Ref: Ro J Rheumatol. 2024;33(4)
DOI: 10.37897/RJR.2024.4.3

Delay in diagnosis in Egyptian axial spondylarthritis patients, contributing factors and worldwide stance

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ABSTRACT

Objectives. Among all rheumatic diseases, axial spondyloarthritis (axSpA) has one of the longest delays between the onset of symptoms and diagnosis. This study aimed to investigate the diagnostic delay in a cohort of Egyptian axSpA patients, specifically the time between symptom onset and access to rheumatology care. Additionally, we aimed to analyze the factors associated with this delay and compare it to diagnostic delays observed in different countries and regions around the world.

Material and methods. This cross-sectional study included 51 axSpA patients diagnosed according to the Assessment of Spondyloarthritis International Society (ASAS) criteria. All participants underwent a comprehensive assessment including history taking, clinical examination, review of laboratory and radiological investigations, and treatment. Activity and functional indices were also applied. We conducted correlative studies to analyze factors associated with the delay in diagnosis. Participants were divided into two groups: early diagnosis and late diagnosis, with a cutoff of 5 years. The two groups were compared regarding demographic data, clinical findings, activity, and functional indices. Relations between the groups were assessed using the independent samples t-test or Mann-Whitney's test for numerical variables.

Results. The median (IQR) diagnostic delay was 7 years (3-10 years). Patient age was significantly correlated with diagnostic delay (P = 0.004). Comparison of the early and late diagnosis groups revealed that older patients were more likely to receive an earlier diagnosis.

Conclusions. A significant delay in the diagnosis of axSpA persists among Egyptian patients. This delay is correlated with disease duration and is more likely to occur when non-rheumatologists are consulted first.

Keywords: axial spondyloarthritis, diagnosis, delay, rheumatology

INTRODUCTION

Axial spondyloarthritis (axSpA) is a disabling inflammatory autoimmune disorder primarily affecting the spine, sacroiliac joints (SIJs), and adjacent soft tissues, such as tendons and ligaments. The onset of axSpA typically occurs in patients younger than 40 years. Diagnosis is based on clinical manifestations, laboratory investigations (such as acute phase reactants, HLA-B27), and imaging studies. The association with HLA-B27 is well established, being present in 85% to 90% of patients [1]. Among rheumatic diseases, axSpA has one of the longest delays between the onset of symptoms and the time of diagnosis [2].

Many factors contribute to this diagnostic delay, including low awareness among physicians and misdiagnosis with other causes of low back pain. Other contributing factors include unusual clinical presentations, normal initial radiographs of the SIJs, and the absence of pathognomonic clinical or laboratory diagnostic tests [3]. Some physicians hesitate to diagnose axSpA without radiographic evidence of sacroiliitis, which may be absent in the early stages of the disease [4]. Radiographic changes typically develop slowly, with about 70% of axSpA patients showing changes after 5 years of symptoms [5]. The implementation of the Assessment of Spondylar-

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Article History:
Received: 12 November 2024
Accepted: 18 December 2024

thritis International Society (ASAS) criteria, with the inclusion of MRI of the SIJs, has facilitated earlier diagnosis of axSpA [6]. However, access to MRI is limited in many countries [2].

Inflammatory back pain (IBP) is a primary symptom in most axSpA patients. Unfortunately, IBP often goes unnoticed by both patients and physicians, partly because non-inflammatory mechanical back pain (MBP) is more common. Differentiating MBP from IBP can be challenging, and patients with IBP who do not present other disease manifestations may be mistakenly diagnosed with MBP [7]. Moreover, primary care physicians, who are often the first point of contact for patients, may lack expertise in identifying IBP among patients complaining of non-specific back pain [8].

The current study aims to investigate the diagnostic delay in a cohort of Egyptian axSpA patients, identify the factors contributing to the delay, assess the impact of this delay on disease outcomes, and review prior reports discussing this issue.

