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INVITED REVIEW

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Rheumatoid arthritis management in the APLAR region: Perspectives from an expert panel of rheumatologists, patients and community oriented program for control of rheumatic diseases

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Abstract

Rheumatoid arthritis (RA) is a major health burden in Asia Pacific affecting the quality of life of patients and consuming healthcare resources. According to recent estimates from the World Health Organization-International League Against Rheumatism-Community Oriented Program for Control of Rheumatic Diseases, prevalence is around 0.3%-0.5%. Management guidelines have helped to improve treatment across this diverse region. To gain better insight into current real-world management applications in view of these guidelines, virtual meetings were conducted in mid-2020 to explore perspectives of rheumatologists and patients, as well as discuss the impact of coronavirus disease 2019 on RA management. Patients and rheumatologists from Hong Kong, Malaysia, Singapore, the Philippines, Thailand, India, Pakistan, and Taiwan were included, representing a diverse mix of healthcare systems, wealth, ethnicity and culture. Despite many countries having prospered in recent years, similar challenges in RA diagnosis and treatment were identified. The daily impact and patient experience of RA were also similar across countries, marked by "silent" pain and disability, and universal misunderstanding of the disease. Late diagnosis and treatment, and barriers to access to appropriate treatment, remain problematic. The experience shared by Taiwan offers a glimmer of hope, however, wherein patient advocacy groups have succeeded in being included in policy-making decisions and securing access to advanced treatment. Real-world solutions that pay heed to the unique local needs and diversity of Asia Pacific are required to improve RA management, which will take time. In the interim, help can be sought from the trained, non-rheumatologist community to reduce some of the disease burden.

KEYWORDS

APLAR region, current management, patient journey, rheumatoid arthritis

1 | INTRODUCTION

Asia Pacific is a vast, diverse region, with a sizeable burden of rheumatoid arthritis (RA), which affects the quality of life of patients and consumes healthcare resources[1-3] The prevalence of RA in Asia Pacific (around 0.30%-0.50%) compared with North America (0.70%) and Europe (0.59%) is relatively lower but, given the large populations, this translates to a huge burden in the region (Figure 1).[4-8]

The World Health Organization-International League Against Rheumatism-Community Oriented Program for Control of Rheumatic Diseases (WHO-ILAR-COPCORD) survey data were collected in phases using a near-similar methodology and in particular a uniform core set of questions (to identify respondents), thereby allowing comparison of point prevalence across countries and regions. The surveys were planned and supervised by rheumatologists and the diagnosis of rheumatic disorders was essentially clinical.

In some countries there is an urban-rural divide but this is likely to become blurred over time with rapid urbanization and modern development, and migration of people to the cities.[9]

In 2007, the opportunities and challenges for rheumatology in Asia Pacific were discussed in an editorial, which noted that "many countries in the Asia Pacific region have failing economies, and are still struggling to establish rheumatology as a medical subspecialty. There is a general lack of awareness about musculoskeletal diseases and their effect on society. Diagnosis and treatment are often delayed because primary-care physicians have limited knowledge of the clinical evaluation and management of rheumatic diseases, and trained rheumatologists are few and far between."[10]

Since 2007, healthcare infrastructure has markedly improved in many low- and middle-income countries (LMICs) in Asia Pacific, whereas higher-income countries (HICs) have become more systematic in their approach to healthcare delivery. In 2015, the Asia Pacific League of Associations for Rheumatology (APLAR) took the lead to develop treatment guidelines specific for the region, which took into account the diversity in healthcare delivery, and other differences across countries. Indeed, the APLAR executive has been at the forefront of improving the rheumatology landscape and has established special interest groups for RA and COPCORD epidemiology, with recent COPCORD publications being readily available online.[11]

From the patient perspective, the management of RA has evolved to incorporate more shared decision-making, individualized therapy, and patient-centered outcomes. Treatment options have increased significantly with the availability of newer advanced disease-modifying antirheumatic drugs (DMARDs). How have these developments benefited RA patients and rheumatology practice in Asia Pacific? To gain more insight into current real-life management and the perspectives of RA patients, a series of virtual meetings was held with experienced rheumatologists (the authors of this article) and their patients (N = 7) from Hong Kong, Malaysia, Singapore, Philippines, Thailand, India, Pakistan, and Taiwan in July 2020, and we expected there to be disparities between affluent countries (eg, Taiwan, Hong Kong, and Singapore) and LMICs (eg, India, Pakistan).

