countries – is a research collaboration between the Axial Spondyloarthritis International Federation (ASIF), the Health and Territory Research (HTR) group of the University of Seville, and Novartis Pharma AG, together with a scientific committee composed of axSpA patient representatives, rheumatologists, psychologists, and health researchers. More information on the design and dissemination of the survey is available in the seminal European[17] and international manuscripts.[18]

Sample selection and recruitment

An online survey was conducted between 2017 and 2022 recruiting unselected patients by Ipsos and local patient organizations. The sample eligibility criteria were: (1) age ≥18 years; (2) residents in the specified country; (3) a self-reported diagnosis of axSpA (either radiographic or non-radiographic axSpA, r-axSpA and nr-axSpA).

Table 1
Variables, asked questions and measurements/categories included in this analysis.

Variables	Questions	Categories/measures
Sociodemographic		
Age	Please specify your age	In years
Gender	Please specify your gender	Male, female
Lifestyle		
Physical activity	Do you do any physical or sporting activity, including walking?	Yes, no
Patient-reported outcomes		
No. of self-reported symptomatic body regions	In which part of your body have you noticed redness, swelling or pain (inflammation) at some point due to spondylitis/spondyloarthritis?	Pelvis, spine, dorsal region, lumbar region, sacroiliac joints, hips, thorax, iritis, mandible, metacarpals, phalanges, pain in toe joints, vertebrae, shoulders, wrists, ankles, knee joints, dorsum of foot, Achilles tendon, sole of foot, tendons, neck, joints in the feet, elbows, the skin, the digestive tract
Employment		
Work choice due to axSpA	Do you think your current or past work choice was in any way determined by your spondylitis/spondyloarthritis?	Yes, No
Difficulty finding a job due to axSpA	Do you think it is or it would be difficult for you to find a job because of your spondylitis/spondyloarthritis?	Yes, No
Diagnosis characteristics		
Diagnostic delay	Calculated based on the age at diagnosis	In years
Extra-musculoskeletal manifestations		
Uveitis	Please indicate whether you have been diagnosed with any of the following:	Uveitis
Inflammatory bowel disease	Please indicate whether you have been diagnosed with any of the following:	Inflammatory bowel disease
Treatment		
NSAIDs	Have you ever been treated with a non-steroidal anti-inflammatory drug (NSAID) for your spondylitis/spondyloarthritis?	Yes, no
bDMARDs	Have you ever been treated with a biologic for your spondylitis/spondyloarthritis?	Yes, no
csDMARDs	Have you ever been treated with a conventional synthetic disease-modifying antirheumatic drug (DMARD) for your spondylitis/spondyloarthritis?	Yes, no

NSAIDs: non-steroidal anti-inflammatory drugs; bDMARDs: biological disease-modifying antirheumatic drugs; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs.

Collected data

The variables of the present study are grouped into seven areas: sociodemographic characteristics, lifestyle, disease characteristics, patient-reported outcomes, employment, diagnosis characteristics, extra-musculoskeletal manifestations and treatments (Table 1).

The main outcome of the present analysis was disease activity as measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), which is a self-administered questionnaire that evaluates disease activity in patients with axSpA. The overall BASDAI ranges from 0 to 10. Cut-off point at 4 indicates active disease (BASDAI $\geq$4).[5]

Patient-reported outcomes were collected from the following scales:

- *Spinal Stiffness Index*: an index has been developed by the University of Seville specifically for the IMAS survey to assess the degree of spinal stiffness experienced by patients in the spinal column, distinguishing between the cervical, dorsal, and lumbar areas. The index ranges between 3 and 12 points. Higher values of the index indicate greater spinal stiffness.[19]
- *Functional Limitation Index*: an index has been developed by the University of Seville specifically for the IMAS survey to assess the degree of limitation in 18 activities of daily life. The index ranges between 0 and 54 points. Higher values of the index indicate higher functional limitation.[19]
- 12-Item General Health Questionnaire (GHQ-12) is a screening measure of common mental health disorders in the general population, including symptoms of anxiety, depression, social dysfunction, and loss of confidence.[20,21] The overall GHQ-12 ranges from 0 to 12. Cut-off point at 3 indicates risk of poor mental health (GHQ score $\geq$3).

