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REVIEW

Disease burden and treatment challenges of psoriatic arthritis in Africa and the Middle East

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Abstract

Psoriatic arthritis (PsA) is a chronic, inflammatory arthropathy occurring in up to 30% of patients with psoriasis, and is characterized by multiple manifestations including peripheral arthritis, enthesitis, dactylitis, spondylitis, and psoriatic skin and nail disease. This complex and heterogeneous disease is poorly understood and its diagnosis and treatment are suboptimal, particularly in Africa and the Middle East, where very few studies into the impact of PsA have been carried out. This article aims to highlight the disease burden of PsA in the region as well as to identify unmet clinical needs. A non-systematic review was carried out in the PubMed database and the most relevant publications were selected. Expert rheumatologists practicing in Africa and the Middle East provide an insight into the challenges of treating PsA in daily practice, along with recommendations for improvements.

Keywords Africa · Disease burden · Middle East · Prevalence · Psoriatic arthritis · Spondyloarthritis

Introduction

Psoriatic arthritis (PsA) is a member of the spondyloarthritis family of diseases and affects approximately 30% of patients with psoriasis [1]. This chronic immune-mediated inflammatory disease is characterized by multiple manifestations including peripheral arthritis, enthesitis, dactylitis, spondylitis, and psoriatic skin and nail disease [1, 2], which may occur alone or in combination [3]. Since PsA is a clinically diverse and heterogeneous disease, both in presentation and severity [4], management is particularly challenging and requires an interdisciplinary approach [5]. Recent advances in the understanding of the immunological mechanisms underlying PsA are providing new insights into the pathogenesis of the disease [6], enabling the development of targeted therapies that can improve patient outcomes [7].

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However, there is still much to learn and both the diagnosis and treatment of PsA remain suboptimal [7]. This is particularly true for the large and diverse region of Africa and the Middle East, where very few studies into PsA have been carried out, and consequently the extent of the disease burden is poorly understood and improvements in the management and treatment of PsA are much needed [5].

The objective of this review is to highlight the disease burden of PsA in Africa and the Middle East and to identify unmet clinical needs and the physical and psychosocial impact of PsA in the region.

Literature search strategy

Non-systematic literature searches were conducted using PubMed (https://www.ncbi.nlm.nih.gov/pubmed), incorporating all studies published on or before March 01, 2019 (10 year limit) based on the following search terms: (Africa OR sub-Saharan Africa OR Algeria OR Bahrain OR Egypt OR Iran OR Iraq OR Jordan OR Kuwait OR Lebanon OR Libya OR Middle East OR Morocco OR Oman OR Qatar OR Saudi Arabia OR South Africa OR Syria OR Tunisia OR United Arab Emirates OR Yemen) AND psoriatic arthritis AND prevalence OR burden. A search replacing 'psoriatic arthritis' with 'spondyloarthritis' was also performed. A search of African Journals Online (https://www.ajol.info) was also conducted based on the following search terms: psoriatic arthritis OR spondyloarthritis. Additionally, the African Journal of Rheumatology, published African League Against Rheumatism (AFLAR) Congress abstracts (2013), and recent Asia Pacific League of Associations for Rheumatology (APLAR) Congress abstracts (2015–2018) were reviewed for relevant studies. The literature search results were manually reviewed for relevance, and articles reporting PsA in countries outside of Africa and the Middle East were excluded. References in all relevant articles were examined to identify other articles of interest and, in addition to the searches, the authors drew on their knowledge of the wider literature to provide context. Figure 1 shows a flowchart of the non-systematic literature selection process and the 12 articles initially identified from the literature search are detailed in Table 1.

The authors, who are expert rheumatologists practicing in Africa and the Middle East, also provide an insight into the challenges of treating PsA in daily practice from personal experience, along with recommendations for improvements.