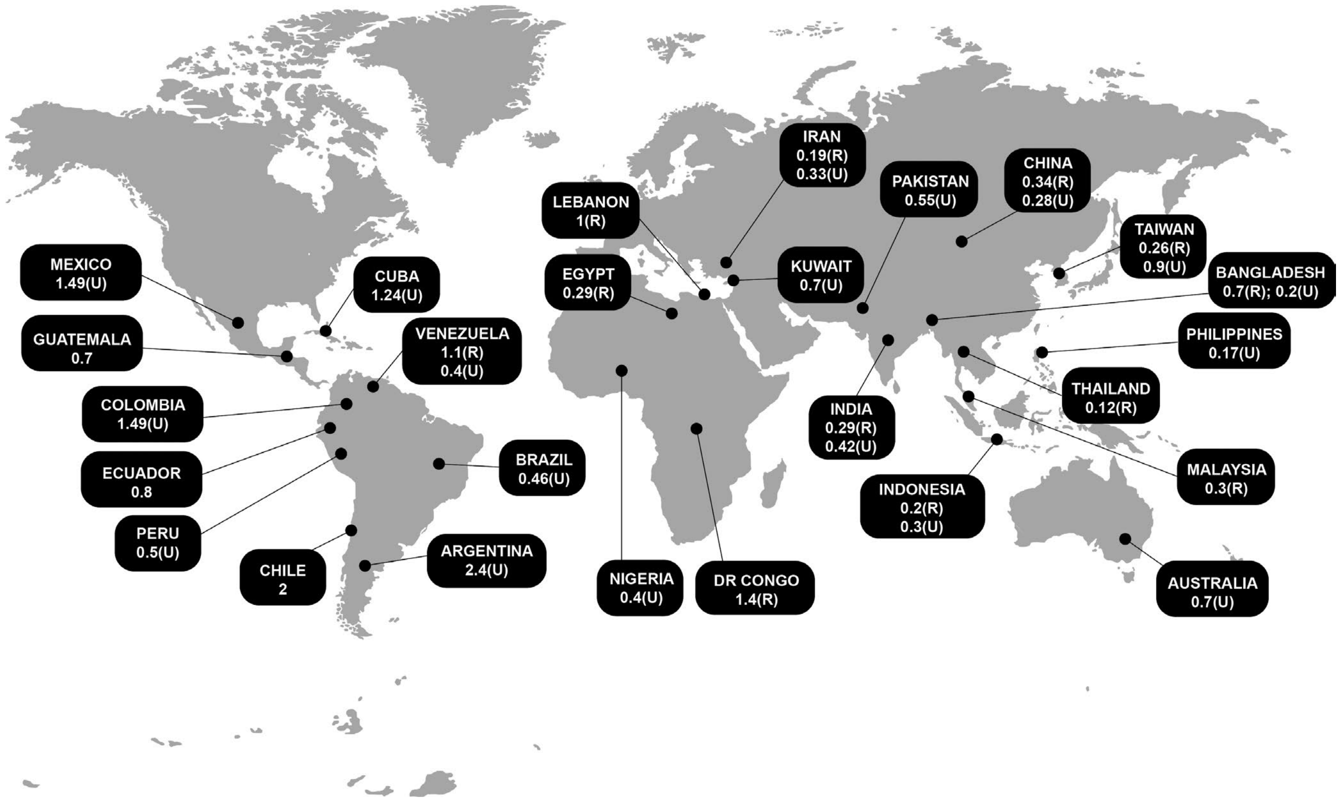

FIGURE 1 WHO-ILAR-COPCORD prevalence map of rheumatoid arthritis.[4] Prevalence rates for Asia-Pacific countries were determined from population surveys conducted from 1988 to 2015. U, urban; R, rural

Previously unpublished data from WHO-ILAR-COPCORD (available at www.copcord.org), courtesy of Arvind Chopra, one of the authors, were included to support this commentary.