Statistical analysis

The total number of patients who responded the BASDAI scale was 5295 (Fig. 1), which were divided into patients with active disease (BASDAI $\geq$4) versus patients without active disease (BASDAI <4). Continuous variables are presented as means and standard deviations while categorical variables are presented as frequency and percentage. Mann–Whitney, Chi-square tests, and multivariable logistic regression analysis were used to evaluate the relationship between active disease and candidate variables. In addition, we performed an assessment of the interaction between the candidate variables. Due to the multiple significant interactions found when analyzing the variables associated with active disease distinguishing between gender, the logistic regression model was stratified by gender. Specifically, significant interactions by gender were found between active disease and the following variables: physical activity, spinal stiffness, functional limitation, diagnostic delay, presence of inflammatory bowel disease, difficulty finding a job due to axSpA, and mental health GHQ-12 scores (Fig. 1). The

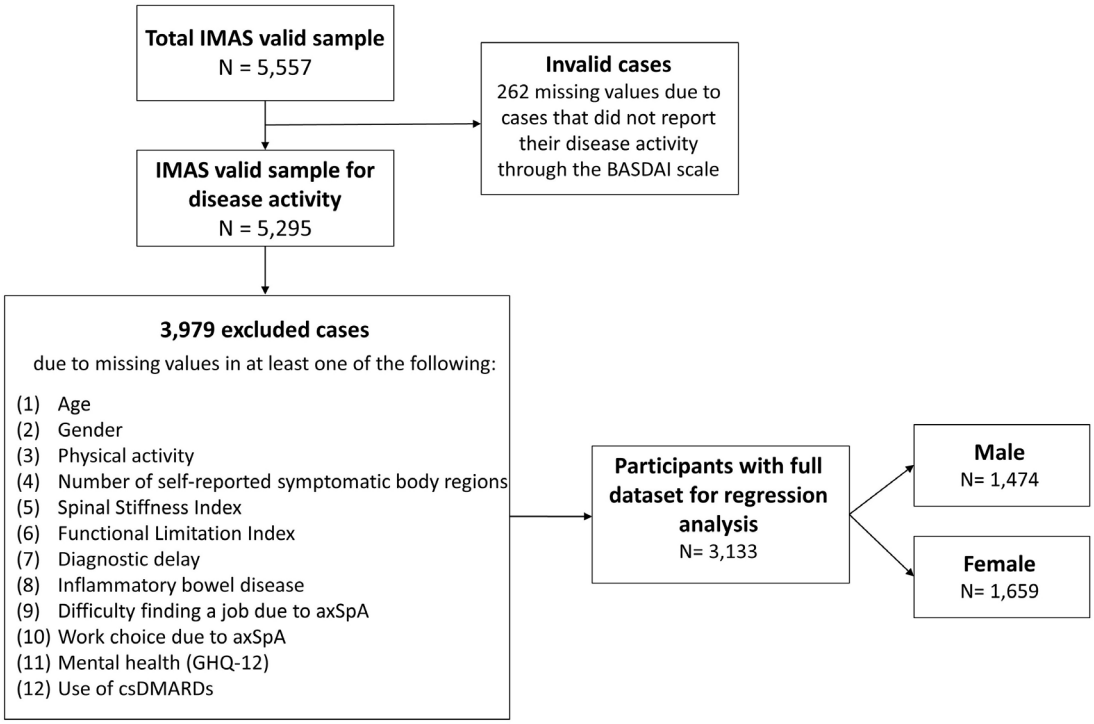


Fig. 1. Flowchart of the study sample selection.

odd-ratios (OR) and corresponding 95% confidence intervals (CIs) were reported. SPSS 26.0 version was used to carry out the analysis.

Results

Of 5295 patients, mean BASDAI was 5.4 (SD 2.1) with 75% having active disease (BASDAI ≥4). Specifically, 96.2% of patients reported axial affection with a mean of 5.7 out of 10, while 88.8% reported peripheral affection with a mean of 4.6 out of 10 (Table 2).

In South Africa, 87.0% of patients reported having active disease, compared to 68.5% in Asia (Fig. 2). Patients with active disease were frequently younger, females, with less physical activity, with greater number of self-reported symptomatic body regions, greater spinal stiffness, higher functional limitation, longer diagnostic delay, higher prevalence of inflammatory bowel disease, greater work choice due to axSpA, higher difficulty finding a job due to axSpA, poorer mental health and greater use of csDMARDs (Table 3). Bivariate analyses between independent variables and active disease for each region are available in Supplementary Table 1.

There was a significant interaction between gender and age (OR = 0.98, $p < 0.001$), physical activity (OR = 0.77, $p < 0.001$), spinal stiffness (OR = 1.19, $p < 0.001$), functional limitation (OR = 1.01, $p < 0.001$), diagnostic delay (OR = 0.99, $p = 0.031$), presence of inflammatory bowel disease (OR = 1.33, $p = 0.005$), difficulty finding a job due to axSpA (OR = 1.60, $p < 0.001$) and mental health GHQ-12 scores (OR = 1.11, $p < 0.001$). Therefore, we performed an additional regression analysis stratified by gender to assess factors associated with active disease showing in both genders an association between active disease and higher functional limitation, greater spinal stiffness, difficulty finding a job due to axSpA and worse mental health. In addition, only for males, younger age and shorter diagnostic delay, and only for females, no physical activity and presence of inflammatory bowel disease were associated with active disease (Table 4).

