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Abstract

Background: Multiple sclerosis is a complex and intractable neurological disease associated with substantial morbidity, healthcare utilization, management cost, and loss of productivity. There has been an alarming increase in the number of multiple sclerosis cases in Arab countries in recent years, which has spurred an increase in local research.

Aims: To analyse the multiple sclerosis research profile in Arab countries.

Methods: A total of 781 publications focusing on multiple sclerosis research in Arab countries from 1983 to 2021 were extracted from the Web of Science database and analysed using bibliometric techniques.

Results: Publication on multiple sclerosis research increased sharply in the last decade, globally and in the Arab countries. However, Arab countries have only contributed 0.8% of the overall number of publications. Keyword pattern analysis showed that magnetic resonance imaging, optical coherence tomography, expanded disability status, demyelination, and epidemiology were the major themes of multiple sclerosis research in Arab countries. Case–control, cohort, and descriptive studies were the most prevalent study designs. However, there was a notable paucity of meta-analyses, randomized controlled trials, and clinical trials.

Conclusion: Arab countries can improve their regional expertise and add a wealth of

knowledge to global multiple sclerosis resources by diversifying their current research initiatives, and tracking recent advances in pathogenesis, diagnosis, and management of multiple sclerosis.

Keywords: sclerosis, neurology, Arab countries, Web of Science, research, scientometrics

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Introduction

Multiple sclerosis is a complex autoimmune disease that targets the nervous system, and affects ~0.03% of the human population (1). The pathological course of multiple sclerosis is largely characterized by chronic inflammation, demyelination, axonal damage, and neurodegeneration. Clinically, multiple sclerosis symptoms manifest as sensory, motor, and cognitive dysfunction, and affected individuals are mostly aged 15–45 years (2). Multiple sclerosis is a chronic disease with no curative treatment and causes massive loss of productivity and disruption of social life. The global healthcare burden and cost of managing multiple sclerosis-induced neurological disabilities and comorbidities are huge (3). Epidemiological data collected in 2016 suggested a 10.2% increase in multiple sclerosis incidence since 1990, with 2.2 million new cases (4). Hence, multiple sclerosis has emerged as a disease of serious global concern, with data projecting a worldwide increase in incidence and economic impact (4).

Historically, multiple sclerosis was considered a rare disease in Arab countries (Algeria, Bahrain, Comoros, Djibouti, Egypt, Iraq, Jordan, Kuwait, Lebanon, Libya, Mauritania, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, and Yemen). However, recent data indicate that the incidence of multiple sclerosis in Arab countries is higher than the low-risk category (≥30/100 000) of Kurtzke's

classification, and is estimated to increase in the future (5). In common with other countries, Arab countries are also facing a surge in multiple sclerosis cases and their consequent morbidity (6). This explains the increase in multiple sclerosis research in Arab countries in the past few years. Although there have been many epidemiological, genetic, neurological, diagnostic, and clinical studies of multiple sclerosis conducted in Arab countries, there has been no narrative or systematic review of its overall scope and trends (7–9). Therefore, this study used bibliometric mapping to analyse the multiple sclerosis research profile in Arab countries, identify research gaps and highlighted opportunities in multiple sclerosis research for local and international researchers.

Methods

We conducted a bibliometric analysis of the scientific literature on multiple sclerosis produced by 22 Arab countries between 1983 and 2021. The relevant literature was identified in Web of Science, using the following search query in the core collection: TS= (multiple sclerosis OR experimental autoimmune encephalomyelitis) AND CU= (Algeria OR Comoros OR Djibouti OR Egypt OR Iraq OR Jordan OR Lebanon OR Libya OR Mauritania OR Morocco OR Palestine OR Somalia OR Sudan OR Syria OR Tunisia OR Bahrain OR Kuwait OR Oman OR Qatar OR Saudi Arabia OR United Arab Emirates OR Yemen). The literature search was performed on 17 August 2021, at the Imam Abdulrahman bin Faisal University, and retrieved 1734 records in the English language, including 1046 research articles, 395 meeting abstracts, 208 reviews, 31 letters, 29 editorials, 24 early access articles, 24 proceedings papers, 5 book chapters, 4 corrections, 1 note, and 1 retracted publication. Some records were found in 2 categories in Web of Science; for example, early access articles were also listed as research articles. Therefore, the count and percentage of the total retrieved records and records listed in different categories may have differed.