METHODOLOGY

Fifty-one adult axSpA patients, diagnosed according to the ASAS criteria [9], were enrolled in the study after presenting to the Rheumatology outpatient follow-up clinic between September 2021 and April 2022. All patients underwent history taking, with particular focus on the duration between symptom onset and diagnosis. Clinical examination, including musculoskeletal assessment, was performed, and laboratory investigations were conducted, including CBC, ESR, CRP, liver and kidney function tests, and HLA-B27 testing. A comprehensive treatment history was obtained, including the use of non-steroidal anti-inflammatory drugs (NSAIDs) and biological DMARDs. Radiological investigations included X-rays of both sacroiliac joints and the dorsolumbar spine (anteroposterior and lateral views), as well as MRI of the sacroiliac joints. Functional scores and disease activity were evaluated using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [10] and Bath Ankylosing Spondylitis Functional Index (BASFI) [11].

The study was conducted in accordance with local ethical committee standards and the Declaration of Helsinki. All participants provided informed consent. Study approval number: 23-SRec-RCPU2020.

Statistical methods

Descriptive analysis was performed, with numerical variables summarized as medians and interquartile ranges or means and standard deviations, as appropriate. Non-numerical variables were presented as frequencies and percentages. Relations between the two groups were assessed using the independent samples t-test or Mann-Whitney's test for numerical variables, and the Chi-square test or Fisher's exact test for non-numerical variables. A p-value of less than 0.05 was considered statistically significant. Data analysis was performed using STATA version 15.1.

RESULTS

The current study included 51 axSpA patients, of whom 7 (13.73%) were female and 44 (86.27%) were male. The median (IQR) age of the patients was 34 years (30–43), with ages ranging from 21 to 58 years. Among the axSpA patients, 43 (84.31%) were employed, and 38 (74.51%) lived in urban areas.

Regarding educational level, 6 patients (11.76%) were illiterate or had only attended primary school, 27 patients (52.94%) had completed middle or secondary school, and 17 patients (33.33%) were university graduates. The median (IQR) diagnostic delay for axSpA patients was 7 years (3–10), with a range from 2 months to 21 years.

Age was significantly correlated with diagnostic delay. Table 1 shows the correlation between the delay in diagnosis and other disease characteristics.

TABLE 1. Correlation of diagnostic delay with age, age at onset, activity and functional scores

Variable	Correlation coefficient	P-value
Age	0.3	**0.04**
Age of onset	-0.12	0.4
BASDAI	0.12	0.4
BASFI	0.1	0.7

Significant (P-value<0.05), highly significant (P-value<0.001)

Patients were divided into two groups based on the duration of diagnostic delay, with a cutoff value of 5 years. The two groups were compared across several aspects, as shown in Table 2.

Eighteen patients were in the early diagnosis group (<5 years), while 33 patients were in the late diagnosis group (≥5 years). There was a statistically significant difference between the early and late di-

TABLE 2. Comparison of early and late diagnosis groups with 5 years cutoff delay

Variable		Early diagnosis (<5 years) (n=18)	Late diagnosis (≥5 years) (n=33)	P-value
Age at disease onset (median (IQR)		0.1	22 (19-27)	25 (20-35)
Gender	Males	15 (83.3%)	29 (87.9%)	0.7
	Females	3 (16.7%)	4 (12.1%)	
Residence Number (%)	Urban	13 (72.2%)	25 (75.8%)	0.8
	Rural	5 (27.8%)	8 (24.2%)	
Disease duration (median (IQR))		0.0002	14 (10-18)	**5 (3-13)**