Discussion

The present study assessed the disease activity of 5295 axSpA patients from 27 countries around the globe and found a mean disease activity of 5.4 and active disease in 75% of the patients. Active disease was more likely at a younger age, female gender, a higher number of self-reported symptomatic body regions, greater spinal stiffness, higher functional limitation, shorter diagnostic delay, presence of inflammatory bowel disease, difficulty finding a job due to axSpA, work choice due to axSpA and poorer mental health. In the multivariable linear regression stratifying by gender, higher functional limitation, greater spinal stiffness, difficulty finding a job due to axSpA (with greater weights in males) and worse mental health were associated with active disease in both genders. However, only for males, younger age and shorter diagnostic delay, and only for females, no physical activity and the presence of inflammatory bowel disease were associated with active disease.

The mean disease activity of IMAS patients (5.4) was one point higher than a recent study (4.5) that also included patients from different regions of the world such as Europe, China, Latin America, Canada and Arab countries, although in both studies the proportion of patients with high disease activity was lower in Asia.[12] This could be to the fact that the Asian patients in the IMAS cohort reported a shortest delay in diagnosis and, therefore, were able to initiate effective treatment earlier to reduce disease activity. In addition, almost 9 out of 10 patients in IMAS South Africa had an active disease. This may be due to the fact that the South African patients in the IMAS cohort waited more than 10 years before diagnosis which, in addition to being unacceptable, could severely restrict the quality of life of these patients.

Active disease was higher in female IMAS patients. This could be due to the fact that female patients experience a longer diagnostic delay, greater functional limitations – although they

Table 2
The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) items ($n = 5347$, unless specify).

BASDAI questions	Mean	SD	$n > 0$ (%)
Q1. Level of fatigue	5.9	2.5	5137 (96.1)
Q2. Neck, back and hip pain	5.7	2.5	5144 (96.2)
Q3. Pain other than neck, back and hip	4.6	2.7	4747 (88.8)
Q4. Discomfort	4.8	2.8	4814 (90.0)
Q5. Morning stiffness severity	5.3	2.7	5018 (93.8)
Q6. Morning stiffness duration, $n = 5295$	4.2	2.9	4750 (89.7)
BASDAI overall, $n = 5295$	5.4	2.1	5252 (99.2)

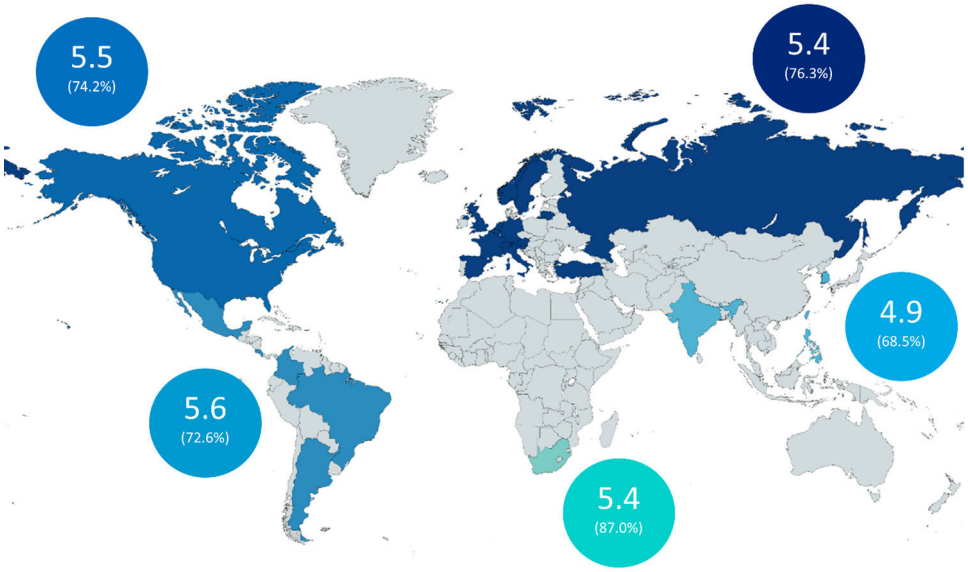


Fig. 2. Mean of disease activity and proportion of active disease by region ($n = 5295$). Data shown in the circles refer to the mean of disease activity (% active disease, BASDAI ≥4). BASDAI: Bath Ankylosing Spondylitis Disease Activity Index.

