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REVIEW

The Impact of Spondyloarthritis on Health-Related Quality of Life and Healthcare Resource Utilization in Saudi Arabia: A Narrative Review and Directions for Future Research

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Abstract: Spondylarthritis (SpA) is an umbrella term that encompasses a wide range of rheumatological disorders. Several studies demonstrated that SpA is associated with increased healthcare resource utilization (HCRU) and a lower health-related quality of life (HRQoL). This review aimed to summarize the current literature regarding the multidimensional impact of SpA on HRQoL and HCRU in Saudi Arabia and explore the correlation of the extent of severity of SpA with HRQoL and HCRU. Although the prevalence of SpA varies across different populations and is correlated with HLA-B27 prevalence, the magnitude of SpA in the Saudi population has not been extensively evaluated. Few studies have investigated the impact of SpA on HRQoL and HCRU in Saudi Arabia and the Middle East. There is a need to study the cost-effectiveness of various SpA treatment strategies, including biologic disease-modifying anti-rheumatic drugs (bDMARDs), to prioritize healthcare spending in the Saudi healthcare system. Data on SpA in Saudi Arabia and the Middle East region are mainly based on expert views, with few population-based studies compared to other regions. Therefore, there is an imperative need to develop high-quality, national-level epidemiological studies that assess the following: (1) more accurate estimates of the current prevalence of SpA in Saudi Arabia, including the prevalence of axial SpA and psoriatic arthritis; (2) the phenotypes/clinical characteristics of SpA, including disease severity and extra-articular involvement; (3) the impact of SpA on the HRQoL of the patients and the factors that can predict the extent of impaired HRQoL in such population, which can represent the first step in developing psychological interventions that should be personalized to this patient population; (4) the impact of implementing formal assessment of disease activity on the management of the patients and, subsequently, their HRQoL; and (5) the HCRU and costs for patients with SpA, and how treatment patterns can affect this cost.

Keywords: spondylarthritis, psoriatic arthritis, health-related quality of life, healthcare resource utilization, Saudi Arabia

Introduction

Spondylarthritis (SpA) is an umbrella term for several related rheumatologic disorders that affect the whole axial skeleton joints and large peripheral joints. According to the pattern of spinal symptoms, the disorder can be generally classified into axial SpA -affecting mainly the spine with or without radiographic changes of the sacroiliac joints- and peripheral SpA -manifested predominantly by asymmetrical peripheral arthritis and enthesopathy-.[1] SpA encompasses a wide range of inflammatory conditions which may have extra-articular domains, such as inflammatory bowel disease (IBD)-related arthritis, reactive arthritis, psoriatic arthritis (PsA), and ankylosing spondylitis (AS), which is the prototype of SpA and the most commonly studied subtype.[2] The grouping of different rheumatological diseases under the umbrella of SpA is based on the shared clinical characteristics and the role HLA-B27 allele in the pathogenesis of SpA. Previous

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experiments demonstrated that the HLA-B27 transgenic rats were more susceptible to multisystem inflammatory disorders similar to the SpA multisystem involvement.[3] The prevalence of SpA shows wide geographic disparity; previous registries showed that the prevalence of SpA ranges from 9 to 30 per 10,000 general population worldwide.[4] In a recent global systematic review, the prevalence of SpA was reported to range from 20 to 161 per 10,000 general population, with the highest prevalence in Northern Arctic communities.[5]

