

REVIEW

Challenges and opportunities in the early diagnosis and optimal management of rheumatoid arthritis in Africa and the Middle East

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Abstract

Early diagnosis and early initiation of disease-modifying antirheumatic drug (DMARD) therapy slow the progression of joint damage and decrease the morbidity and mortality associated with rheumatoid arthritis (RA). According to the European League Against Rheumatism (EULAR) guidelines, treatment should be initiated with methotrexate and addition of biological DMARDs such as tumour necrosis factor (TNF) inhibitors should be considered for RA patients who respond insufficiently to methotrexate and/or other synthetic DMARDs and have poor prognostic factors. Africa and the Middle East is a large geographical region with varying treatment practices and standards of care in RA. Existing data show that patients with RA in the region are often diagnosed late, present with active disease and often do not receive DMARDs early in the course of the disease. In this review, we discuss the value of early diagnosis and remission-targeted treatment for limiting joint damage and improving disease outcomes in RA, and the challenges in adopting these strategies in Africa and the Middle East. In addition, we propose an action plan to improve the overall long-term outlook for RA patients in the region.

Key words: Africa and Middle East, early diagnosis, low disease activity, remission, rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with progressive joint damage and considerable disability. The global prevalence of RA is approximately 0.3–1.2%, with the highest prevalence

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observed in American Indian tribes and Alaskan Indians, and the lowest in African and Asian countries.^{1,2}

The burden of RA in Africa and the Middle East has not been accurately estimated because of scant data on incidence and prevalence, as well as a shortage of up-to-date registries on the diagnosis and treatment of RA.² Africa and the Middle East is a large region that encompasses countries in north and south Africa, as well as those in western Asia, including Bahrain, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Oman, Palestinian Territories, Qatar, Saudi Arabia, Syria, the United Arab Emirates (UAE) and Yemen.

RA is associated with both direct and indirect costs that have substantial impacts on patients and their families. The direct costs are in terms of the expenses related to drugs, hospital visits and physician fees for managing the disease and physical disability, while the indirect costs are in terms of lost productivity and lost wages due to work disability or even unemployment. In addition, RA patients also suffer from disease-related quality of life impairment, the cost of which is difficult to estimate. Early diagnosis and intensive treatment can help to achieve remission or low disease activity (LDA), and enable individuals to continue working and lead productive lives. Thus, remission has valuable individual, social and financial implications for RA-affected individuals.³

In this review, we discuss the value of early diagnosis and remission-targeted treatment for limiting joint damage and improving disease outcomes in RA, and the challenges and opportunities in adopting these strategies in Africa and the Middle East. We also propose an action plan to improve the overall long-term outlook for RA in the region.

EARLY DIAGNOSIS AND TREATMENT OF RA

Improved outcomes with early treatment initiation

Permanent structural damage is known to occur early in the course of active RA, and early initiation of disease-modifying antirheumatic drugs (DMARDs) has been shown to slow the progression of joint damage and improve long-term outcomes and overall quality of life of patients.⁴ According to the European League Against Rheumatism (EULAR) guidelines, treatment should be initiated with methotrexate, and addition of biological DMARDs such as tumour necrosis factor (TNF) inhibitors should be considered for RA patients who respond

insufficiently to methotrexate and/or other synthetic DMARDs and have poor prognostic factors.⁵