Table 3
Bivariate analysis to assess possible relationships with active disease in axSpA patients ($n = 5295$, unless specified).

	Mean ± SD or *n* (%)		*p*-Value
	Not active disease (BASDAI <4) 1324 (25.0%)	Active disease (BASDAI ≥4) 3971 (75.0%)	
Sociodemographic			
Age	44.7 ± 13.6	43.5 ± 12.6	**0.017**
Gender, *n*: 5293; female	570 (43.1)	2363 (59.5)	**<0.001**
Lifestyle			
Physical activity, *n*: 5214; yes	1128 (85.6)	3184 (81.7)	**0.001**
Patient-reported outcomes			
No. of self-reported symptomatic body regions, *n*: 5293	5.4 ± 4.3	8.2 ± 5.3	**<0.001**
Spinal stiffness (3–12), *n*: 5253	6.2 ± 2.5	8.0 ± 2.3	**<0.001**
Functional limitation (0–54), *n*: 5294	12.5 ± 12.7	21.2 ± 15.0	**<0.001**
GHQ-12 (0–12)	2.4 ± 3.1	5.5 ± 4.1	**<0.001**
Employment			
Work choice due to axSpA, *n*: 4805; yes	405 (33.2)	1830 (51.1)	**<0.001**
Difficulty finding a job due to axSpA, *n*: 4314; yes	446 (43.3)	2613 (79.5)	**<0.001**
Disease characteristics			
Diagnostic delay, *n*: 5187	6.6 ± 8.5	7.7 ± 9.2	**<0.001**
Extra-musculoskeletal manifestations			
Uveitis, *n*: 4788; yes	285 (23.1)	859 (24.2)	0.435
Inflammatory bowel disease, *n*: 4894; yes	123 (9.8)	599 (16.5)	**<0.001**
Treatment (ever received)			
NSAIDs, *n*: 4729	933 (79.2)	2845 (80.1)	0.497
csDMARDs, *n*: 4649	482 (41.7)	1601 (45.8)	**0.014**
bDMARDs, *n*: 4772	565 (47.3)	1800 (50.3)	0.074

NSAIDs: non-steroidal anti-inflammatory drugs; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biological disease-modifying antirheumatic drugs.
Bold values represent statistical significance ($p < 0.05$).

Table 4
Logistic regression analysis to determine factors associated with active disease ($n = 3133$).

	Multivariable logistic regression OR (95% CI)	
	Male $n = 1474$	Female $n = 1659$
Age	**0.98 (0.97, 0.99)**	0.99 (0.98, 1.01)
Gender, female	–	–
Physical activity engagement, no.	0.79 (0.55, 1.12)	**1.54 (1.01, 2.35)**
Number of self-reported symptomatic body regions	1.03 (0.99, 1.06)	1.03 (0.99, 1.06)
Spinal stiffness (3–12)	**1.25 (1.17, 1.32)**	**1.45 (1.35, 1.59)**
Functional limitation (0–54)	**1.02 (1.01, 1.03)**	**1.02 (1.01, 1.03)**
Diagnostic delay	**0.97 (0.95, 0.99)**	0.99 (0.97, 1.01)
Inflammatory bowel disease, yes	1.37 (0.92, 2.03)	**1.61 (1.04, 2.51)**
Difficulty finding a job due to axSpA, yes	**2.65 (1.98, 3.56)**	**1.75 (1.26, 2.41)**
Work choice due to axSpA, yes	1.21 (0.91, 1.62)	1.29 (0.95, 1.76)
Mental health GHQ-12 scores (0–12)	**1.17 (1.12, 1.22)**	**1.20 (1.15, 1.26)**
csDMARDs (ever received), yes	1.08 (0.83, 1.41)	1.11 (0.83, 1.48)

csDMARDs: conventional synthetic disease-modifying antirheumatic drugs.
Bold values represent statistical significance ($p < 0.05$).

have less structural damage to the spine – as well as a lower trend of adherence to treatment and a poorer response to treatment.[22]

Patients with active disease in IMAS cohort experienced significant disease burden in terms of symptomatic body regions and spinal stiffness and functional limitations for both genders and diagnostic delay for males. Functional limitation of IMAS patients was also associated with severe pain, as measured by BASDAI items Q2 and Q3.[23] Disease activity may damage the sacroiliac joint, influencing the functional status and mobility of the spine.[24] In addition, high disease activity is associated with accelerated radiographic progression of the spine especially in early axSpA.[25]