Three independent reviewers scanned the individual articles and screened out 492 irrelevant articles that were not related to multiple sclerosis. The data were exported into Microsoft Excel (Redmond, WA, USA), and manually screened by 2 independent reviewers to identify articles based on their study design. A total of 781 relevant documents were included in the analysis. We used the bibliometric tools VOSviewer, Biblioshiny, Bibexcel, Microsoft Excel, and Microsoft Acess (Redmond, WA, USA) to measure various aspects of the literature on multiple sclerosis research in Arab countries, including research productivity of a country, type of institution where the research was conducted, citation score, chronological distribution of research, keyword analysis, funding, and research design.

Results

Publication and citation trends in multiple sclerosis research in Arab countries and globally

Figure 1 shows the trends in publications and citations on multiple sclerosis research in Arab countries between 1983 and 2021. There was a slow increase in the number of publications, which did not reach double figures until 2010. However, the citation scores shows an upward trend. For example, from 1983 to 2009, only 55 of 781 (7%) publications were recorded with 1928 of 10 229 (18.85%) citations. The publication count showed an increasing trend after 2011. The highest number of publications (n = 126, 16.13%) was in 2020, followed by 2018 (n = 105, 13.44%) and 2019 (n = 98, 12.54%). The highest citation score was recorded in 2015 (n = 1261), followed by 2017 (n = 1188) and 2019

(n = 1032). The highest h-index of 20 was recorded in 2017, followed by 18 in 2015 and 16 in 2018. The h-index is a scientometric indicator that measures the number of publications of a researcher and the citation impact of those publications.

There was a similar pattern in global multiple sclerosis research productivity (Table 1). Between 1900 and 1980, only 1167 papers were published worldwide, which comprised only 1.3% of the total global contribution to multiple sclerosis research up to 2021. The last decade witnessed significant growth in global multiple sclerosis research productivity, with 55% of the entire output since 1900 being published between 2011 and 2021. However, the annual growth rate in publications in Arab countries was only 0.88% between 1980 and 2021, which was significantly lower than in the rest of the world (2.43%).

Top 10 Arab countries and institutions for research collaboration and productivity

Table 2 lists the top 10 Arab countries for number of publications and citations on multiple sclerosis research. Some single papers were considered more than once when counting the number of publications because of collaboration among different countries. The same was applicable to organizational productivity and collaboration. There may also have been some possibility of error in country and organizational counting because of spelling variations. Egypt was the leading country for multiple sclerosis research, followed by Saudi Arabia, Kuwait, and Lebanon. Kuwait had the highest citation score, followed by Saudi Arabia and Lebanon. However, Qatar scored the highest citations/publications ratio, followed by UAE and Bahrain. This indicated that the citation impact of Qatar, UAE, and Bahrain was higher than that of countries with the largest number of publications. Although Egypt was ranked first for publication count, it was ranked ninth in the citation impact list.

Al-Amiri Hospital, Kuwait, was the most prominent institution in terms of research productivity and institutional collaboration, followed by Cairo University, American University of Beirut, and Ibn Sina Hospital. Among the top 10 Arab institutions, 4 were from Kuwait, 3 from Saudi Arabia, 2 from Egypt, and 1 from Lebanon.

Comparison of global and Arab multiple sclerosis research

We compared the global distribution of multiple sclerosis research published from 1900 to April 2021 and indexed in the Web of Science database. When comparing the global output of multiple sclerosis research (88 850 publications), the USA ranked first, contributing 37.15% of the total, followed by Germany (10.25%), UK (10.21%), Italy (10.07%), Canada (6.94%), France (4.67%), Netherlands (4.63%), China (4.56%), Spain (3.79%), Japan (3.76%), and Arab countries (0.88%).