Numerous studies have shown that intensive DMARD treatment is more beneficial than conventional treatment in patients diagnosed with early RA. A study in Iran showed that combination therapy with methotrexate and chloroquine plus low-dose prednisolone was associated with an American College of Rheumatology (ACR)70 response of 71–79%. Furthermore, the efficacy of this treatment strategy did not fade over time, with no significant difference in the ACR70 response rates at 6 months, 1, 2, 3, 4 and 5 years.⁶ In addition, emerging data show that the long-term outcomes of RA patients are significantly improved if DMARDs are initiated immediately after development of signs of early inflammatory arthritis. Etude et Suivi des Polyarthrites Indifférenciées Récentes (Study and Follow-up of Early Undifferentiated Polyarthritis, ESPOIR) was a French observational study in RA patients that evaluated the impact of a time lag between arthritis onset (first patient-reported swollen joint) and DMARD initiation on radiological progression 12 months after treatment initiation. It was observed that patients who started DMARDs within 3 months of symptom development showed significantly less radiological progression than those who started treatment later (mean progression after adjustment for propensity scores, 0.8 units *vs.* 1.7 units; $P = 0.033$). Thus, a delay of only 3 months in DMARD initiation after development of first symptoms had an adverse effect on the long-term prognosis of RA. Furthermore, there was a trend for early treatment to be especially beneficial for patients with an unfavorable prognosis.⁴

Improved outcomes with treatment aiming at a specific target

Remission is now considered an achievable goal in RA and achieving this goal early and rapidly after initiating treatment can arrest radiological progression of RA. Thus, international guidelines recommend that remission be the goal of treatment in early RA. For patients with long-standing established disease, LDA or minimal disease activity is a more feasible goal, as complete remission may be difficult to achieve.^{5,7,8}

In Europe, at least four different 'strategy trials' have demonstrated that patient outcomes are significantly better with intensive DMARD therapy directed at tight control of disease activity compared with conventional management in which the decision to treat is based only on the discretion of the treating physician.^{9–12}

CHALLENGES IN THE OPTIMAL MANAGEMENT OF RA IN AFRICA AND THE MIDDLE EAST

Scarce epidemiological data

There is a scarcity of large epidemiological studies pertaining to RA in Africa and the Middle East and most available data on prevalence, severity and management of RA are derived from small population and hospital studies. Existing data show that the prevalence of RA varies widely across different countries in the region.^{13–16}

A systematic literature review performed in 2010 found only 10 population studies and 11 hospital studies relevant for calculating the prevalence and burden of RA in Africa. The overall estimated crude prevalence rate of RA was 0.42%, translating into a burden of 4.3 million people with RA. However, as only two studies had been performed since 1990, the disease projections were based on earlier data and not considered accurate.¹³

The Community Oriented Program for Control of Rheumatic Diseases (COPCORD) is an International League of Associations for Rheumatology (ILAR) initiative launched in collaboration with the World Health Organization (WHO) to gather data from developing nations on pain and disability in rheumatic disorders. A COPCORD study in Lebanon found a high RA burden of 1% in the Lebanese population, highlighting the need for early detection and treatment of the condition.¹⁴ Population studies by the same group in rural and urban Iran found a low prevalence of 0.19 and 0.33%, respectively, and a high prevalence of rheumatic complaints in the population.^{15,16}

Variation in disease severity and management practices across the region

The severity of RA varies greatly across African and Middle Eastern countries. In addition, the management practices also vary, in accordance with the healthcare infrastructure and socioeconomic status of patients. Of note, most countries do not have their own consensus guidelines for RA management.^{17–28}

Furthermore, among clinicians who do not have a special interest in RA, there is low awareness of international treatment recommendations and, consequently, of implementation of these guidelines. Practitioners with an interest in RA follow international treatment guidelines whereby treatment is targeted at remission and initiated with DMARDs and stepped up with additional DMARDs or biologic

drugs. However, delayed referral and limited access to basic drugs such as methotrexate pose significant barriers to implementing the guidelines in many countries.²⁹ As such, there are no published data on the pharmacological treatment strategies, the maximum dosages of drugs employed, and surgical treatment for managing RA in African and Middle Eastern countries.