With respect to extra-musculoskeletal manifestations, IMAS patients with active disease were associated with the presence of inflammatory bowel disease, although stratifying by gender, this was only significant in the case of females. This may be due to the higher prevalence of inflammatory bowel disease among women with AxSpA.[26]

Higher disease activity can disrupt the working life of patients with axSpA, with greater weight of difficulty in finding a job due to axSpA for males. In addition, difficulty finding a job due to axSpA was associated with pain severity, assessed by BASDAI items Q2 and Q3, in IMAS patients.[23] This could be due to the existence of a higher proportion of males who tend to perform manual labor, which requires greater physical effort.[27] We found higher disease activity was associated with job loss,[28] greater work impairment,[29] absenteeism,[30] and decreased work productivity.[31] In this sense, the most frequent work-related issues in patients with axSpA were sick leave, difficulty fulfilling working hours and missing work for doctor's appointments. In addition, a higher number of work-related issues was associated with higher disease activity.[32] As it emerges, disease activity in patients with axSpA should not only be considered with respect to the disease burden, but also to the impact on patients' quality of life, especially the working life, as these patients are much more restricted than the general population.

IMAS axSpA patients with higher disease activity suffered poorer mental health for both genders although with a slight greater impact on females. In this context, higher disease activity was associated with moderate–severe depressive symptom,[33] risk of anxiety,[34] and risk of mental disorders.[35] Moreover, a strong association between higher disease activity and poorer mental health was found.[36] Although more attention is currently being paid to the mental health of axSpA patients, their psychological status should be closely examined, especially in view of the significant effect on disease burden and disease activity.

In the IMAS cohort, the use of NSAIDs and bDMARDs was not significantly associated with active disease, which may indicate that these treatments may have the disease under control. Previous studies have shown that treatments such as NSAIDs and bDMARDs are targeted to reduce inflammation and progression of disease activity.[37,38] It should be noted that non-pharmacological treatments are also beneficial in reducing disease activity and improving patients' quality of life.[39] Thus, optimal treatment of axSpA should include a combination of pharmacological and non-pharmacological treatments.

Assessment of disease activity plays an essential role in management decisions of axSpA due to its wide association of symptoms across body regions, spinal stiffness, functional limitation, working impact and mental health. Disease activity should be measured by validated tools such as the BASDAI scale or ASDAS (Ankylosing Spondylitis Disease Activity Score) which has demonstrated better psychometric properties,[40] despite which, many healthcare professionals continue to use the BASDAI scale to measure patients' disease activity.

High disease activity according to BASDAI may not be due to inflammatory activity, but to other issues, such as non-nociceptive pain mechanisms (non-disciplastic, neuropathic), structural damage, mechanical/degenerative problems in the spine. Therefore, it is essential that axSpA patients communicate effectively with their physicians to describe their symptoms. Based on this evidence, the healthcare professional can adjust the treatment regimen to control disease activity, reduce symptoms and improve the patient's quality of life. Treatments should include non-pharmacologic therapy, work-related guidance, anti-inflammatory drugs, and in case of failure of these, biologics, or specific targeted therapies to control inflammation.

IMAS is an international survey of axSpA patients, including 5557 respondents from 27 countries worldwide, making it the largest sample and coverage to date. This study includes an important number of factors associated with disease activity, the identification of which may aid improvements in the management and follow-up of axSpA patients by rheumatologists and other HCPs. However, IMAS has some limitations. First, the survey was based on self-reported data and was unable to confirm the patients' diagnosis. Secondly, information on the symptomatic body regions and extra-musculoskeletal manifestations were self-reported by patients. Furthermore, there is an overrepresentation of the European region compared to other regions such as Asia or South Africa. Finally, the lack of comparison of the BASDAI with other scales with better psychometric properties such as the ASDAS is another limitation of the study.

Conclusions

Worldwide, 75% patients with axSpA reported clinically active disease according to BASDAI, with higher proportion of patients with active disease in South Africa and lower proportion in Asia. The causal relationship between the identified factors and clinical disease activity is complex and may vary from patient to patient, although a significant association has been found with respect to symptomatic body regions, spinal stiffness, and functional limitation of patients. In addition, disease activity may be affecting patients' mental health and employment status. Regarding the assessment of active disease, significant interactions were found between female gender and age, number of self-reported symptomatic body regions, spinal stiffness, functional limitation, inflammatory bowel disease, difficulty finding a job due to axSpA, and mental health GHQ-12 scores. Our results underline the complexity of the clinical disease activity concept in axSpA and the need for a holistic approach in the patient management, care, and treatment.

CRediT authorship contribution statement

All authors had full access to all study data, participated in the drafting and revision of the article, and approved the final version to be published.