Keyword analysis

Co-occurrence of keywords refers to the common presence, frequency of occurrence, and close proximity of keywords in research papers. Figure 2 shows co-occurrence of keywords in the multiple sclerosis literature. Among the 781 records considered in this study, 635 (81.30%) research papers had 1686 keywords, while 145 (18.56%) lacked author keywords. The keyword multiple sclerosis was excluded from the network graph because it was frequently used. For keywords with spelling variations, one standardized term was used. Some 1638 author keywords with at least 7 occurrences in the literature were considered to generate the network visualization graph.

In the network visualization, the size of the circle and labels represented the frequency of the keywords in the literature. Some items may not have been displayed in the network graph to avoid overlapping. The colours of the keywords were determined by the clusters to which they belonged. Lines between the keywords represent the links. Figure 2 presents the 35 most-used keywords based on their co-occurrence and associational link strength. The latter indicated the number of links of a keyword with other keywords. Thirty-five keywords met the threshold of appearing at least 7 times and were distributed into clusters 1 (n = 9) 2 (n = 9), 3 (n = 5), 4 (n = 4), 5 (n = 3), 6 (n = 3), and 7 (n = 2). Demyelination, disability, relapsing–remitting MS, depression, Expanded Disability Status Scale, epidemiology, and diagnosis had the highest occurrence and link strength in each cluster.

Popular research designs

Table 3 presents the research design and subtype adopted by multiple sclerosis researchers in Arab countries. Observational was the most frequent research design, appearing in 263 (33.67%) publications, followed by descriptive in 189 (24.19%), experimental in 187 (23.94%), and review in 132 (16.90%), and clinical trial was the least used research method. Case–control, cohort, and case reports were widely used subtypes, and meta-analysis and case study were the least popular.

Discussion

Our bibliometric analysis showed that multiple sclerosis research in Arab countries had a progressively upward trend since 2010, with a marked spike after 2014 to the present. This increase mirrors the global research trend over the same period. However, despite the rise in multiple sclerosis publications in Arab countries, the combined output of all Arab countries constituted only 0.88% of the global research output in the Web of Science database.

The current analysis did not include any Arabic articles on multiple sclerosis. We searched Google Scholar without a language filter and some Arabic language databases, such as Al Manhal, Dar almundumah, and AskZad, using Arabic versions of our keywords. Our search still did not yield a single Arabic article on multiple sclerosis, reflecting a limited attention to this crucial topic in Arab countries.

There are two possible explanations for the delayed

and limited attention of Arab researchers to multiple sclerosis research. First, until the earlier preliminary studies in Libya and Kuwait that indicated a rising prevalence of multiple sclerosis in Arab countries in the 1980s, it was presumed to be a disease of cold climates and was not considered important by Arab researchers. Second, unlike in western countries, scientific research has not previously been a high priority in Arab countries, which allocated only 0.3% of their gross domestic product to research and development (10). However, the rapidly changing social and cultural dynamics in most Arab countries are now favouring an increased emphasis on education and learning. The progressive increase in multiple sclerosis research in Arab countries shows the potential for future growth in this area. If the current trend continues, Arab countries could become important players in expanding knowledge and understanding of multiple sclerosis worldwide.

Our data indicated that Egypt, Saudi Arabia, Kuwait, and Lebanon were the most productive countries, while Qatar, UAE, and Bahrain had the highest citation impact. In the citation analysis, the top 10 Arab countries received a reasonable citation score (> 600), reflecting the high impact of their work in the field.

Our keyword distribution analysis suggested that a significant proportion of the Arab multiple sclerosis research has been directed at detection, diagnosis, and rehabilitation. A manual screening of all the selected publication records showed that observational case–control studies, cohort studies, and descriptive studies were the dominant methods used in Arab multiple sclerosis research. In contrast, there was a dearth of clinical trials, randomized controlled trials, and meta-analyses. In the following section, we discuss the latest trends in

multiple sclerosis research that have not received much attention in Arab countries and offer future prospects for research.