Clinically, patients with axial SpA present with chronic inflammatory low back pain, which can limit lumbar flexion due to the fusion of several vertebrae.[6] Besides, SpA patients can present with a wide range of extra-articular manifestations.[7] Cutaneous manifestations, multiorgan involvement, and increased risk of cardiovascular diseases were also noted in patients with SpA.[8–10] According to the Assessment in SpondyloArthritis International Society (ASAS) criteria, the classification of axial SpA depends on the presence of sacroiliitis by MRI plus one clinical feature ("imaging arm") or the presence of HLA-B27 plus two clinical features ("clinical arm").[11] Imaging of the sacroiliac joint is an important element in the diagnosis of Axial SpA. While X-rays can only show late lesions in the sacroiliac joint, magnetic resonance imaging (MRI) shows early post-inflammatory changes, such as erosions, sclerosis, ankyloses, and fatty lesions via T1 and T2 weighted sequences.[2] Computed tomography (CT) is considered the gold standard modality for detecting structural damage, particularly erosions.[12] Active inflammation can be detected as bone marrow edema in both sides of SIJ in the STIR sequence.[13] The Ankylosing spondylitis disease activity can be measured by various scales, including Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Functional Index (BASFI), and Bath Ankylosing Spondylitis Metrology Index (BASMI).[14–16] Besides, various, well-validated, assessment scores were developed for PsA, such as Disease Activity in Psoriatic Arthritis (DAPSA), clinical DAPSA (cDAPSA), and Composite Psoriatic Disease Activity Index (CPDAI).[17] Recommendations for first-line therapy of axial SpA include Non-Steroidal Anti-inflammatory Drugs (NSAIDs), such as naproxen, diclofenac, ibuprofen, indomethacin, and piroxicam, and non-pharmacological treatment, such as physiotherapy and exercises. The second-line includes bDMARD therapy in the form of TNF-α, Janus kinase (JAK), and interleukin (IL)-17 inhibitors.[18] Finally, analgesics, including paracetamol and opioid-(like) drugs, and surgery can be regarded in resistant cases.[2] With regard to PsA treatment, the current guidelines recommend TNF-α inhibitors, IL-12/23, JAK, and T-cell inhibitors in case of inadequate response to conventional synthetic DMARDs.[18–20] However, the application of these interventions in the real-world is still limited.

On the other hand, patients with peripheral SpA present mainly with peripheral joint involvement. According to the current literature, patients with PsA can present with five different patterns of joint affection, with asymmetric mono-articular or oligoarticular arthritis being the most dominant pattern. Other patterns of involvement include distal interphalangeal joint involvement, symmetric polyarthritis, and arthritis mutilans. Besides, common clinical features of peripheral SpA include dactylitis, enthesitis, and cutaneous manifestations.[21]

According to several studies, including those from the Middle East and Saudi Arabia, SpA, including AS, can negatively impact the health-related quality of life (HRQoL) of the patients.[22–25] A distinct feature of different subtypes of SpA is the extra-articular involvement, which adds further burdens on HRQoL.[2] Besides, SpA is associated with an increased healthcare resource utilization (HCRU), particularly among patients who do not initiate biologic disease-modifying antirheumatic drugs (bDMARDs) early.[26–28]

Saudi Arabia is the largest country in the Arabian Peninsula, with more than 34 million inhabitants.[29] While the prevalence of rheumatic diseases in Saudi Arabia appears to be similar to the Western world, there are notable differences between Saudi and Western patients regarding disease patterns and outcomes.[30] Recently, SpA has gained more attention in Saudi Arabia with an increasing number of published studies exploring its epidemiology and clinical patterns.[31] In this narrative review, we aimed to summarize the current published literature regarding the multidimensional impact of SpA, including axial and peripheral subtypes, on HRQoL and HCRU in Saudi Arabia. Besides, we explored the correlation of delayed diagnosis and disease severity with HRQoL and HCRU. This review also offers directions for future research addressing the current landscape and impact of SpA in Saudi Arabia.

Discussion

The Epidemiology of SpA in Saudi Arabia and the Middle East and North Africa (MENA)

Globally, the prevalence of SpA was reported to range from 20 to 161 per 10,000 general population, with the highest prevalence in Northern Arctic communities.[5] It was also noted that South Asia (22 per 10,000 general population) and South-East Asia (20 per 10,000 general population) had a lower prevalence than Europe and the United States (US).[5] The same global study showed that the pooled prevalence of SpA, including AS, was 32 and 11 per 10,000 general population, respectively, in the Middle East and North Africa (MENA) region.[5] Concerning peripheral SpA, a recent global systematic review highlighted that the prevalence and incidence of PsA were 133 per 100,000 general population and 83 per 100,000 person-years, respectively.[32]