Ethical approval

This article does not contain any studies with animal subjects. All participants were asked to provide explicit opt-in consent prior to participating in the EMAS survey.

Data sharing statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Patient and public involvement

Participant data was anonymized.

Funding

This study was supported by Novartis.

Declaration of competing interest

Marco Garrido-Cumbrera Grant/research support from: Novartis, Denis Poddubnyy Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Fernando Sommerfleck Speakers bureau: Abbvie, Eli Lilly, Janssen, Novartis, Consultant of: Abbvie, Novartis, Janssen, Christine Bundy Speakers bureau: AbbVie, Celgene, Janssen, Lilly, Novartis and Pfizer, Souzi Makri Consultant of: ovartis, GSK and Bayer, Shashank Akerkar Speakers bureau: Pfizer, Novartis, Eli Lilly, Jansen, Jo Lowe Grant/research support from: No personal funding, but ASIF has received funding from Novartis, UCB, Lilly, Abbvie, Boehringer Ingleheim, Pfizer, Janssen, Elie Karam: None declared, José Correa-Fernández: None declared, Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Eli Lilly, Galapagos, MoonLake, MSD, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Novartis.

Acknowledgements

We would like to thank all axial spondyloarthritis patients and patient organizations who participated in the IMAS study.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi: https://doi.org/10.1016/j.reuma.2024.10.002.

References

1. Navarro-Compán V, Sepriano A, El-Zorkany B, van der Heijde D. Axial spondyloarthritis. Ann Rheum Dis. 2021;80:1511–21, http://dx.doi.org/10.1136/annrheumdis-2021-221035.
2. Merjanah S, Igoe A, Magrey M. Mimics of axial spondyloarthritis. Curr Opin Rheumatol. 2019;31:335–43, http://dx.doi.org/10.1097/BOR.0000000000000613.
3. Walsh JA, Magrey M. Clinical manifestations and diagnosis of axial spondyloarthritis. J Clin Rheumatol. 2021;27:E547–60, http://dx.doi.org/10.1097/RHU.0000000000001575.
4. Landewé R, van Tubergen A. Clinical tools to assess and monitor spondyloarthritis. Curr Rheumatol Rep. 2015;17:1–7, http://dx.doi.org/10.1007/S11926-015-0522-3/FIGURES/2.
5. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol. 1994;21:2286–91.
6. Ramiro S, Nikiphorou E, Sepriano A, Ortolan A, Webers C, Baraliakos X, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis. 2022;82:19–34, http://dx.doi.org/10.1136/ard-2022-223296.
7. Chung HY, Machado P, Van Der Heijde D, Apos D, Agostino MA, Dougados M. Smokers in early axial spondyloarthritis have earlier disease onset, more disease activity, inflammation and damage, and poorer function and health-related quality of life: results from the DESIR cohort. Ann Rheum Dis. 2012;71:809–16, http://dx.doi.org/10.1136/annrheumdis-2011-200180.
8. Chung HY, Machado P, Van Der Heijde D, D'Agostino MA, Dougados M. 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. 2011;70:1930–6, http://dx.doi.org/10.1136/ARD.2011.152975.
9. Moltó A, Etcheto A, Van Der Heijde D, Landewé R, Van Den Bosch F, Bautista Molano W, et al. Prevalence of comorbidities and evaluation of their screening in spondyloarthritis: results of the international cross-sectional ASAS-COMOSPA study. Ann Rheum Dis. 2016;75:1016–23, http://dx.doi.org/10.1136/ANNRHEUMDIS-2015-208174.
10. Van Der Horst-Bruinsma IE, Zack DJ, Szumski A, Koenig AS. Female patients with ankylosing spondylitis: analysis of the impact of gender across treatment studies. Ann Rheum Dis. 2013;72:1221–4, http://dx.doi.org/10.1136/annrheumdis-2012-202431.
11. Webers C, Essers I, Ramiro S, Stolwijk C, Landewé R, Van Der Heijde D, et al. Gender-attributable differences in outcome of ankylosing spondylitis: long-term results from the Outcome in Ankylosing Spondylitis International Study. Rheumatology. 2016;55:419–28, http://dx.doi.org/10.1093/RHEUMATOLOGY/KEV340.
12. Poddubnyy D, Sieper J, Akar S, Muñoz-Fernández S, Haibel H, Hojnik M, et al. Characteristics of patients with axial spondyloarthritis by geographic regions: PROOF multicountry observational study baseline results. Rheumatology (Oxford). 2022;61:3299–308, http://dx.doi.org/10.1093/rheumatology/keab901.
13. Benavent D, Capelusnik D, Ramiro S, Molto A, López-Medina C, Dougados M, et al. Does gender influence outcome measures similarly in patients with spondyloarthritis? Results from the ASAS-perSpA study. RMD Open. 2022;8:1–11, http://dx.doi.org/10.1136/rmdopen-2022-002514.
14. Bautista-Molano W. Radiographic progression in axial spondyloarthritis: is it the expression of a helpful measure of structural involvement outcome? Rev Colomb Reumatol (Engl Ed). 2018;25:224–7, http://dx.doi.org/10.1016/J.RCREUE.201904004.
15. Aouad K, Ziade N, Baraliakos X. Structural progression in axial spondyloarthritis. Jt Bone Spine. 2020;87:131–6, http://dx.doi.org/10.1016/J.JBSPIN.201904006.
16. Poddubnyy D, Protopopov M, Haibel H, Braun J, Rudwaleit M, Sieper J. High disease activity according to the Ankylosing Spondylitis Disease Activity Score is associated with accelerated radiographic spinal progression in patients with early axial spondyloarthritis: results from the GErman SPondyloarthritis Inception Cohort. Ann Rheum Dis. 2016;75:2114–8, http://dx.doi.org/10.1136/annrheumdis-2016-209209.
17. Garrido-Cumbrera M, Poddubnyy D, Gossec L, Gálvez-Ruiz D, Bundy C, Mahapatra R, et al. The European Map of Axial Spondyloarthritis: Capturing the Patient Perspective-an Analysis of 2846 Patients Across 13 Countries. Curr Rheumatol Rep. 2019;21, http://dx.doi.org/10.1007/s11926-019-0819-8.