Variable		Early diagnosis (<5 years) (n=18)	Late diagnosis (≥5 years) (n=33)	P-value
Awareness of rheumatology	Unaware	16 (88.9%)	31(94%)	0.6
	Aware	2 (11.1%)	2 (6%)	
Education	Illiterate and primary school	2	5	0.7
	Middle and secondary school	5	22	
	University	4	13	
Specialty visited first (number (%0))	Orthopedics	15 (83.3%)	33 (100%)	**0.4**
	Rheumatology	2 (11.1%)	0	
	Others	1 (5.6%)	0	
Schober test (number (%))	Limited	13 (72.2%)	28 (84.8%)	0.3
	Non limited	5 (27.8%)	5 (15.2%)	
Occiput to wall (Median (IQR))		0.2	5 (0-10)	0 (0-6)
BASDAI (Mean ±SD)		0.4	4.73 ±2.17	4.23 ±2.21
BASFI (Median (IQR))		0.9	2.6 (1.5-4.2)	2.5 (1-4)
X ray changes (number (%))	0.5	32 (97%)	16 (88.9%)	Sacroiliitis
	0.4	6 (18.2%)	5 (27.8%)	Bamboo spine
Sacroiliitis in MRI (number (%))		1	32 (97%)	18 (100%)

Significant (P-value<0.05), highly significant (P-value<0.001)

agnosis groups in terms of disease duration (p = 0.0002) and the specialty visited first (p = 0.04).

DISCUSSION

Axial spondyloarthritis (axSpA) is known for one of the longest diagnostic delays among chronic diseases in general and rheumatic diseases in particular. Despite increased awareness, diagnostic delay remains a distinct feature of this disease [12]. The estimated global mean diagnostic delay is 6.7 years, which is unacceptably long [13].

Although axSpA is a slowly progressive disease, it can be debilitating, and the lack of functionality after years of untreated disease is overwhelming. Complications include severely restricted spinal movement, joint damage—especially to the hips and knees—osteoporosis, and skeletal fractures. Not only are its skeletal manifestations dire, but extra-skeletal manifestations can be equally dangerous. These include iritis, aortic regurgitation, and cerebrovascular events.

In the last decade, many effective biological treatments have become available, which can reduce the progression of axSpA. Therefore, early diagnosis is crucial to begin adequate treatment and achieve better outcomes [14].

Due to the impact of diagnostic delay on outcomes for axSpA patients, the current study aimed to evaluate the diagnostic delay in a cohort of axSpA patients, identify the factors causing the delay, assess the effect of this delay on disease outcomes, and review previous reports on this topic.

The median (IQR) diagnostic delay in patients with axSpA was 7 years (3–10), ranging from 2 months to 21 years. Upon reviewing the current literature, we found that diagnostic delay in axSpA varies significantly depending on the location and timing of the study. Our results are similar to recent studies conducted in Egypt and neighboring countries. A study by Abdelrahman and Mortada (2020) in Egypt reported a mean diagnostic delay of 5.7 years [15]. Another Egyptian study by Nageeb and colleagues (2022) found the mean diagnostic delay to be 7.66 years [14]. Studies from the Middle East also show comparable results. An Iranian study by Fallahi and Jamshidi (2016) reported an average diagnostic delay of 7.88 years [16], and a Moroccan study reported an average delay between 6 and 10 years [17]. A more recent study from Morocco in 2022 reported an average diagnostic delay of 6.5 years [18].

In contrast, diagnostic delays in Europe have significantly improved in recent years. According to a UK study, the time to diagnosis was 9.5 years in 2015 but decreased to 2.2 years by 2021.

In a US study of patients with ankylosing spondylitis (AS), among 235 patients, approximately 37% (87 patients) had been diagnosed within 1 year, 32% (71 patients) were diagnosed within 2–9 years, and 32.8% (77 patients) were diagnosed after ≥10 years from seeking medical attention [19]. Table 3 shows the diagnostic delay reported in previous studies.

The causes of diagnostic delay in axSpA are multifactorial and can be categorized into factors related to disease presentation, demographic features of the patients (age, gender, educational level, awareness of the disease, family history, level of activity, body mass index), and those related to the regional healthcare system (physician awareness, access to imaging and laboratory testing).

