

CODEN [USA]: IAJPBB

ISSN: 2349-7750

INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.2574449

Available online at: <u>http://www.iajps.com</u>

Review Article

MULTIPLE SCLEROSIS EPIDEMIOLOGY IN ARABIAN GULF REGION: A SYSTEMATIC REVIEW

Albatoul Fahad Almulhim¹, Cereen Fahad Almulhim¹, Sukaina Mohammad Al Haddad¹, Fatimah Ali Alshehri¹, Abrar Mohana'a AlHussain ¹ ¹King Faisal University

Abstract:

Background: Multiple sclerosis (MS) is a chronic inflammatory multifocal demyelinating disease of the central nervous system (CNS) with progressive neurodegeneration. MS is one of the world's most common neurologic disorders and consider to be the most common cause of non-traumatic disability in young adults. According to Atlas multiple sclerosis of WHO, the median estimated prevalence and incidence of MS is greatest in Europe followed by the Eastern Mediterranean, the Americas, the Western Pacific, South-East Asia and Africa. The Arabian Gulf Region is located in a low-risk zone for MS; however, recent studies suggest a moderate-to-high prevalence nearby. **Objective:** In our review we aim to describe and compare demographic and clinical characteristics of MS in Arabian gulf countries (AGCs).

Methods: PubMed database were used for articles selection. All relevant articles related to our review were chosen to cover the following topics: Multiple sclerosis, epidemiology, prevalence, incidence. We excluded other articles, which are not related to our objectives. The data have been extracted according to specific form to be reviewed by the authors

Results and discussion: We enrolled a total of 13 studies according to our inclusion, and exclusion criteria. McDonald's criteria were the most widely used diagnostic criteria in the studies. Most studies were conducted in single hospital-based centers with a defined catchment area. The female/male ratio ranged from 1.1 in Oman to 4.3 in Saudi Arabia. The mean age at disease onset ranged from 25.2 years Kuwait to 32 years Saudi Arabia. MS prevalence ranged from 85.05/100,000 in 2013 to 4/100000 in 2000 reported in Kuwait and Oman respectively.

Conclusion: There is an increase in the prevalence and incidence that were reported in some AGCs such as Kuwait over the years. However, the prevalence and incidence of MS overall in are not well-documented in many countries of Arabian Gulf Region.

Keywords: Multiple Sclerosis (MS), Arabian Gulf Countries (AGCs), Prevalence, Incidence, Clinical course.

Corresponding author:

Albatoul Fahad Almulhim, King Faisal University, 3842 abu suad al jahani - Az Zahra Dist. JEDDAH 23425 - 7686 e-mail: albatoulf@gmail.com, Telephone number: + 966563999678.



Please cite this article in press Albatoul Fahad Almulhim et al., **Multiple Sclerosis Epidemiology In Arabian Gulf Region: A Systematic Review.,** Indo Am. J. P. Sci, 2019; 06(02).

INTRODUCTION:

Multiple sclerosis (MS) is a chronic inflammatory multifocal demyelinating disease of the central nervous system (CNS) with progressive neurodegeneration caused by an autoimmune response to self-antigens in a genetically susceptible individual [1-3].

It is believed to be an immune mediated disease, and although the etiology remains unknown, it is believed to occur from a combination of genetic risk factors and environmental risk factors [4, 5]. MS is one of the world's most common neurologic disorders, and consider to be the most common cause of nontraumatic disability in young adults. It affects approximately 1 000 000 people between 17 and 65 vears old worldwide [6]. A Systemic review involving different studies from different countries showed the weighted mean incidence rate among women was 3.6 cases per 100,000 person-years, and among men was 2.0 cases per 100,000 person-years [7]. As any other autoimmune disease, MS is more common in women than in men and female: male ratio has increased over the last decades from 1.4 in 1955 to 2.3 in 2000. This corresponds to a lifetime risk of 2.5% in women compared to 1.4% in men, with women affected 2-5 years earlier than men [7-9]. According to Atlas multiple sclerosis of WHO, the median estimated prevalence and incidence of MS is greatest in Europe followed by the Eastern Mediterranean, the Americas, the Western Pacific, South-East Asia and Africa [10]. Based on the Kurtzke classification, the Arabian Gulf Region is located in a low-risk zone for MS; however, recent studies suggest a moderate-to-high prevalence nearby (31-55 MS per 10,0000 individuals), with an increase in incidence and prevalence in recent years [11, 12].