18. Garrido-Cumbrera M, Poddubnyy D, Sommerfleck F, Bundy C, Makri S, Correa-Fernández J, et al. International Map of Axial Spondyloarthritis (IMAS): results from the perspective of 5557 patients from 27 countries around the globe. RMD Open. 2024;10:e003504. https://doi.org/10.1136/rmdopen-2023-003504
19. Garrido-Cumbrera M, Navarro-Compán V, Zarco P, Collantes-Estévez E, Gálvez-Ruiz D, Braçe O, et al. Atlas of axial spondyloarthritis in Spain 2017: study design and population. Reumatol Clin. 2019;15:127–32, http://dx.doi.org/10.1016/j.reuma.2018.08.003.
20. Goldberg D. The detection of psychiatric illness by questionnaire: a technique for the identification and assessment of non-psychotic psychiatric illness. London: Oxford University Press; 1972.
21. Hankins M. The reliability of the twelve-item general health questionnaire (GHQ-12) under realistic assumptions. BMC Public Health. 2008;8:7, http://dx.doi.org/10.1186/1471-2458-8-355.
22. Chimenti MS, Alten R, D'Agostino MA, Gremese E, Kiltz U, Lubrano E, et al. Sex-associated and gender-associated differences in the diagnosis and management of axial spondyloarthritis: addressing the unmet needs of female patients. RMD Open. 2021;7:e001681, http://dx.doi.org/10.1136/RMDOPEN-2021-001681.
23. Garrido-Cumbrera M, Navarro-Compán V, Sommerfleck F, Bundy C, Makri S, Correa-Fernández J, et al. POS0508 what factors are associated with pain intensity in axial spondyloarthritis? Results from the International Map of Axial Spondyloarthritis (IMAS). Ann Rheum Dis. 2024;83:917–8, http://dx.doi.org/10.1136/ANNRHEUMDIS-2024-EULAR. 2467.
24. Protopopov M, Sieper J, Haibel H, Listing J, Rudwaleit M, Poddubnyy D. Relevance of structural damage in the sacroiliac joints for the functional status and spinal mobility in patients with axial spondyloarthritis: results from the German Spondyloarthritis Inception Cohort. Arthritis Res Ther. 2017;19:240, http://dx.doi.org/10.1186/S13075-017-1453-3/TABLES/2.
25. Poddubnyy D, Protopopov M, Haibel H, Braun J, Rudwaleit M, Sieper J. High disease activity according to the Ankylosing Spondylitis Disease Activity Score is associated with accelerated radiographic spinal progression in patients with early axial spondyloarthritis: results from the GErman SPondyloarthritis Inception Cohort. Ann Rheum Dis. 2016;75:2114–8, http://dx.doi.org/10.1136/ANNRHEUMDIS-2016-209209.
26. Stolwijk C, Van Tubergen A, Castillo-Ortiz JD, Boonen A. Prevalence of extra-articular manifestations in patients with ankylosing spondylitis: a systematic review and meta-analysis. Ann Rheum Dis. 2015;74:65–73, http://dx.doi.org/10.1136/annrheumdis-2013-203582/-/dc1.
27. Vendramin P, Valenduc G. Occupations and ageing at work. An analysis of the findings of the fifth European Working Conditions Survey. European Trade Union Institute; 2020.
28. Barlow JH, Wright CC, Williams B, Keat A. Work disability among people with ankylosing spondylitis. Arthritis Rheum. 2001;45:424–9, http://dx.doi.org/10.1002/1529-0131(200110)45:5<424::AID-ART361>3.0.CO;2-7.