Previous reports have focused on the relationship between specific factors and the delay in diagnosis. The most commonly cited contributing factors are physician- and patient-related, with “wrong diagnosis” being the most frequently identified cause of delay [13].

A review by Barnett et al. indicated that healthcare providers at the primary and secondary care levels were largely to blame. In fact, most patients (62%) sought medical advice within the first year of experiencing symptoms related to axSpA. However, there is a notable delay in diagnosis after patients consult healthcare practitioners. Research shows

TABLE 3. Delay in axSpA reported in the previous studies addressing delay in AS/axSpA

year	Study location	Sample size	Population of the study	Delay in years	Cause of delay			Patients' assessment	Reference
					Health care -related	Patient-related	Disease- related		
2024	Spain	82	Spanish axSPA patients through electronic records	10.1	NA	NA	NA	BASDAI, ASDAS	Arévalo et al 2024 [29]
2023	Europe and Latin America	3553	Multicenter cohort including AS and PSA patients	5	NA	NA	Uveitis and IBD in AS patients	NA	Michelena et al 2024 [30]
2023	Europe, North America, Latin America, Asia and Africa	5327	Patients with axSPA included in International Map of Axial Spondyloarthritis (IMAP)	7.4	Diagnosed by rheumatology specialist, many physicians visits before diagnosis	Females, young age	Uveitis, longer disease duration	NA	Poddubnyy et al 2023 [31]
2023	Brigham, USA	554	AxSPA patients Brigham-Boston USA	6.8	NA	lower social levels	Uveitis before diagnosis	NA	McDermott et al 2024 [32]
2023	Taiwan	112	AS patients through online survey	3	NA	NA	NA	BASDAI	Yen et al 2023 [33]
2023	China	1295	Chinese AS patients	3	misdiagnosis	Patients who came from less developed regions	Peripheral arthritis at diagnosis	NA	Zheng et al 2024 [34]
2024	United Kingdom	14	British AS patients through telephone Microsoft teams	15.5	Misdiagnosis	lack of awareness	NA	NA	Hay et al 2024 [35]
2024	Poland	117	Rheumatology and Immunology department Jagiellonian and Krakow University Hospitals	5.5	NA	Lack of awareness	NA	NA	Zimba et al 2024 [36]
2007	Spain	824	12 rheumatology centers from 8 different cities	8	NA	NA	NA	NA	Collantes et al, 200737]
2008	Turkey	111		6.05		NA	IBP, family history, HLA-b27	NA	Dincer et al, 2008[22]
2009	India	70	Rheumatology clinic of spinal injury center	6.9	Physician awareness (Misdiagnosis with non-specific back pain)	Specialty visited first (Orthopedics, GP, rheumatologists)	Absence of extraarticular manifestations, juvenile-onset	Significant BASFI, BASDI. BASMI	Aggarwal and Malaviya., 2009.[38]
2009	Turkey	279	rheumatology clinics of 5 university hospitals	5.08	NA	NA	NA	NA	Ozgocmen et al, 2009[39]
2012	Italy	135	Rheumatology clinic	9	NA	NA	NA	NA	Salvadorin et al, 2012[40]
2012	Turkey	393	Rheumatology clinics in 4 cities	8.1	Physician awareness (Misdiagnosis)	Physiatrist, 25% (n = 99) an orthopedist, and 16% (n = 63) a neurosurgeon	Age	NA	Gerdan et al, 2012 [7]
2012	Morocco	100	Department of Rheumatology of El Ayachi University Hospital	4.12	Physician awareness (Wrong diagnosis)			BASMI, BASFI, BASRI	Ibn Yacoub et al., 2012 [24]
2013	Denmark	1335		5.3 0.8					Sørensenm et al, 2015[41]
2014	Iran	60	Emam Reza Hospital-Tabriz, Iran	6.2	Misdiagnosis	NA	Absence of uveitis, HLA-B27 negativity	No correlation with BASDI, positive with BASFI	Hajialilo et al, 2014[25]