Other than the above study, only a few others have reported the prevalence of SpA in the MENA region. A previous report from Iran showed a prevalence of 23 and 12 per 10,000 of the general population for SpA and AS, respectively;[33] while, in the same country, nearly 9% of the psoriasis patients were reported to have PsA.[34] Data are even more scarce in the Gulf region. In a single-center report from Kuwait, it was estimated that the prevalence of PsA was 0.01% (95% CI 0.00–0.17%).[35] Another study from Kuwait found a prevalence of 8 patients per 10,000 population.[36] Based on a cross-sectional study of 3985 patients from primary health care clinics, the prevalence of PsA was reported to be 0.3% in the United Arab Emirates (UAE).[37] To date, very limited national data about the epidemiology of SpA in Saudi Arabia exist. In a previous report by Elnady et al,[38] it was reported that the incidence of PsA was 4.3% among psoriasis patients.

Clinical Patterns of SpA

The clinical patterns and spectrum of SpA disorders are believed to be affected by geographical and ethnic disparities.[39] There is some evidence of more severe disease and delayed diagnosis among patients from the Middle East, compared to the Western population.[25] A study on 518 patients from Morocco, Algeria, and Tunisia reported that in patients with sacroiliitis, inflammatory back pain, peripheral involvement, and extraarticular disease such as psoriasis, were associated with a high prevalence of hip involvement (30.3% at 5 years and 39.4% at 10 years).[40] A prospective cohort study on 22 patients from Jordan, which followed up patients for four years, revealed mild to moderate disease with few systemic complications. Only one patient progressed to a Bamboo spine.[41] In a recent review by Bedaiwi et al,[42] it was noted that PsA patients present with substantial physical involvement and symptomatic burden in the MENA region; however, there was no comparison conducted with other populations.

In a study conducted by Bedaiwi et al[43] in Saudi Arabia, it was observed that among patients with AS who were previously diagnosed at a tertiary center, only 36.1% demonstrated low disease activity; on the other hand, 40.6% of PsA patients had high disease activity, at the start of the study. Another study in Saudi collected the data of 15 AS patients from King Khalid University Hospital for four years.[44] All patients presented with radiographic sacroiliitis; nearly 60% and 33% of the patients had enthesitis and peripheral arthritis, respectively. In addition, eye affection was present in 20% of the cases. A small study was performed in 1982 on 194 patients admitted to the rheumatology clinic at King Khalid University Hospital and reported four SpA patients, which had no-to-mild movement limitations;[30] the report did not present any other clinical feature for these four patients. Elnady et al,[38] reported that using ultrasonography, nearly 40% of Saudi patients with PsA had subclinical enthesitis and synovitis before the development of PsA; nonetheless, the author did not report the clinical features of the patients with PsA. Omair et al,[31] assessed the prevalence of HLA-B27 positivity among axial SpA patients from five centers in Saudi Arabia over a period of 26 years. One hundred and thirty-four patients were included; HLA-B27 was positive in 60.4% of the entire cohort; 69% of patients with AS and 25.9% of patients with non-radiographic axial SpA. Nearly 19.4% of all patients had extra-articular manifestations.

Delayed Diagnosis of SpA

Without effective treatment, SpA leads to irreversible structural damages in joints, with subsequent impairment of physical and emotional well-being, as well as increased economic cost and HCRU.[27,45,46] Accordingly, early diagnosis represents a cornerstone in the efforts to minimize the clinical, economic, and emotional burden of SpA. However, globally, there is an

average of 5–14 years of delay between the onset of disease symptoms and the time of diagnosis.[47–52] In the USA, it was reported that patients with PsA experienced a diagnostic delay of nearly 2.5 years.[53] One of the contributing factors to diagnostic delay is the lower awareness of inflammatory back pain among primary care physicians. For example, low back pain has a global prevalence of 9%, and nearly 54–80% of adults experience low back pain once in their lifetime.[54–56] Moreover, chronic back pain (defined as pain lasting for more than three months) is one of the common symptoms in primary health care, adding difficulty to early diagnosis.