29. Osterhaus JT, Purcaru O. Discriminant validity, responsiveness and reliability of the arthritis-specific Work Productivity Survey assessing workplace and household productivity within and outside the home in patients with axial spondyloarthritis, including nonradiographic axial spondyloarthritis and ankylosing spondylitis. Arthritis Res Ther. 2014;16:R164, http://dx.doi.org/10.1186/ar4680.
30. Boonen A, Brinkhuizen T, Landewé R, Van Der Heijde D, Severens JL. Impact of ankylosing spondylitis on sick leave, presenteeism and unpaid productivity, and estimation of the societal cost. Ann Rheum Dis. 2010;69:1123–8, http://dx.doi.org/10.1136/ard.2009.116764.
31. Strömbeck B, Jacobsson LTH, Bremander A, Englund M, Heide A, Turkiewicz A, et al. Patients with ankylosing spondylitis have increased sick leave – a registry-based case–control study over 7 yrs. Rheumatology. 2009;48:289–92, http://dx.doi.org/10.1093/RHEUMATOLOGY/KEN497.
32. Garrido-Cumbrera M, Bundy C, Navarro-Compán V, Makri S, Sanz-Gómez S, Christen L, et al. Patient-reported impact of axial spondyloarthritis on working life: results from the EMAS survey. Arthritis Care Res (Hoboken). 2020;73:1826–33, http://dx.doi.org/10.1002/acr.24426, acr.24426.
33. Redeker I, Hoffmann F, Callhoff J, Haibel H, Sieper J, Zink A, et al. Determinants of psychological well-being in axial spondyloarthritis: an analysis based on linked claims and patient-reported survey data. Ann Rheum Dis. 2018;77:1017–24, http://dx.doi.org/10.1136/ANNRHEUMDIS-2017-212629.
34. Kilic G, Kilic E, Ozgocmen S. Relationship between psychiatric status, self-reported outcome measures, and clinical parameters in axial spondyloarthritis. Medicine (Baltimore). 2014;93:e337, http://dx.doi.org/10.1097/MD.0000000000000337.
35. Garrido-Cumbrera M, Gálvez-Ruiz D, Delgado-Domínguez CJ, Poddubnyy D, Navarro-Compán V, Christen L, et al. Impact of axial spondyloarthritis on mental health in Europe: results from the EMAS study. RMD Open. 2021;7:e001769, http://dx.doi.org/10.1136/RMDOPEN-2021-001769.
36. Garrido-Cumbrera M, Delgado-Domínguez CJ, Gálvez-Ruiz D, Blanch-Mur C, Navarro-Compán V. The effect of axial spondyloarthritis on mental health: results from the atlas. J Rheumatol. 2019;46:1284–9, http://dx.doi.org/10.3899/jrheum.180868.
37. Heldmann F, Dybowski F, Saracbasi-Zender E, Fendler C, Braun J. Update on biologic therapy in the management of axial spondyloarthritis. Curr Rheumatol Rep. 2010;12:325–31, http://dx.doi.org/10.1007/S11926-010-0125-Y/METRICS.
38. Kroon FPB, van der Burg LRA, Ramiro S, Landewé RBM, Buchbinder R, Falzon L, et al. Non-steroidal anti-inflammatory drugs (NSAIDs) for axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis). Cochrane Database Syst Rev. 2015;2015, http://dx.doi.org/10.1002/14651858.CD010952.PUB2/MEDIA/CDSR/CD010952/IMAGE_N/NCD010952-CMP-005-11.PNG.
39. Perrotta FM, Musto A, Lubrano E. New insights in physical therapy and rehabilitation in axial spondyloarthritis: a review. Rheumatol Ther. 2019;6:479–86, http://dx.doi.org/10.1007/S40744-019-00170-X.
40. Navarro-Compán V, Boel A, Boonen A, Mease PJ, Dougados M, Kiltz U, et al. Instrument selection for the ASAS core outcome set for axial spondyloarthritis. Ann Rheum Dis. 2023;82:763–72, http://dx.doi.org/10.1136/ANNRHEUMDIS-2022-222747.