year	Study location	Sample size	Population of the study	Delay in years	Cause of delay			Patients' assessment	Reference
					Health care -related	Patient-related	Disease- related		
2015	Middle East	169	Egypt, Kuwait, Qatar, and Saudi Arabia	4.9					Hammoudeh et al, 2015 [42]
2016	Iran	163		7.88	NA	NA	Enthesitis, HLA-B27 negativity	BASFI, BASDI, BASMI, AS Quality of life, chest expansion, sacroiliac grading	Fallahi et al, 2016[16]
2017	France	479	Two tertiary referral sentence	4.9	NA	NA	higher age at onset, less frequent peripheral arthritis or more frequent enthesis pain	NA	Masson behar et al, 2017[43]
2019	European Map of Axial Spondyloarthritis (EMAS)	2846	The major sample sizes had been found in Spain, France, Norway, and Russia	7.4				BASDI, general stiffness index, global limitation index	Garrido-Cumbrera et al, 2019[44]
2019	Germany	1677	health insurance data in Germany	5.7	NA	NA	Young female, at symptom onset, psoriasis negative HLA27	NA	Redeker et, 2019 [45]
2020	India	100	Rheumatology clinic	5	NA	NA	NA	NA	Reedy et al,2020 [46]
2021	Saudi Arabia	94	Rheumatology clinic of King Khalid University Hospital in Riyadh, Saudi Arabia	6.69				BASDI, ASDAS	Bedaiwi et al., 2021[27]
2021	Korea	1012	26 tertiary care hospital	1		Specialty visited first (Orthopedic, Rheumatology)	longer disease duration, proportion of patients aged over 40 years, and proportion of patients with a herniated disc		Hur et al, 2021[47]
2024	Egypt	51	Tertiary care hospital	7		Specialty visited first	Disease duration	No correlation between Delay and BASDI or BASFI	The current study

that healthcare professionals—including those in primary and secondary care, as well as musculoskeletal radiologists—often lack adequate knowledge, awareness, and confidence in detecting and identifying the key features and risk factors of axSpA [13].

Some reports have studied diagnostic delay on a regional basis. Rachid et al. examined the reasons for diagnostic delay in Africa and the Middle East, identifying low awareness among physicians and patients, the requirement for radiographic evidence of sacroiliitis for diagnosis, and limited access to MRI in some countries as the main causes of delay [2]. In our study, awareness was reported by only 7.8% of patients. Deodhar et al. (2022) also noted that decreased awareness of AS is one of the reasons behind the declining incidence rates of the disease [20].

Regarding patient-related factors, the specialty visited when the patient first experienced symptoms was the most studied. Our study showed that 94.1% of patients first visited orthopedic surgeons, while only 2 patients (3.9%) consulted rheumatology specialists at the onset of symptoms. This result is consistent with the findings of Nakashima et al. (2016), where 62% of patients first visited orthopedic surgeons [21]. Similarly, Gerdan et al. (2012) found that only 4% of patients presented to rheumatologists for their first visit, while 30% consulted physiotherapists, 25% orthopedists, and 16% neurosurgeons [7].

These findings are echoed by Dincer et al. (2008), who reported that diagnostic delay was significantly higher in patients who visited specialists other than rheumatologists [22]. Those who consulted general practitioners, orthopedists, neurologists, and neurosurgeons were more likely to be diagnosed with common low back pain. Non-rheumatological specialists are less adept at differentiating inflammatory back pain (IBP) from other spondyloarthropathy symptoms compared to rheumatologists.

Patients with axSpA often seek treatment in specialties such as orthopedics, neurosurgery, or neurology, as these specialties are trusted for the management of back pain. Additionally, delays may occur in the private sector due to the cost of visits and necessary investigations. General care providers and family medicine specialists can also delay referral to rheumatologists, particularly in the private sector [23].