Historically, the presence of different criteria for the diagnosis of the different entities within SpA was one of the factors that contribute to delayed diagnosis. For example, Rome criteria, New York, and modified New York criteria require the presence of radiographic evidence of sacroiliitis, which occurs in the late stages of AS.[57–60] On the other hand, the ASAS criteria differentiate peripheral from axial SpA with higher sensitivity and specificity. Radiographic evidence of sacroiliitis was not essentially required to diagnose Axial SpA.[8,61] Likewise, the lack of accepted diagnostic and classification criteria for PsA was reported to be a contributing factor to delayed diagnosis.[62] However, the introduction of CASPAR criteria could mitigate this impact on the time of diagnosis.[63]

One of the main reasons for the delayed diagnosis is the delayed referral of patients from primary health care physicians to rheumatology specialists due to several factors, including delayed clinical suspicion of the disease in patients, absence of nearby rheumatology specialists, long waiting lists, and patient reluctance to see specialists.[64,65] Accordingly, the adoption of outdated criteria can delay diagnosis, with new criteria needing to be adopted by physicians to limit the delay in diagnosis.[66] In an Egyptian study, investigators compared patients with a diagnosis of axial SpA before the beginning of 2010 (when ASAS criteria became widely available and in use) and patients with a diagnosis of axial SpA after the beginning of 2010, to assess the impact of wide application of ASAS on delay diagnosis in axial SpA. The adoption of the ASAS criteria resulted in a decrease in the delay of diagnosis compared to before 2010 (4.6 years of delay vs 11.3 years), respectively. Moreover, the wide application of ASAS criteria was associated with younger age at the time of diagnosis, less direct cost, lower number of doctor's visits, and lower disease activity scores.[67]

Several studies assessed the clinical impact of delayed diagnosis of Axial SpA. Patients with delayed SpA diagnosis suffered from increased activity of SpA, impaired physical function, and more structural damage compared with patients with early diagnosis.[68] A statistically significant association was found between worse BASDAI and BASFI scores and delayed diagnosis in different studies.[47,67,69,70] Likewise, other spinal mobility measures were also affected as the Schober test and lateral lumbar flexion.[71–73] Response to treatment was less favorable in patients with delayed SpA diagnosis, as assessed by BASDAI score and radiologic assessment.[74] Radiographic disease progression in SpA patients was significantly associated with delayed diagnosis compared with early diagnosis.[47,71,74,75] Delayed diagnosis of SpA was also associated with an increased number of doctors' visits and an increased number of patients who underwent unnecessary spinal surgery.[76] Similarly, the delayed diagnosis in the setting of PsA was found to be associated with a more symptomatic burden.[53]

In a Saudi study conducted by Bedaiwi et al, which included 94 patients who were diagnosed with SpA, the delay in diagnosis of AS was reported to be 6.69 ± 5.83 years, while the delay was 3.67 ± 6.42 years in PsA and 2.00 ± 1.60 years in enteropathic arthritis. There was no statistically significant relationship between HLA-B27 positivity and the delay of diagnosis or age at diagnosis. Notably, there was no statistically significant correlation between the delay in diagnosis and disease severity scores.[43] In Omair et al[31] study, the delay in diagnosis among Saudi patients with axSpA was 3 (1–6) years. Such diagnostic delay was associated with a higher symptomatic burden.

Regional experts from different Arab countries, including Saudi Arabia, reported that there is an actual need to train general practitioners and specialists in orthopedics and internal medicine about inflammatory back pain and how to diagnose SpA in its early stages. This targeted training would minimize the diagnostic delay by reducing the time from the onset of symptoms to referral to a rheumatologist and eventual diagnosis.[16] The causes of delayed diagnosis should be examined to decrease this delay in Arab and Saudi populations with its associated health and economic burden.

HRQoL and Psychosocial Burden of SpA

The Burden of SpA on HRQoL

HRQoL is an integral part of the adequate management of chronic diseases. It is generally defined as "a multidimensional assessment of how disease and treatment affect a patient's sense of overall function and well-being".[77] According to the

US Food and Drug Administration (FDA), the HRQoL is defined as "a multidomain concept that represents the patient's general perception of the effect of illness and treatment on physical, psychological, and social aspects of life".[78]