Multiple sclerosis is a perplexing disease because of our partial understanding of its etiology and pathogenesis. Although it has been established that some genetic and environmental predictors are linked to high susceptibility to multiple sclerosis (2), scientists are still unsure about why and how these factors trigger the disease. It has also not been determined whether autoimmunity to the myelin epitopes is a cause or a consequence of another underlying pathological event (11). Marked variation in the pathology, disease course, and response to treatment has been observed between the relapsing–remitting and progressive forms of multiple sclerosis. The latest studies have attempted to establish the distinctive biomarkers and regulators that drive the course of each form of multiple sclerosis (12). Some recent data support the theory that the inflammatory microenvironment in the progressive form of multiple sclerosis is dominated by microglial activation, B cell hyperactivity, antibody production, and cytokine release (13). Mitochondrial dysfunction and disruption of cationic conduction are known to exacerbate axonal injury in progressive multiple sclerosis (14). Although informative, these data do not explain the upstream cascade of events that drives molecular and genetic heterogeneity in multiple sclerosis. Further immunobiological and genetic studies are ongoing in this direction. Another direction of research is to identify further multiple sclerosis susceptibility markers. Some recent studies have investigated the role of the gut microbiome, epigenetic factors, sex-specific genes, and an anti-inflammatory protein, ubiquitin, in multiple sclerosis risk (15–17).

Demyelination and neurodegeneration are 2 major features of multiple sclerosis that lead to profound neurologic deficits. Currently, researchers are trying to elucidate the precise contribution and behaviour of resident microglia and astrocytes to maintaining neuronal integrity. Although these immune cells have protective and destructive roles in neurodegeneration, it is unknown which biological cues induce them to behave in certain ways (18). Understanding the cross-communication between neurons and immune cells is also crucial to identifying targets for repair or reversal of the neuronal damage (18).

Other recent research has investigated ways to enhance endogenous remyelination or neuroprotective mechanisms in the central nervous system, by transplanting autologous peripheral nerve Schwann cells, olfactory bulb ensheathing cells, or mesenchymal stem cells (19,20). Mesenchymal stem cells have the potential to induce remyelination and neuroprotection in multiple sclerosis because of their pluripotent nature and anti-inflammatory activity. A recently introduced human monoclonal antibody, opicinumab, that binds to LINGO-1 on oligodendrocytes has shown remyelination potential in clinical trials. This area has received little attention in Arab research to date (21) and it would be worthwhile to investigate the clinical efficacy of opicinumab and related drugs among Arab patients.

Previous studies have implicated epigenetic modifications such as DNA methylation, histone modification, and miRNA-associated gene expression in multiple sclerosis pathogenesis (22). These findings have led to the emergence of the concept of epigenetic therapy. Animal studies have shown that histone deacetylase inhibitors (e.g. trichostatin and vorinostat) and DNA methyltransferase inhibitors (e.g. decitabine) were effective in reducing central nervous system demyelination, and neuronal and axonal loss. These promising medications are candidates for human trials in the near future (23,24).

Multiple sclerosis management has always been challenging because of the unavailability of effective or curative therapies. Currently available disease-modifying drugs have been moderately effective (30–55%) in controlling disease exacerbations, as well as the progression of disability in relapsing–remitting multiple sclerosis. However, they have not achieved the same level of success in progressive multiple sclerosis. Sodium channel blockers (e.g. lamotrigine, phenytoin, and carbamazepine) and glutamate receptor antagonists have reduced axonal damage and improved oligodendrocyte survival in animal models (25,26). Glial-cell-line-derived neurotrophic factors (e.g. insulin-like growth factor 1 and brain-derived neurotrophic factor) and MitoQ, a specific inhibitor of mitochondrial reactive oxygen species production, have also exhibited axonal protective properties (27,28). These drugs are potential candidates for the treatment of progressive multiple sclerosis. Compared with disease-modifying drugs, B-cell-based therapies, including anti-CD20 monoclonal antibodies (e.g. rituximab, ocrelizumab, and ofatumumab) have shown superior efficacy, and better toxicity profile, long-term benefits, patient adherence, and flexibility in dosing regimens in relapsing–remitting and progressive MS. These medications are undergoing clinical trials and need to be studied in a larger patient population including in Arab countries (28,29).