Another patient-related factor is educational level. In our study, educational level did not affect diagnostic delay when comparing the late and early diagnosis groups. Ibn Yacoub et al. (2012) reported similar results [24], while Fallahi and Jamshidi (2016) found that a lower educational level led to a longer diagnostic delay [16]. Other studies by Dincer et al. (2008), Gerdan et al. (2012), and Mboussi et al. (2022) also showed a higher average diagnostic delay in patients with lower educational levels [7,18,22].

Regarding disease-related factors, the most common presenting symptom in our patients was axial manifestations, reported in 46 patients (90.2%), followed by peripheral joint affection and enthesitis. Similarly, Hajialilo et al. (2014) reported that low back pain was the first presenting symptom in 51.7% of patients with ankylosing spondylitis, followed by buttock pain (23.3%), morning stiffness (20%), and peripheral arthritis (5%) [25]. Nakashima et al. (2016) also reported that back pain was the most common initial symptom, occurring in 54% of patients, followed by coxalgia [21]. The fact that most of our patients' initial presentation was axial may be an important factor associated with diagnostic delay in our cohort. Ziade et al. (2022) reported that diagnostic delay was lower in cases of pure peripheral SpA compared to pure axial or combined forms of SpA [26]. On the other hand, Ibn Yacoub et al. (2012) found that 17% of patients had extra-articular manifestations, and 40% had uveitis. However, they did not find a correlation between extra-axial manifestations during the disease course and diagnostic delay [24].

We also examined the relationship between disease duration and diagnostic delay. In our study, older age was positively correlated with diagnostic delay ($p = 0.04$), but age at disease onset did not significantly affect diagnostic delay. Bedaiwi et al. (2021) reported that diagnostic delay was correlated with age at disease onset [27].

Next, we explored the impact of diagnostic delay on disease activity and functional indices. Our study showed no correlation between diagnostic delay and disease activity or function (BASDAI and BASFI). Similar results were reported by Bedaiwi et al. (2021), Ibn Yacoub et al. (2012), and Dincer et al. (2008) [22,24,27]. However, Abdelrahman and Mortada (2020) found that diagnostic delay was significantly associated with higher disease activity (BASDAI) and functional index (BASFI) [15]. Hajialilo et al. (2014) also reported significant differences in BASFI between early and late diagnosis groups [25]. Seo et al. (2015) found that the modified Schober index was worse in the delayed diagnosis group [28].

Among all rheumatic diseases, axSpA has the longest diagnostic delay, with some reports indicating delays of up to 10 years. Although awareness among patients and healthcare providers is improving, much work remains to be done, especially in less-developed countries. We need to ensure that patients with inflammatory back pain are easily recognized and properly managed. Improving knowledge of axSpA and other spondyloarthropathies is essential, and the role of rheumatologists in diagnosing and managing these patients must be emphasized to provide the best treatment options and outcomes.

Limitations

This study was limited by a small sample size and time constraints, as well as some obstacles in the healthcare system. We hope that future studies can be conducted with a larger sample size, fewer time limitations, and improved healthcare systems.

CONCLUSION

In Egyptian patients with ankylosing spondylitis (AS), diagnostic delay continues to be a significant challenge. This delay is influenced by factors such as the duration of the disease and the specialty visited first. Patients often seek care from non-rheumatology specialists, which contributes to delays in receiving a timely diagnosis. Addressing these factors through increased awareness among healthcare providers and promoting early referral to rheumatologists could help reduce the diagnostic delay and improve long-term outcomes for patients.

Data access statement:
The data that support the findings of this study are available on request from the corresponding author.

Conflict of interest:
Authors had no conflict to declare.

Financial support:
This research did not receive any specific grant from funding agencies in the public, commercial or non-profit sectors.

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