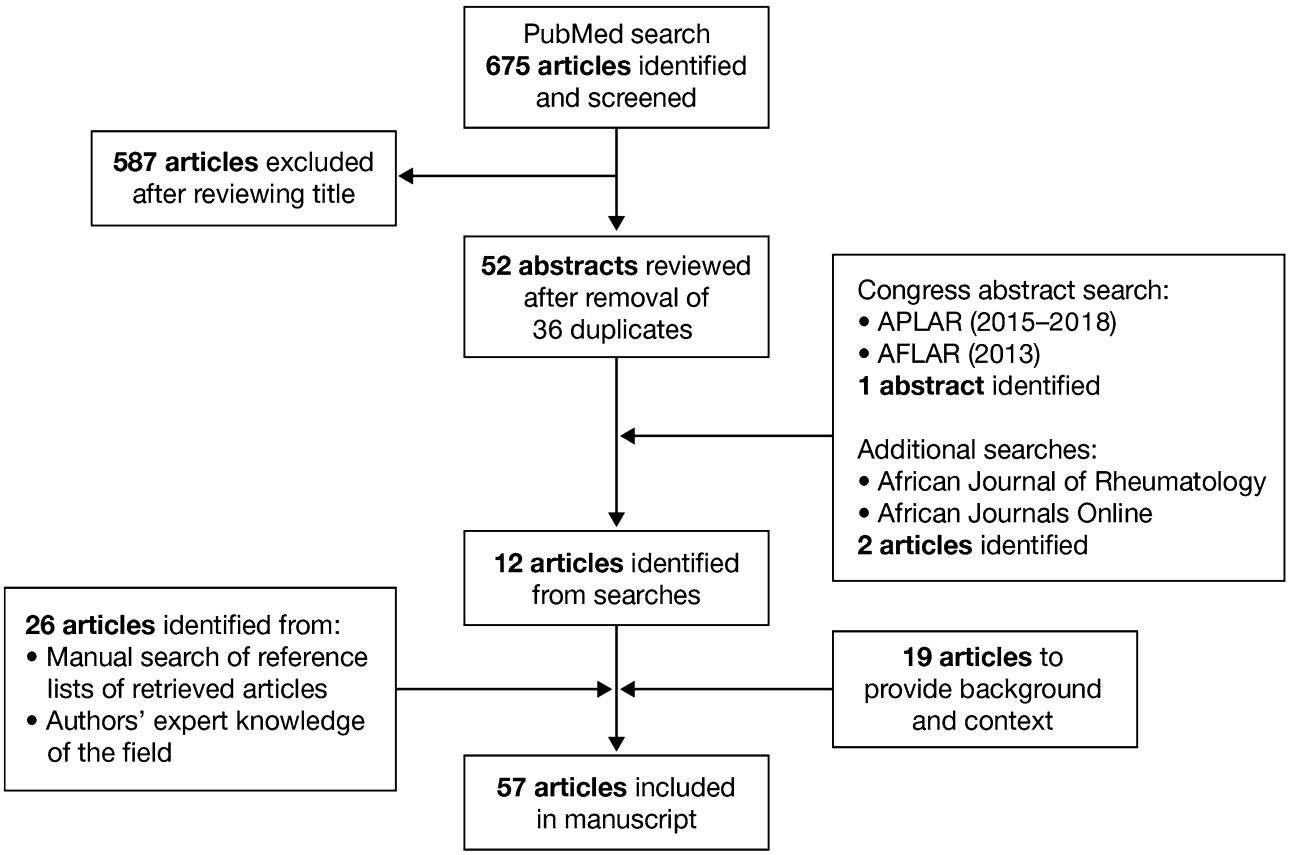

Fig. 1 Flowchart of the non-systematic literature selection process

Table 1 Articles identified in the literature search

Article	Type	Main observations
Abdulghani et al. [5]	Review and expert opinion of dermatologists in Africa and the Middle East	The management of psoriasis and PsA is suboptimal in Africa and the Middle East
Al Hammadi et al. [8]	Survey of expert dermatologists in Africa and the Middle East	There was a lack of consensus in the use of biologics for the treatment of psoriasis and PsA in clinical practice, which was attributed to low physician awareness, high cost, and non-adherence
Conaghan et al. [9]	Multi-national survey of dermatologists and rheumatologists in the Asia–Pacific region and the Middle East	Patients waited an average of 0.9 years for a confirmed diagnosis of PsA, and longer for appropriate treatment ($n=364$)
Elnady et al. [10]	Study of patients with psoriasis from two tertiary medical centers in Saudi Arabia	During a 2-year clinical follow-up of patients with psoriasis, the annual incidence of PsA was reported to be 4.3% ($n=104$)
Harmse et al. [11]	Review of bDMARD use in South Africa	The prohibitive cost of biologics limits their use in resource-poor countries
Jamshidi et al. [12]	Single-center cross-sectional study of PsA in Tehran, Iran	PsA was reported in 29/320 patients with psoriasis (9.1%)
Lebughe et al. [13]	Prospective hospital-based study in the Democratic Republic of Congo	One case of PsA reported among 984 patients (0.1%) attending two rheumatology practices
Maharaj et al. [14]	Single-center study of PsA in South Africa	A study of 384 patients with PsA reported the complete absence of black South African patients with PsA
Mgonda et al. [15]	A cross-sectional hospital-based study in Tanzania	Two cases of PsA among 42 patients with psoriasis (5%) attending specialized skin clinics in Tanzania
Ouédraogo et al. [16]	Review article of PsA in sub-Saharan Africa	No data available on the prevalence of PsA in sub-Saharan Africa
Stolwijk et al. [17]	Systematic review and meta-regression analysis of the global prevalence of spondyloarthritis	There is large variation in the reported global prevalence of PsA Prevalence of PsA in the Middle East and North Africa was reported as 0.01% (95% CI 0.00–0.17%)
Usenbo et al. [18]	Systematic review and meta-analysis of the prevalence of arthritis in Africa	There is a lack of reliable data on the prevalence and burden of PsA in Africa

bDMARD biologic disease-modifying antirheumatic drug, *PsA* psoriatic arthritis

Incidence and prevalence of PsA in Africa and the Middle East