In many countries, RA patients have high disease activity, significant disability and body pain, and impaired quality of life. In South Africa, RA patients from low socioeconomic classes seek care in public care centres which have limited medical facilities. A study showed that these patients had a higher Health Assessment Questionnaire Disability Index, higher disease activity and disease severity scores, and greater frequency of being treated with steroids versus those treated in private care centres. Thus, improved facilities in public care centres are warranted to improve the outcomes of African RA patients who frequent these centres.¹⁷ Another study in South Africa found that RA patients had significant body pain, physical disability and poor quality of life. Furthermore, disease activity correlated with functional disability and health-related quality of life (HRQoL).¹⁸

Existing data show that RA patients are often undertreated in Africa and the Middle East. A study among 100 RA patients presenting at a musculoskeletal clinic in Dubai, UAE, found erosions in 55% and deformities in 26% of patients. The mean Disease Activity Score of 28 joints (DAS28) was 5.2, which was higher than that reported in the West. Despite this, only 43% of patients were receiving DMARD therapy, and a large proportion of patients with early disease were not on DMARDs. Furthermore, there was a significant lag time of 18 months from symptom onset to initiation of DMARD therapy.¹⁹

In contrast to the studies described above, a study evaluating the severity of RA in Lebanon found that radiological damage in the Lebanese RA population was comparable with that reported in Western populations.²⁰ Two small hospital studies in Saudi Arabia also showed that radiographic changes in the hands and feet of RA patients were less severe, and the proportion of patients with erosions (60%) was lower than those reported in Western European and North American studies.^{21,22} Similarly, a study in 100 consecutive RA patients in Kuwait found a low incidence (42%) of radiological erosive arthropathy, with sicca complex being the most common extra-articular manifestation of RA.²³

A small hospital study ($n = 66$) in Oman found that the demographic characteristics of RA patients were similar to those reported in Western countries, with the disease being more prevalent in females than males. However, the seropositivity rate and nodular form of the disease were less frequent and the disease seemed milder in the population studied. The majority of the patients belonged to class 1 or 2 of the ACR functional classification. Of note, 95.45% of the patients were on conventional DMARD therapy.²⁴

There are inconsistent data from different studies on the features and prognosis of young-onset RA (YORA) and elderly-onset RA (EORA).^{30–32} Interestingly, a study in Egypt found that EORA affected more males, and had a more active and less disabling course than YORA. Also, biologics and combination DMARD therapies were used significantly less frequently in the former group, probably due to the presence of comorbidities and high cost of treatment.²⁸

High physical, social, psychological and financial impacts of RA

HRQoL is an outcome measure useful for evaluating the physical, psychological and social impact of a chronic disease as reported by a patient. In a study involving 250 RA patients in Morocco, those with low levels of education and socioeconomic status had significantly lower HRQoL scores than the general population. Patients who received methotrexate and biological drugs exhibited better scores for mental health, and physical and social domains. Furthermore, low HRQoL was significantly correlated with disease duration, joint pain intensity, clinical and biological disease activity, functional disability and radiographic damage. Overall, there was significant deterioration in mental and physical health of patients with RA compared with the general population.³³

RA is known to be associated with significant financial and social burden, for both patients with RA and their families. In a group of 100 Moroccan patients affected with RA, financial difficulties were reported by 91% of patients and resulted in poor treatment compliance (61%) and absenteeism at school (19%). Among patients who had paid jobs ($n = 34$), 65% stopped working within an average of 6.9 years after disease diagnosis; this was predominantly observed in males who were older and had physically strenuous jobs. Other significant adverse impacts due to RA included divorce (in six married women), sexual problems (61%), and problems in performing domestic chores (84%) and participating in leisure activities (46%).³⁴

Few studies have investigated the prevalence of comorbidities among patients with RA in Africa and the Middle East. Established RA patients often have two or more comorbidities which may lead to increased treatment costs, disability and mortality.³⁰ A study in Egypt found increased cardiovascular (CV) risk in a group of patients with RA, particularly in the presence of smoking, obesity, high triglycerides and extra-articular disease severity.³¹ A study among 231 patients with RA in Egypt found a high prevalence of sexual dysfunction among both females (45.7%) and males (53.8%). Furthermore, this disorder was significantly correlated with CV disease (CVD).³²