Patients with SpA can suffer from impaired HRQoL for various reasons, including impaired physical activity, severe debilitating symptoms, chronic pain, treatment-related adverse events, and psychological distress symptoms.[79] In one of the largest studies, 70,334 US veterans were invited via a postal survey to answer questions about the performance of activities of daily living (ADL) and HRQoL using Veterans Short Form-36. Out of them, 664 veterans with SpA (AS = 100 patients, Psoriatic arthritis = 551, and Reactive arthritis = 13) reported significant limitations in dressing, walking, transferring, and overall mean Activities of Daily Living (ADL) limitation, when compared with other veterans without SpA. Moreover, they observed poorer physical function and HRQoL in SpA patients after adjustment for demographic differences and comorbidities. Improving functional status is an important aspect of SpA treatment to improve QoL.[22] Although non-radiographic Axial SpA is associated with less inflammatory changes and shorter disease duration, it poses a similar burden of impaired physical function and HRQoL as radiographic SpA.[80] Surprisingly, non-radiographic Axial SpA patients reported more significant impairment of psychosocial health in the SF-36 survey than radiographic SpA.[80]

Concerning the MENA region, an Egyptian study on 75 patients from four different centers reported significant impairment in the mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score and mean Health assessment questionnaire (HAQ-DI). This impairment was correlated with more severe disease.[24] Another multicenter study, including four different Arab countries (Egypt, Kuwait, Qatar, and Saudi Arabia), collected data from 169 SpA patients. The patients showed a significant impairment in the HRQoL, as assessed by the Ankylosing Spondylitis Quality of Life score (ASQoL). Besides, nearly 15% of patients were unemployed or part-time employed due to disease activity.[25] In their systematic review, Bedaiwi et al reported that patients with PsA from the MENA region had a reduced QoL.[42]

The Effect of Delayed Diagnosis of SpA on HRQoL

Delayed diagnosis of axial SpA was associated with poor HRQoL in several studies.[47,72,81–83] During the period between the onset of symptoms and receiving a diagnosis of SpA, patients experienced depression and distress, and employed patients felt stigmatized in the working environment by the notion of having a "bad back".[81] A higher prevalence of depression was associated with a delay in diagnosis.[82] Grigg et al,[83] reported significant emotional relief (69%) and a more optimistic attitude (66%) when patients were diagnosed after a delay. However, the delay itself was not associated with long-term depression using the Beck Depression Inventory test. In a study on 163 Iranian patients, worse QoL and morning stiffness were correlated with a delay in diagnosis.[47] A study on 121 Turkish patients using the 36-item Short-Form Health Survey (SF-36) stated that a longer delay in diagnosis was associated with worse scores in physical functioning and general health domains of the survey when compared with early diagnosis.[72]

To date, there are no published studies from Saudi Arabia and Gulf region regarding the association between delayed diagnosis and impaired HRQoL amongst SpA patients.

The Effect of Suboptimal Management of SpA on HRQoL

Despite the advance in the management of SpA, previous reports noted suboptimal responses in a considerable proportion of the patients.[84] Suboptimal management of SpA can significantly impair the HRQoL of the patients through the high symptomatic burden and progressive involvement of various systems.[85] In order to guide rheumatologists in the use of new therapies and management strategies, many international guidelines disseminated evidence-based recommendations for the management of SpA, aiming for low disease activity and better HRQoL.[86] However, despite these great advances in the understanding of the importance of early and aggressive treatment, management of SpA in the MENA region remains suboptimal for a combination of reasons.

The lack of formal assessment and monitoring of disease activity status is one of the factors that may contribute to the suboptimal management of SpA in the MENA region. Over the past two decades, a continuous effort was implemented to develop universal and well-validated tools for assessing SpA disease activity.[87] In the setting of axial SpA, the BASDAI, ASDAS, BASFI, and BASMI are commonly used for the assessment and monitoring of the patients.[14–16] Previous reports showed that these scores are predictors of HRQoL in axial SpA patients.[79] A significant correlation was found

between BASFI score and both physical and social function. The role limitation due to emotion was significantly correlated with BASDAI scores.[88] Likewise, a study found a significant negative linear correlation between ASQOL and BASDAI, BASFI, and ASDAS.[89] However, the use of these assessments in daily practice could be limited, especially in areas with limited access to rheumatology services.