There is considerable variation in the reported global incidence and prevalence of PsA [17, 19]. The global annual incidence of PsA has been reported as ranging from 0.1 to 23.1 cases per 100,000 (median 6.4) in the general population [19], while global prevalence rates of PsA are estimated to range from 0.001 to 0.42%, depending on geographic region [17, 19, 20].

There are several factors causing this wide variation in global estimates, including the use of different methodologies used to identify cases of PsA. Those studies with the lowest prevalence estimates have used International Classification of Disease (ICD-9) codes or clinical classification criteria, while those with higher estimates have utilized self-reported diagnosis techniques [20–23]. Another factor that may partially explain the wide differences in the global prevalence is the variable expression of the HLA-B27 allele, which is a genetic biomarker of PsA—populations with a high frequency of this gene are reported to have higher rates of PsA [24]. Additionally, patients with PsA expressing this allele tend to develop musculoskeletal symptoms faster, are more prone to developing enthesitis, dactylitis, and uveitis, and develop an axial disease pattern with more bone marrow edema in sacroiliac joints [24].

The HLA-B27 allele is widespread in the population throughout Europe and Asia, and very highly prevalent in the native populations of arctic and subarctic regions such as Alaska and Greenland, but is effectively absent in the native population of other regions, such as South America, Australia, and parts of Equatorial and Southern Africa [25].

Population-based studies have estimated the prevalence of PsA in the United States to be 0.25% [95% confidence interval (CI) 0.18–0.31%] [20] and in the United Kingdom to be 0.19% (95% CI 0.185–0.193%) [26]. However, a comparison with African and Middle Eastern populations is not currently possible since the majority of research into PsA has been carried out in Western countries and there are very few published studies on the prevalence and burden of PsA in Africa and the Middle East [5, 18], which was evident in our literature search. Consequently, the reported global estimates of incidence and

prevalence may not be reflective of this very large and diverse region [5]. Indeed, the lack of local registries, reliable diagnosis, and reporting of PsA has led to the impression that it is relatively rare in Africa and the Middle East, when in fact the burden of the disease is unknown [16]; a similar observation has been reported for rheumatoid arthritis (RA) [27].