Data show that the relationship between modifiable CV risk factors and atherosclerosis varies among African patients with RA. A study among Black ($n = 193$) and Caucasian ($n = 93$) women with RA in South Africa showed that metabolic syndrome was more prevalent among women of African descent (30.8%) than in Caucasian women with RA (9.7%). However, unlike that in Caucasian women, the condition was not associated with atherosclerosis in Black women with RA.³⁵

Compared with the general population, RA patients have a higher risk of osteoporosis due to the inflammatory nature of the disease, long-term corticosteroid usage and decreased physical activity and exercise.⁷ Small studies in Africa and the Middle East suggest that presence of RA is an independent risk factor for osteoporosis.³⁶ A study in a small group of Saudi Arabian women with RA showed a significant decrease in bone mineral density (BMD) versus healthy controls. Furthermore, the decreased BMD was significantly correlated with increased disease activity, impairment of functional activity and prolonged use of steroids.³⁷ These findings align with those from Western studies.^{38,39}

Low awareness and delayed referral

Studies show that delayed referral and treatment interruption are important challenges in the management of RA in Africa and the Middle East. A study in Nigeria found that there was a mean delay of 63.4 months before symptomatic patients presented to rheumatology clinics. This was attributed to ignorance about RA and its treatment among medical practitioners and nurses. Patients were put on long courses of nonsteroidal anti-inflammatory drugs (NSAIDs) despite having joint deformity, as the practitioners were not aware that NSAIDs did not modify the disease course. In addition, they also had misconceptions about RA diagnosis and believed that the disease could only be diagnosed by

the presence of joint deformities or rheumatoid factor positivity.⁴⁰

Similarly, a study in Senegal ($n = 100$) found that, on average, the time from symptom onset to diagnosis was 54 months. Primary health providers had inadequate knowledge about RA and prescribed inappropriate medications. Consequently, many patients had highly active disease at diagnosis.⁴¹ A small epidemiological study in Morocco found a delay of 20 weeks before symptomatic patients were referred to specialists for evaluation and DMARD therapy. Moreover, at 2-year assessment, 13.6% of the patients had stopped treatment due to financial reasons.⁴²

In the UAE, the Quantitative Standard Monitoring of Patients with Rheumatoid Arthritis (QUEST-RA) database showed that despite being a high 'gross domestic product' country, there was a median delay of 11 months until RA patients first initiated DMARD therapy, and only 10% of the patients received biological therapies.⁴³

Shortage of rheumatologists

Existing data suggest that the prevalence of RA in Africa and the Middle East is comparable with that in other parts of the world; however, management is suboptimal for various reasons. One of the reasons could be the lack of enough trained rheumatologists.²⁹ According to the WHO, there should be at least one rheumatologist per 100 000 people. However, in sub-Saharan Africa (excluding South Africa), there are < 20 rheumatologists for > 800 million people and only two for a population of > 100 million in east Africa.⁴⁴ As such, there are no published data from most countries in the region on the ratio of rheumatologists to the total population.

ONGOING ENDEAVOURS TO IMPROVE RA MANAGEMENT IN AFRICA AND THE MIDDLE EAST

Educational programs

It has been suggested that developing educational programs tailored to patient needs may help to increase knowledge about the disease which, in turn, may serve to increase treatment compliance and reduce RA disease activity. This was observed in a group of 39 RA patients in Morocco who participated in a 3-day per week educational program for one year. After 3 years, the disease activity status was significantly improved in this group versus controls, although there was no significant change in functional status between the two groups.⁴⁵

A meta-analysis showed that education, counselling and behavioral treatment of patients were associated with small but significant short-term benefits in the outcomes of functional disability, joint counts, depression, patient global assessment and psychological status.⁴⁶

In the UAE, significant reductions in the time to RA diagnosis (45.8%; $P = 0.0001$) and time to initiation of DMARD therapy (34.9%; $P = 0.04$) were achieved 5 years after implementing a nationwide program of support groups, awareness programs and public campaigns to improve public knowledge and understanding of RA.⁴⁷

Furthermore, efforts should be made to educate rheumatologists about the long-term advantages of early intensive treatment targeted at remission or LDA. A multidisciplinary approach to RA management should be promoted, whereby rheumatologists work in collaboration with orthopedic surgeons, physiotherapists, cardiologists and physicians to deliver improved management of the disease and its associated comorbidities.