On the other hand, various, well-validated assessment scores were developed for PsA, such as minimal disease activity (MDA), very low disease activity (VLDA), DAPSA, cDAPSA, and CPDAI.[17] According to previous literature, the assessment of these scores should be implanted in routine clinical practice, and they can be used as suitable treatment targets for PsA.[90] Besides, it was found that higher disease activity, as measured by MDA, DAPSA, and cDAPSA was correlated with more impairment in the HRQoL of PsA patients.[91] Despite the beneficial role of formal assessment of PsA disease activity, there is a lack of formal assessment using validated tools in the Saudi Arabia clinical setting.

The most pressing issue in managing SpA arises from a combination of factors, such as a deficit of specialized healthcare professionals,[92] restricted availability of cutting-edge bDMARDs in numerous MENA countries,[93] the absence of SpA management guidelines tailored to local contexts, inadequate healthcare financing, substantial treatment costs, and limited disease awareness among both patients and primary healthcare physicians.[94,95] These obstacles pose significant impediments to efficient SpA treatment and hence, concerted efforts should prioritize addressing these problems to enhance the overall management of SpA.

To date, there are no published studies from Saudi Arabia and Gulf region regarding the association between suboptimal management and impaired HRQoL amongst SpA patients.

Economic and HCRU Burden of SpA

A growing body of evidence has shown a substantial economic impact of SpA and an associated increase in HCRU.[96] According to a US survey in 2012, the annual HCRU cost for patients with AS was 6514 US Dollars.[97] A study published in 2008 on 145 Hong Kong patients revealed an average annual cost of 9120 US Dollars. The overall costs included direct costs (doctor visits, diagnostic workup, hospital care, drugs, and out-of-pocket expenses) and indirect costs (work disability and household work). None of the participants ever used bDMARDs treatment. Indirect costs accounted for 62% of the total cost, while diagnostic workup accounted for 32% of the direct cost, followed by doctor visits (22% of the direct cost).[88]

Delayed diagnosis of axial SpA was associated with increased HCRU. Increased costs were either direct costs associated with increased specialist visits, preventable spinal surgeries, and treatment. Seo et al,[74] reported increased social disabilities in patients with delayed diagnosis of more than eight years compared with patients diagnosed in less than eight years. Social disability was defined as the change of jobs, leaving jobs due to disease, discontinuation of academic studies, and the requirement of another person to help homemakers.[74] Work disability was greater in SpA patients with delayed diagnosis when compared with early diagnosis.[70,72,83,98,99] In a retrospective study on Health Search Database in Italy, 1084 patients were identified with a delay in diagnosis of three years. During this delay, approximately €153,000 were spent on services related to specialist visits and drugs not related to SpA. If this database represents the Italian population, it is expected that over €5.4 million were unduly spent on healthcare services for 38,232 SpA patients in three years (2010–2013).[100] Grigg et al,[83] estimated the healthcare cost associated with delayed diagnosis to be more than 3000 USD in 26% of patients with early diagnosis (<5 years delay) compared with 44% of patients (5–10 years of delay) and 67% of patients (> 10 years of delay). Additionally, increased delay in diagnosis was associated with indirect costs related to loss of employment. The risk of work disability increased by 6% per year of delay in diagnosis.[70] There was no relationship between diagnostic delay and TNF inhibitor use.[101] Likewise, delay in PsA diagnosis exerted a notable burden on HRCU as reported by several previous reports. In one report, it was noted that direct HRCU costs correlated positively with the progression of PsA, highlighting the critical role of early diagnosis in reducing HRCU costs in these patients.[102]

Concerning the MENA region data, a study on 121 Turkish AS patients was performed to investigate factors that determine work disability. The frequency of hip and spine involvement was higher in the work-disabled group. Other factors such as older age of onset of the disease, diagnostic delay, and spinal and hip mobility impairment were associated with work disability.[72] In 2018, an Egyptian study estimated the effect of delayed diagnosis on health care

costs, which was 9879 ±3827 USD for delayed diagnosis compared with 2373 ±881 USD for early diagnosis. This cost was in the form of medical consultations, medications, investigations, physiotherapy, and surgical treatment. Additionally, the delayed diagnosis was associated with a significantly higher number of doctor visits and HCRU in the form of preventable spinal surgery. Moreover, loss of work was higher in patients with delayed diagnosis when compared with early diagnosis.[67] Another study on 90 Egyptian AS patients was performed to assess the prevalence and risk factors associated with work disability. Nearly 40% of patients were not working due to AS. Different factors were associated with disability, including delayed diagnosis, lower educational level, manual work, rural living, peripheral arthritis manifestation, and psychological factors.[99] To date, there are no published studies from Saudi Arabia that assessed the HRCU costs of SpA and the impact of the delayed diagnosis on costs.