In a recent systematic review and meta-regression analysis, the prevalence of PsA in the Middle East and North Africa was reported to be 0.01% (95% CI 0.00–0.17%) [17]. However, this estimate was based on a single population study from Kuwait, in which one case of PsA was identified in a survey of 7670 adults [28]. A cross-sectional population-based study of 3985 patients attending primary healthcare clinics in the United Arab Emirates estimated the prevalence of PsA to be 0.3% [29], while an Iranian single-center cross-sectional study of 320 patients with psoriasis reported that 9.1% had PsA [12]. A population-based study of > 3000 adults in Lebanon used the Community Oriented Program for the Control of Rheumatic Diseases (COPCORD) methodology, which estimated the prevalence of spondyloarthropathies to be 0.3%; however, the survey did not specifically identify any cases of PsA [30]. During a 2-year clinical follow-up of patients with psoriasis from two tertiary medical centers in Saudi Arabia, the annual incidence of PsA was reported to be 4.3% ($n = 104$) [10]. This was the only study identified in our search that reported annual incidence rates in Africa and the Middle East.

The prevalence of PsA in the general population of sub-Saharan Africa is unknown, but it has been reported sporadically in isolated studies [16]. Hospital-based studies have reported the prevalence of PsA to be 1% (95% CI − 0.10 to 2.10) in patients with HIV in urban Uganda ($n = 300$), 0.01% (95% CI − 0.01 to 0.02) among 12,494 outpatients in a rheumatology clinic in urban Cameroon [18, 31, 32], and 0.1% (one occurrence) of 984 patients attending two rheumatology practices in the Democratic Republic of Congo [13]. A cross-sectional hospital-based study reported two cases of PsA among 42 patients with psoriasis (5%) attending specialized skin clinics in Tanzania [15]. A single-center study of 384 patients in South Africa reported no black South African patients with PsA, rather all patients attending the clinic were mixed race, or of Indian or European descent. The authors suggested that this lack of susceptibility could be due to yet-to-be-identified protective genes in this population [14]. This inconsistent and sporadic reporting highlights the need for more epidemiological studies of PsA in Africa and the Middle East.

Diagnosis and management of PsA in Africa and the Middle East

Prior to the introduction of the criteria developed by the ClASsification of Psoriatic ARthritis (CASPAR) study group [33], the lack of universally accepted diagnostic and classification criteria for PsA hindered the understanding of the burden of PsA [34].

Guidelines published by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) provide recommendations for the management of PsA [35, 36]. A limitation of the EULAR guidelines is that they are focused on the management of the musculoskeletal manifestations of PsA, while the management of psoriatic skin disease is not addressed [37]. Clinical guidelines for PsA jointly developed by ACR/NPF were recently published and are the first to include new therapeutic agents for the treatment of PsA, such as inhibitors of interleukin (IL)-17 and Janus kinase. These guidelines provide treatment recommendations for the management of both musculoskeletal disease and severe psoriasis [36].

Recommendations published by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) are preferred by some clinicians as they encompass key PsA disease domains (i.e., arthritis, spondylitis, enthesitis, dactylitis, skin disease, and nail disease), and these recommendations are frequently implemented in the Africa and Middle East region [2]. According to GRAPPA, the ultimate goals of therapy for patients with PsA are (1) to achieve the lowest possible level of disease activity in all domains of disease, (2) to optimize functional status, improve quality of life and wellbeing, and prevent structural damage to the greatest extent possible, and (3) to avoid or minimize complications, both from untreated active disease and from therapy. They recommend that all major disease domains of PsA are considered, including examining the impact of the disease on pain, function, quality of life, and structural damage. GRAPPA recommends that clinical assessments should include patient-reported outcome measures, a comprehensive medical history, and physical examination, along with laboratory tests and imaging techniques [2].