National rheumatology societies and medical organizations

National rheumatology societies, existing in many countries in Africa and the Middle East, are important stakeholders in RA management and provide excellent platforms for sharing experiences, exchanging ideas and updating knowledge about inflammatory rheumatic conditions. In many countries, these and other non-profit medical organizations are actively involved in designing and implementing programs to improve the diagnosis and overall management of RA.

For instance, the Ligue Algérienne Anti Rhumatismale (Algerian League Against Rheumatism, LAAR) and the Société Algérienne de Rhumatologie (Algerian Society of Rheumatology) are two Algerian organizations involved in educating health professionals by organizing annual congresses and disseminating information about the signs of early RA and latest advances in rheumatology. In South Africa, the South African Rheumatism and Arthritis Association (SARAA) promotes research, education, awareness and knowledge of the prevention and management of rheumatic diseases by organizing biannual congresses and regular continuing medical education programs, and publishing RA management guidelines. In addition, the Arthritis Foundation of South Africa, a non-profit organization, provides non-medical support to people with arthritis, their families and carers in South Africa. In Tunisia, the educational programs organized by La Ligue Tunisienne

Anti Rhumatismale (The National Rheumatology Society, LITAR), a scientific non-profit organization, have led to significant improvements in RA management practices in this country.

In Qatar, Kuwait, South Africa and the UAE, national rheumatology societies have established registries and early RA clinics, data from which will help to better understand the reasons for delayed referrals, estimate the true burden of RA and associated complications, and guide rheumatologists on the need to modify treatment strategies according to disease activity. In addition, sharing these data with patients and primary care practitioners will serve to improve the awareness of RA.

Self-management

Self-management in RA entails taking control of living with the condition and is considered important for the physical and psychological well-being of affected individuals. In the UK, implementation of the Arthritis Self-Management Program was associated with significant improvement in the perception of control over arthritis at 4 months of follow-up. Subjects who received the intervention had significantly better cognitive symptom management, communication with physicians, dietary habits, exercise and relaxation, and were less depressed compared with those in the control group. At 12 months, they reported significant improvement in pain and decreased visits to the general practitioner.⁴⁸ We believe it will be worthwhile to introduce such a program in Africa and the Middle East to empower RA patients to better cope with and manage their RA.

CONCLUSION

Early diagnosis and treatment targeted at remission or LDA are key to improving the long-term outlook of patients with RA. Early initiation of DMARD therapy slows progression of joint damage, and decreases morbidity and mortality associated with RA.

In light of the existing barriers to early diagnosis and optimal treatment of RA in Africa and the Middle East, we propose the following action plan to improve the overall long-term outlook for RA patients in the region:

- 1 Treat RA early and aggressively with combination of traditional DMARDs in patients with poor prognostic markers, particularly those in resource-poor regions.
- 2 Initiate educational programs to improve the identification of early RA and rates of specialist referral so that treatment can be initiated earlier.

- 3 Design and implement longitudinal epidemiological studies to better estimate the prevalence and burden of RA in the region.
- 4 Develop educational programs for rheumatologists to increase awareness of remission or LDA-targeted treatment and improve the long-term prognosis of RA patients.
- 5 Develop national recommendations for detecting and monitoring comorbidities in RA patients.
- 6 Adopt a multidisciplinary approach to RA management by working in collaboration with other care providers, including orthopedic surgeons, physiotherapists and physicians.
- 7 Incorporate rheumatology training in undergraduate and postgraduate medical education programs to meet the need of trained rheumatologists.

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DISCLOSURES

None.

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