Serious toxicity associated with the current disease-modifying drugs has necessitated efforts to find more effective and safe medications for multiple sclerosis. Antigen-specific therapy is an ideal approach to specifically target and silence the autoreactive T-cell repertoire without causing general immunosuppression and toxicity (30).

Multiple sclerosis is a chronic disease with inevitable progression to significant cognitive and neurological dysfunction involving paraesthesia, hyper-reflexia, facial weakness, optic neuritis, and paroxysmal symptoms including Lhermitte’s symptoms, trigeminal neuralgia, pain, spasticity, depression, fatigue, bladder dysfunction, sexual dysfunction, and cognitive impairment (31,32). We found limited research in this area.

This study had some limitations. First, there were the typical limitations inherent in a bibliometric study, which have been discussed previously (33). Second, we analysed articles indexed in the Web of Science database only, which created some research bias in the collected data because other databases such as PubMed, Google Scholar, Scopus, and EBSCO could have revealed another set of records. Third, our study was limited to assessing the overall research productivity, its pattern, academic impact, and prospective opportunities. We did not seek to assess the scientific quality and socioeconomic impact of the publications. This would have been more time-consuming and required more advanced technical resources.

Conclusion and implications

This study assessed publications of multiple sclerosis research in Arab countries and discussed recent advances in the field to help steer future research in the region. Egypt, Saudi Arabia, Kuwait, and Lebanon were the leading Arab countries for multiple sclerosis research. Observational (case–control and cohort) and descriptive studies were the predominant study designs in Arab multiple sclerosis research. There has been little research involving randomized control trials, meta-analyses, and clinical trials of newly approved drugs and more research is warranted. Multiple sclerosis research in Arab countries had a slow onset and low output before 2010, but the growth curve shows strong potential for future expansion. Arab countries need to diversify their current basic sciences, and translational and clinical research to address the unresolved questions in multiple sclerosis. Pursuit of the latest hotspots would open new avenues of multiple sclerosis research in the region, improve specialized expertise for better patient care, and add a wealth of knowledge to the multiple sclerosis literature. Multiple sclerosis is a promising area of research globally as well as in Arab countries. With growing interest and investment in scientific research, more resources, collaboration opportunities, and new talent, Arab countries are well placed to contribute significantly to the exciting and dynamic field of multiple sclerosis research for global benefit.

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Tendances actuelles et perspectives de la recherche sur la sclérose en plaques dans les pays arabes

Résumé

Contexte : La sclérose en plaques est une maladie neurologique complexe et incurable qui est associée à une morbidité substantielle, au recours à des soins de santé, à des coûts de prise en charge et à une perte de productivité. On observe une augmentation alarmante du nombre

de cas de sclérose en plaques dans les pays arabes ces dernières années, ce qui a stimulé une intensification de la recherche locale.

Objectifs : Analyser le profil de recherche sur la sclérose en plaques dans les pays arabes.

Méthodes : Au total, 781 publications consacrées à la recherche sur la sclérose en plaques dans les pays arabes entre 1983 et 2021 ont été extraites de la base de données Web of Science et analysées à l'aide de techniques bibliométriques.

Résultats : Les publications concernant la recherche sur la sclérose en plaques ont fortement augmenté au cours de la dernière décennie, à l'échelle mondiale et dans les pays arabes qui ne contribuent toutefois que pour 0,8 % du nombre total de publications. L'analyse des modèles par mots-clés a montré que l'imagerie par résonance magnétique, la tomographie par cohérence optique, le statut d'invalidité étendu, la démyélinisation et l'épidémiologie étaient les principaux thèmes de la recherche sur la sclérose en plaques dans les pays arabes. Les études cas-témoins, descriptives et de cohortes étaient les méthodes d'étude les plus répandues. Cependant, les méta-analyses, les essais contrôlés randomisés et les essais cliniques étaient nettement insuffisants.

Conclusion : Les pays arabes peuvent améliorer leur expertise régionale et apporter d'importantes connaissances aux ressources mondiales concernant la sclérose en plaques en diversifiant leurs initiatives de recherche actuelles et en suivant les progrès récents dans la pathogenèse, le diagnostic et la prise en charge de la sclérose en plaques.

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