GRAPPA recommendations may be more applicable for use in Africa and the Middle East, a diverse and large area that includes both resource-poor and resource-rich countries, because it provides ‘standard’ and ‘expedited’ therapeutic recommendations for each clinical domain; the standard treatment for axial disease would begin with nonsteroidal anti-inflammatory drugs and progress to biologic disease-modifying antirheumatic drugs (bDMARDs; e.g., tumor necrosis factor, IL-17, or IL-12/23 inhibitors) in inadequate responders, while the expedited option would initiate treatment with bDMARDs directly [2]. Hence, GRAPPA’s ‘standard’ arm could be the initial treatment option for the resource-poor countries, while GRAPPA’s ‘expedited’ treatment recommendations may be most appropriate in resource-rich countries.

The International League of Associations for Rheumatology (ILAR) group supports projects that advance rheumatology in countries where there is an exceptional need [38]. As current treatment guidelines may not be directly applicable in resource-poor countries, such as those in Central/South America and Africa, ILAR has recently adapted the GRAPPA and EULAR guidelines for this purpose. These adapted recommendations are mainly based on GRAPPA, with some EULAR recommendations, and have incorporated input from local regional experts [39]. While these adapted recommendations may not be useful throughout the whole of Africa and the Middle East, they are a step toward developing regional guidelines. The lack of consistency when applying treatment guidelines for PsA management in Africa and the Middle East likely means that different practices are being implemented within individual countries, and between physicians within the same hospitals.

Physical and psychosocial disease impact of PsA in Africa and the Middle East

The physical and psychosocial disability associated with PsA places a substantial burden on patients due to its diverse clinical spectrum. In addition to debilitating joint damage, the presence of psoriatic skin disease can cause patients embarrassment, self-consciousness, and depression [40]. The substantial burden of PsA on patient quality of life has been reported in studies carried out in North America and Europe [41]. However, further research is required in Africa and the Middle East as we were unable to identify any studies specifically addressing the physical and psychosocial disease impact of PsA in the region. A population-based study highlighted the substantial burden of musculoskeletal pain and rheumatic disorders in Lebanon, reporting that 6.4% (95% CI 4.2–8.5%) of patients had functional disability and 26.0% (95% CI 22.3–30.1%) required treatment ($n = 500$); however, the authors noted that research in this area and recognition by health authorities in the region is seriously lacking [42, 43].

Sleep disturbance is a common symptom of PsA [40, 44] and while there are no specific studies investigating its impact in Africa and the Middle East, a cross-sectional study of Moroccan patients with ankylosing spondylitis reported that inflammatory pain and depression are risk factors for sleep problems ($n = 110$) [45], a finding that could potentially be extrapolated to PsA. There is a requirement for clinical studies to be conducted in Africa and the Middle East to assess the impact of PsA on sleep disturbance.

PsA has been described as a systemic disease because, alongside the inflammatory skin and joint manifestations, comorbidities are common and are associated with a reduced quality of life. It is estimated that around 40% of patients with PsA have three or more comorbidities, which may include cardiovascular disease, metabolic syndrome, obesity, diabetes, fatty liver disease, depression, and anxiety [46, 47].

Unmet needs in the management of PsA in Africa and the Middle East

As there are very limited data available on the prevalence and incidence of PsA in Africa and the Middle East, there is a need to develop registries across this region to monitor patients with PsA and gather real-world data on the extent and impact of the disease.

In sub-Saharan Africa, a shortage of qualified health professionals is a contributory factor to the lack of rheumatology services, and there is an urgent need to improve rheumatology training and services [48]. Initiatives such as the International League Against Rheumatism (ILAR)—East Africa Initiative and East, Central and Southern Africa College of Physicians (ECSACoP) aim to enhance medical training in this region through collaboration with the international rheumatology community, and these partnerships are vital for the development of rheumatology care in sub-Saharan Africa [49–51].

There is also a need for specific guidelines to be developed for the management of PsA in Africa and the Middle East, as the current published guidelines are primarily focused on the United States and Europe. Two recent editorials detail multiple obstacles faced by rheumatologists practicing in Africa and the Middle East, including a lack of disease awareness among both patients and healthcare professionals, drug accessibility, inadequate health funding, and a lack of rheumatologists [27, 52]. While these obstacles are applicable to the management of PsA, treatment is further complicated by the requirement for both a rheumatologist and a dermatologist to provide care to patients and by the presence of multiple clinical domains, each of which may require a different therapy [2].