2 | THE RA PATIENT JOURNEY, MARKED BY “INVISIBLE” PAIN AND DISABILITY, AND LOW AWARENESS

Patients were asked to describe their journey from diagnosis to treatment, and how RA had impacted their lives and that of their families. Very similar experiences emerged regardless of where patients came from, their personal means and background. Notably, the majority of patients were diagnosed late, some beyond 2 years from symptom onset. Patients had difficulty finding the right information about RA or sought treatment solely for pain relief including use of traditional Chinese medicines and acupuncture, which delayed diagnosis. All the patients were on DMARD treatment, but this may not be the case in large stretches of the region where medical services are sparse and medical practice is non-specialized. In these scenarios, patients tend to be managed with painkillers and steroids for prolonged periods, which is consistent with several COPCORD population surveys that reported surreptitious and often rampant use of steroids (sometimes mixed with herbal remedies) to treat RA. In terms of advanced DMARD therapy (biologics and targeted-synthetic DMARDs), some had received biologic therapy in the past, some were still receiving biologic therapy, and some had never tried because of cost, but felt that this type of treatment would be beneficial. Moreover, the RA patient journey was shown to be an isolating and lonely one. RA can be perceived as an “invisible” illness, and it is difficult to imagine the severity and type of pain that RA patients feel when, on the outside, they “look normal”. Patients referred to having “silent pain” that was difficult even for family members to believe, let alone comprehend.

Throughout the work day, an RA patient may feel morning stiffness, breakthrough pain, and occasional nausea or other medication adverse effects while appearing “normal”. The lack of understanding around RA extends further to employers and the workplace, and there are no concessions for RA patients when they are feeling unwell. It is not surprising that many RA patients give up work prematurely, often at the height of their careers, as the result of symptoms and increasing disability. In the last decade, despite goals of inclusivity and diversity having been indoctrinated into most workplaces, there remains a growing need for recognition from employers, as well as protection of RA patients in the workplace. Moreover, this loss in peak productivity and its consequences on the economic and social health of a country have yet to be fully appreciated by governments.[12-17]

Individuals with RA can also be misinformed and lack understanding on the pathophysiology of their disease, which can hamper outcomes by delaying diagnosis and the provision of adequate treatment. In the minds of many RA patients, the pain caused by RA *is* the disease, which is a double-edged sword. While pain alerts patients and reminds them to be compliant with their medication, the reverse—stopping medication—often happens when they are not in pain. It is very important that patients are educated about the “silent” progression of RA even when pain is absent. Many RA patients also do not grasp that, despite the absence of pain, poor disease control can still increase the risk of bone destruction and disability. More needs to be done to ensure that patients understand why it is important to reach treatment goals.

Perhaps the defining feature of the RA patient journey in Asia Pacific is invisibility: the pain is invisible, the damage is invisible until it has progressed to significant disability, the patient population is often invisible, and the patient voice is imperceptible and fragmented because there are few patient support and advocacy groups. Where patient groups exist, activities tend to center on lifestyle support and experience sharing. In the arena of advocacy, patient groups in Singapore, Hong Kong, the Philippines, and Malaysia have tried to get involved, but their influence has been limited, with little say in the decisions that directly affect them. In India, patient support (eg, Mission Arthritis India) mainly focuses on education but patients have no influence on public health policy. Yet, to increase awareness and understanding of RA and to improve outcomes, patients in Asia Pacific must be seen and heard. The success of RA patient advocacy groups in Taiwan, which have made good use of social media platforms such as LINE, WeChat, and Facebook to stay connected and vocal—and through which they have been included in policy decision-making and secured greater and longer access to effective advanced DMARD therapy[18]—demonstrates that patients, given the opportunity, have a valid voice, and can work with physicians and policy-makers to improve their own outcomes. Taiwan serves as an effective model for multi-stakeholder collaboration, which can be applied to both HICs and LMICs in Asia Pacific.

3 | CHALLENGES IN THE MANAGEMENT OF RA IN ASIA PACIFIC

Rheumatologists were asked to provide their opinion on RA management in their respective countries to illuminate challenges in current practice. They also provided specific details on epidemiology, diagnosis of RA, the treatment pathway for patients and access to advanced DMARD therapy.

The challenges in RA management in HICs and LMICs in Asia Pacific are interlinked, like pillars underlying a vast structure. Viewed this way, improvements to one pillar should benefit and strengthen the support of the whole structure, and the more pillars that are improved, the greater and stronger the structure becomes. Hence, improvements in RA management, ideally, should not be made in isolation, although small isolated improvements are still beneficial.

The first major challenge lies in the shortage of rheumatologists in some Asia-Pacific countries, which contributes to late diagnosis and delayed appropriate treatment. This challenge was also mentioned in the APLAR guidelines.[1] Indeed, in countries like India, RA is largely neglected in public health, there are no national arthritis programs,[19] and public funding is often diverted to other diseases (eg, infectious diseases, diabetes, hypertension, cancer). In this respect, the comments of the 2007 editorial still ring true in 2020.[10] The shortage of rheumatologists is more evident in LMICs like the Philippines, Thailand, India, and Pakistan where an urban-rural divide exists. Rural areas are at a major disadvantage in terms of availability of and access to rheumatologists and rheumatology services, which often leads to misdiagnosis or late diagnosis.