A factor that can contribute to increased HCRU for the management of SpA in the MENA region is the lack of a local budget impact model and the accessibility to new bDMARDs therapy. The use of bDMARDs was found to be an independent negative predictor for HCRU in the PsA setting.[97] Moreover, the introduction of new bDMARDs, including Mirikizumab, Bimekizumab, and Ustekinumab, could participate in reducing the HCRU.[103,104] On June 5, 2023, the European Medicines Agency (EMA) approved the use of bimekizumab in patients with PsA, axSpA, non-radiographic axSpA, and AS. This approval relied on the results of the BE OPTIMAL and the BE COMPLETE trials, which demonstrated the improvements in the bimekizumab group vs placebo in signs, symptoms and disease activity.[105,106]

In some parts of the MENA region, the availability of bDMARDs is still limited; besides, the high cost of bDMARDs represents a financial restriction for their use in some MENA countries.[107] Moreover, the availability of well-trained rheumatologists may affect the country's profile in using bDMARDs.[94] Thus, the currently published literature demonstrates significant variations in the rate of utilization of bDMARDs amongst SpA patients, which reflect substantial variations in the factors that affect biologics use across different MENA countries. In Qatar, it was found that nearly 40% of the axial SpA patients received TNF-α inhibitors, which is mainly attributed to the free healthcare system for citizens and residents.[108] This rate was notably lower in other MENA countries, where the private sector accounts for a considerable proportion of the healthcare system.[25]

However, there are no published separate data about the utilization of bDMARDs and its impact on HRCU in Saudi Arabia. In a multinational study that involved Saudi Arabia, nearly 20% of the patients who were prescribed bDMARDs, did not receive the treatment as prescribed.[25]

Conclusion and Future Directions

In the present review, we summarized the published literature from Saudi Arabia and MENA regarding the epidemiology, clinical features, clinical practice, and impact of SpA on HRQoL and HCRU. It can be concluded that the data regarding these aspects are scarce in Saudi Arabia and other MENA countries. Besides, the association between delayed diagnosis and HRQoL among Saudi patients with SpA has not been studied yet. Data are also limited regarding the SpA disease patterns within the kingdom and how disease severity affects the HRQoL. On the same token, we could not identify published studies that estimated the direct costs and HCRU in SpA patients within Saudi Arabia. Regional studies from the MENA have highlighted that the cost of SpA management varies substantially, reflecting at least partially the disparity in the availability of bDMARDs. However, there are no currently published national studies to reflect the HCRU and cost-effectiveness of bDMARDs use amongst Saudi patients with SpA. Such findings run in parallel with a recent consensus, which gathered experts from different countries in the Arab and MENA region, reporting a lack of published data on SpA.[16]

To fill this evidence gap, there is an imperative need to develop a high-quality, national-level, epidemiological, and health economic studies that assess the following: (1) accurate and updated prevalence of SpA; (2) the clinical characteristics of SpA patients, as well as the magnitude of disease severity and extra-articular involvement; (3) the impact of SpA on the HRQoL of the patients and the factors that can predict the extent of impaired HRQoL in such population, which can represent the first step in developing psychological interventions that are personalized to this patient population; (4) the impact of implementing formal assessment of disease activity scores evaluation on the management of the patients and, subsequently, its impact on their HRQoL; and (5) the HCRU and costs for patients with SpA, and how treatment patterns can affect this cost. Establishing local registries for patients with SpA in the

Kingdom could help in covering this gap of knowledge. Besides, educational measures should be implemented to increase the awareness about the red-flag signs for patients with low back pain among healthcare practitioners, which can minimize the delay in diagnosis, improve assessment measures, and prompt effective management.

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