Delays in the referral of patients with PsA to rheumatologists is a challenge in Africa and the Middle East which, similarly to RA, is likely to be a result of multiple patient-related and physician-related factors [53]. One such factor may be primary care practitioners and dermatologists not recognizing the symptoms of PsA due to a lack of training in identifying the disease. This is a serious concern for rheumatologists, because when patients are eventually evaluated, they are often already suffering from advanced arthritis and joint deformity [54]. The results of a multi-national survey carried out in the Middle East found that patients waited an average of 0.9 years for a confirmed diagnosis of PsA, and longer for appropriate treatment ($n = 364$) [9]. This highlights the urgent need for consistent and reliable diagnostic criteria to be implemented in the region.

The role of specialist nurses is to help patients understand their treatment, assist clinicians, and aid communication

between the multidisciplinary team [55], which in addition to rheumatologists and dermatologists may include a physiotherapist, a dietician, a psychologist, and a social worker. However, access to such resources is not widespread in Africa and the Middle East and is dependent on the healthcare service available in each country [52]. The logistics of running a multidisciplinary clinic within an outpatient clinic setting and the limited availability of interested dermatologists, specialist nurses, and clinic coordinators are limiting factors (author opinion).

While all medications licensed for the treatment of PsA are available in some African and Middle Eastern countries, their prohibitive cost limits their use in resource-poor countries [11]. There is also considerable variability in patient accessibility to treatment, since, even in clinics where all treatments and services are available and funded, the actions of individual patients and the route that they take to gain access to services remain an important factor (author opinion). In the absence of studies on the diagnosis of PsA in the region, we can draw parallels with studies carried out on the diagnosis of RA. For example, a study carried out in the United Arab Emirates found that patients with early RA were referred to a rheumatologist faster by a secondary specialist than by a general practitioner [56], and a recent observational study performed in Saudi Arabia identified that early referral to a rheumatologist was an important factor in the timely diagnosis and treatment of RA [57]. Therefore, establishing early referral criteria that can support primary care physicians and dermatologists to identify the signs of PsA is required to provide earlier and better care.

A further challenge in the management of PsA in Africa and the Middle East is the lack of patient understanding of their disease, which affects their adherence to medication. Rheumatologists find that patients are not aware of available treatment options, which may be due to a shortage of patient education programs and nursing staff. Many patients suffering from PsA are seen by dermatologists only and are never referred to a rheumatologist because they are more concerned about their skin disease and have not sought help for other symptoms (author opinion).

In addition to the considerable differences in health services between countries in Africa and the Middle East, there also exists significant healthcare system complexities and variability within the same country; in the United Arab Emirates for example, there are three different government healthcare providers in addition to the private health sector. In Egypt, there is limited funding for most of the state and university hospitals, whereas a small number of military and police hospitals are better resourced. While affluent patients can access the benefits of the private health sector, this is unaffordable for the majority of patients in the region, who rely on government hospitals (including university hospitals and clinics), which cannot fund expensive treatments. As would be expected, there is a wide variation between the standard of medical services provided by the private hospitals and the government or university hospitals, which is reflected in the options made available to patients. Patients with health insurance can be treated with bDMARDs if they meet the eligibility criteria, yet many patients in this region do not have either insurance coverage or government support. These patients cannot easily access the services that they require, such as radiological investigations or treatment with bDMARDs, resulting in patients with undertreated PsA (author opinion).

Sickness compensation is not available in all regions; in the United Arab Emirates, there is a federal committee for medical fitness that grants light duties and early retirement based on a patient's disability that is refractory to recommended treatment. In Lebanon, sickness compensation is dependent on the employer, with only those few patients working in certain industries, such as banks, receiving this benefit (author opinion).