To address the shortage of rheumatologists in some countries, healthcare providers have found creative solutions, such as the training of non-rheumatologists to help with diagnosis and parts of routine follow up. In Thailand, the Thai Rheumatism Association developed evidence-based recommendations on RA diagnosis and management for non-rheumatologists,[20] and local medical societies in India and Pakistan are working with associations such as APLAR and COPCORD to develop and implement formal training courses for non-rheumatologists. For example, in Pakistan, a tertiary-care rheumatology center developed a 9-month course for family physicians using a blended learning technique, which was partly funded by a grant from ILAR. The curriculum was developed using American College of Rheumatology Rheum 2 modules and international guidelines.[21] This model can be replicated to address the extreme shortage of experts in the field of rheumatology in other LMICs. Meanwhile, in some centers, such as the one at the University of Santo Tomas Hospital in the Philippines, education workshop modules to establish efficient networking with non-rheumatologists, as well as trained clinic assistants, have increased resources for providing physician and patient education.

A second challenge lies in the implementation of the treat-to-target (T2T) approach—the reference standard for RA management—in which individualized care and the attainment of treatment goals are prioritized.[22-25] However, in the public health sector of Asia-Pacific countries, regardless of wealth, most rheumatologists do not have sufficient consultation time to implement a T2T approach. This is compounded by the shortage of rheumatologists in some countries as mentioned above, a shortage of facilities to enable regular follow up, and resistance towards intensification of treatment, which is discussed further in the third challenge, below. In LMICs where RA is managed at the primary-care level, the management needs to be surveyed and evaluated, because it is likely that no specific, consistent strategy is being followed to treat the disease. Only a small fraction of RA patients in these countries are likely to be treated with reasonable standards of care.

In short, the many limitations in healthcare infrastructure and delivery that exist currently in Asia Pacific, particularly in LMICs, combine to make the T2T approach difficult to implement in real-life practice. A solution may be to modify the T2T approach, tailoring it to RA clinical practice in Asia Pacific, without compromising effectiveness. Another may be to use the T2T approach with conventional DMARDs earlier in the course of disease, which can lead to remission in up to one-third of patients.[26]

A third challenge involves the under-utilization of biologics and other advanced DMARDs in the region. In real-life practice, the usage of biologics and other advanced DMARD therapies amount to around 5% in the represented countries, whereas the data would suggest that a greater proportion of the RA population is indicated for advanced DMARD treatment.[27] This implies considerable undertreatment of a proportion of patients with moderate to severe RA, though more data are needed to support this. The APLAR guidelines give more attention to the role of conventional DMARDs, as these are more accessible and affordable for many countries in the APLAR region.[1] The guidelines also highlight the elevated risk of biologic-associated infection in Asian populations, particularly tuberculosis,[28] which must be taken into account when managing RA patients in the region, but which may also deter use.

Cost is an obvious barrier to greater uptake of advanced DMARD therapy in all countries, regardless of wealth or resources.[29] Other barriers include clinical inertia on the part of physicians, and reluctance of patients to intensify treatment even in the presence of active disease, some of whom are unwilling to "risk" new treatments.[22,30] These barriers underscore the fact that the value and clinical benefits of advanced DMARD therapy are under-appreciated, even though biologics have been available for almost two decades and the development of biosimilars has the potential to expand access to more patients. The best approach to overcome these barriers may be to continue to reinforce evidence from clinical trials and real-world data to convince clinicians and patients, and change behaviors, prejudices, and mindsets.

Several ethnic and traditional medicinal systems are in popular practice in the APLAR region and many have existed since antiquity. Some of these (such as the Chinese traditional system and Indian Ayurveda) are encouraged and promoted by the respective national healthcare systems. These treatments are considered holistic and individualized, but often compete with modern medicine, because they are widely perceived by the general public to be safer with some patients taking these medicines for prolonged periods. As such, it is important to determine and evaluate the clinical benefits of some of these alternative therapies using modern science, necessitating a comprehensive, integrative research agenda.

It is prudent to add, however, that several non-pharmacologic modalities of treatment are important in the management of RA. Diet, exercise, and physiotherapy are pivotal to patients but are often neglected by doctors in clinical practice. Traditional methods of physical and mental fitness (such as tai chi and yoga) are popular and their potential benefits should be recognized and integrated into guidelines and recommendations.

3.1 | The impact of COVID-19 on RA management in Asia Pacific

At the time of our meetings in 2020, it was imperative to include the impact of coronavirus disease 2019 (COVID-19) into the discussions. Every aspect of healthcare has been affected by COVID-19 and rheumatology practice is no exception.[31,32] Rheumatologists have had to adapt rapidly to an evolving situation, as clinics closed and fear among patients set in. Through this process, a major lesson has been the utilization of telemedicine in rheumatology, with increasing understanding among clinicians regarding its capacity to support practice, especially in providing continuity of care.[33] Most rheumatologists in the region have used telemedicine during the COVID-19 pandemic and patients have responded well, with some even expressing a preference to continue with telemedicine after COVID-19. On the one hand, telemedicine's obvious limitation lies in confirming a new diagnosis, which usually requires in-person consultation (indeed, COVID-19 has likely created a sizeable backlog of new cases, which countries will have to prepare for once the pandemic subsides). On the other hand, telemedicine will likely continue to play a role in the routine follow up of patients with stable RA, which is more convenient for patients and reduces the in-clinic burden on doctors and staff. Moreover, as digital technology continues to advance, new opportunities for telemedicine will arise. For example, in Malaysia, an automated repeat-prescription system linked to pharmacies, without the need for a face-to-face doctor consultation, greatly supported the use of telemedicine during lockdown, enabling patients with stable disease to continue getting their medications without having to set foot in a clinic. Nevertheless, in some LMICs, patients may live in areas that are remote or underdeveloped, and without internet access or even reliable sources of electricity; many of these patients may also not be digitally savvy. Hence, the uptake of telemedicine should be guided by individual patients' preferences, access to digital resources, and their level of comfort with using telemedicine.

4 | WHERE DO WE GO FROM HERE?

The experience shared by both patients and rheumatologists allows us to qualitatively assess and discuss how far we have come in the management of RA in Asia Pacific and the challenges that still need to be overcome, as well as providing important insight into the patient journey. In the development of the APLAR guidelines, the views of one patient representative were consulted;[1] perhaps to increase the applicability of guidelines in real-life practice in the future, this approach should continue to be incorporated to ensure that management recommendations are sensitive to the needs of the people they seek to help. In the APLAR guidelines, problems with access to advanced DMARD treatment, largely related to affordability, were noted, and alternatives to these agents were provided. It is beyond the scope of guidelines to recommend other approaches for overcoming issues of access but, from our discussions, there may be a real opportunity to effect change through patient advocacy in countries where governments and public health systems are beginning to realize that involving patients in policy decisions can improve long-term outcomes and care. Many countries in Asia Pacific, on face value, claim to include patients in their healthcare policy-making; however small the window, this opportunity should be explored further with more organized, consolidated patient group efforts. Greater collaborations with bodies such as APLAR, and learning from patient groups in places like Taiwan on how to amplify the patient voice, may also help to improve awareness, disease education, and patient autonomy and responsibility, and may improve treatment and care, including increasing access to advanced DMARD therapy when needed.

From the rheumatologists' perspective, many challenges remain the same, such as the shortage of rheumatologists, late diagnosis, and late or suboptimal treatment. Real-world, tailored, and pragmatic solutions are needed in Asia Pacific to improve outcomes, such as the training of and networking with non-rheumatologists; it may be a while before the rheumatology workforce is sufficient to meet the disease burden. WHO-ILAR-COPCORD needs to further explore ways to serve its primary purpose in determining disease burden and risk factors, imparting education to the community and doctors, and implementing control and preventive strategies at a grass-root level.

One legacy of COVID-19 is the march of telemedicine onto the global stage and, post-pandemic, rheumatologists must determine how and in whom telemedicine should be best used. Finally, if we are to improve patient outcomes on a wider scale, the RA population of Asia Pacific must become "visible". Policy-makers need to hear and see these patients, and understand how their decisions profoundly affect not only the individual and their families, but also the health and productivity of a state or nation. Reducing the RA burden means that a whole society benefits, and actions must be taken to achieve this.

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CONFLICT OF INTEREST

AC, HYL, MAS, SS, RJ, BS, and KWGL all have no conflicts of interest; SVN is on the speaker bureau for Pfizer, Johnson & Johnson, and Novartis; ST has received consultant fees, speaking fees, and honoraria from Novartis, Pfizer, Roche, and Zuellig Pharma, and serves on advisory board for Pfizer; LTC has received speaker fees and honoraria from Amgen, Johnson & Johnson, Pfizer, and Eli Lilly; JW is an employee of Pfizer.

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