Healthcare budget restraints, insurance restrictions, low incomes, and the absence of sickness compensation schemes all limit access to new therapies. Also, some clinicians experience difficulties in convincing insurance companies to consider new biologic therapies if they are in the same class as an existing therapy. However, it should be noted that insurance companies have a lower threshold for approving biologics for PsA than for psoriasis (author opinion). A recent survey of expert dermatologists in the region reported a lack of consensus in the use of biologics for the treatment of psoriasis in clinical practice, which was attributed to low physician awareness, high cost, and non-adherence [8]. The main sources of funding for PsA treatment in the region are insurance coverage, charities, supportive programs from pharmaceutical companies, and government support (author opinion).

Recommendations for improvement in PsA treatment and management in Africa and the Middle East

Based on our first-hand experience of the healthcare system and the challenges of treating and managing patients with PsA in Africa and the Middle East, we propose the following personal recommendations for improvement:

1. The development of specific guidelines for the management of PsA in Africa and the Middle East. These guidelines should consider the health resources in each country and also take into account different socio-economic situations, which vary widely in the region.
2. The introduction of specialized multidisciplinary clinics involving both a rheumatologist and a dermatologist to aid the early diagnosis of PsA.

(a) Improve early diagnosis through increased screening of patients with psoriasis. Ensuring that all patients receive effective treatment for PsA immediately following diagnosis will positively improve patient outcomes. Ideally, patients should be reviewed promptly, offered regular evaluation by appropriate specialists, and have treatment adjusted as needed in order to achieve the goals of therapy.

(b) The introduction of a screening questionnaire for PsA in dermatology clinics. This may help to identify patients that have symptoms of rheumatic disease and facilitate early referral to a rheumatologist. Some rheumatologists and dermatologists in the region have agreed to use the Early ARthritis for Psoriatic patients' (EARP) questionnaire, or the Psoriasis Epidemiology Screening Tool (PEST), which is available via the GRAPPA smart phone application. Other rheumatologists already implement a low threshold for accepting referrals of patients with PsA, agreeing that a patient presenting with psoriasis and joint pain (± lower back pain) should be assessed, and this should also be implemented by dermatologists.

3. A patient education and awareness program in the form of a collaboration between patients and medical societies to enhance both patient and primary physicians' education. This could be implemented by providing patients with leaflets and reading materials to understand more about PsA and treatment management. The introduction of early referral educational programs for primary care and general practitioners and educating pharmacists, nurses, and regulatory authorities on PsA disease burden and the impact on patient quality of life may be beneficial.
4. Improved access to biologics and other new therapies to treat PsA. To allow more patients access to new therapies, more rheumatology clinics are required, along with wider insurance coverage, and increased cooperation between the government and private sectors.

Conclusions

PsA is poorly understood and under-recognized in Africa and the Middle East due to a paucity of quality research, which was evident in our literature search. This review represents a further step towards unveiling the burden of PsA in Africa and the Middle East, and proposes recommendations for improvements in PsA treatment and management in the region. This includes the requirement to establish regional PsA guidelines to define the standard-of-care required, introducing specialized multidisciplinary clinics to aid early diagnosis and appropriate treatment management, encouraging patient and physician education of PsA, and increased cooperation between governments and private sectors to improve access to new therapies. Furthermore, the burden of PsA should be listed on the research agenda of African and Middle Eastern countries to provide much needed data that can be used in the future to obtain health funders' support for this chronic disease.

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Compliance with ethical standards

Conflicts of interest M Bedaiwi—received speaker fees from AbbVie and Pfizer Inc. I Al Homood—received speaker's fees and advisory board honoraria from AbbVie, Lilly, Novartis and Pfizer Inc. A El-Garf—received speaker's fees and advisory board honoraria from AbbVie, Janssen, Novartis, Pfizer Inc, Roche and UCB. I Uthman—received speaker fees from AbbVie, Janssen, Newbridge, and Pfizer Inc. J Al Saleh—received research grant from AbbVie and Pfizer Inc. N Sunna, R Nassier, and H Mohamed—employees and shareholders of Pfizer Inc.

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