This study is aimed to describe and compare demographic and clinical characteristics of MS in Arabian gulf countries (AGCs). This study conduction will help to build a reference of the prevalence, demographical and clinical characteristics data of MS in AGCs.

MATERIAL AND METHODS: Screening and Eligibility Criteria

Inclusion criteria: The following criteria were used to select papers for inclusion in this systematic review: (1) the population defined primarily as those living in the Arabian Gulf region refers to the six member states of the Gulf Cooperation Council (GCC) countries namely Bahrain, Kuwait, Oman, Qatar, Saudi Arabia (KSA), and the United Arab Emirates (UAE) [13]. (2) MS was defined according to the aproved international diagnostic criteria that is used at the time

of the study (McDonald's criteria [14] or Poser's criteria) [15]. (3) The articles were selected based on the relevance to the research project which should include one of the following topics "multiple sclerosis, epidemiology, prevalence, incidence". (4) Articles in English language were included in this study.

Exclusion criteria: All other articles which did not suit with these topics as their primary end or repeated studies, reviews studies.

Analysis: No software was used. The data extracted based on specific form that contain (Study country (author), study period, source of data, diagnostic criteria, number of cases, female/male ratio, mean age at disease onset, prevalence rates, incidence rates in these studies), these data were reviewed by the authors to describe and compare demographic and clinical characteristics of MS in AGCs and to compare with early studies.

Search Strategy

PubMed was chosen as the search database for the articles selection, because it is one of the major research databases within the suite of resources that have been developed by the National Center for Biotechnology Information (NCBI). The following topics were used: ("Multiple Sclerosis"[Mesh]) AND "Multiple Sclerosis/epidemiology"[Mesh]) AND "United "Saudi Arabia"[Mesh] OR Arab Emirates"[Mesh] OR "Qatar"[Mesh] OR OR "Bahrain"[Mesh] OR "Kuwait"[Mesh] "Oman" [Mesh] AND (clinical Study [ptyp] AND "1985/01/01" [PDate]:"2018/12/31" [PDate])

A 35 articles were shown (Saudi Arabia :7 articles, UAE:3, Qatar: 2, Kuwait: 21, Oman: 2, Bahrain:0). The chosen articles were screened by titles, and reviewing the abstracts yielded 13 articles which were enrolled.

RESULTS:

We enrolled a total of 13 studies according to our inclusion, and exclusion criteria as described above. All of the included studies compared the demographic and clinical characteristics of MS in AGCs. Table 1 shows study country (author), study period, source of data, diagnostic criteria, number of cases, female/male ratio, mean age at disease onset, prevalence rates, incidence rates in these studies.

Our search on epidemiology of MS in AGCs yielded no results in Bahrain. Single hospital-based studies covering mainly capital cities were the only source of information on MS epidemiology in Oman, Qatar, and Saudi Arabia. Multicenter hospital-based studies and Single hospital-based studies were the source of information on MS epidemiology in Kuwait and UAE. We have presented these studies separately in the table 1.

Table 1: Comparative analysis of MS epidemiology in AGCs in multicenter hospital-based studies and single hospital center studies

Study country (author)	Study period	Source of data	Diagnostic criteria	Number of cases	Female/male ratio	Mean age at disease onset	Prevalence /100,000	Incidence/ 100,000
<i>Saudi</i> <i>Arabia</i> (Yaqub and Daif.) [16]	1983-1986	Single hospital- based center	Poser's criteria	16	4.3:1	29	-	-
Saudi Arabia (Daif et al.) [17]	1986- 1995	Single hospital- based center	Poser's criteria	89	1.34: 1	27.7 ± 7.8	25	-
Saudi Arabia (Halawani et al) [18]	2017-2018	Single hospital- based center	McDonald's criteria	80	1.85: 1	32	-	-
<i>Kuwait</i> (Alroughani et al) [19]	2010-2013	Multicenter hospital based	McDonald's criteria	1176	1.8:1	-	85.05	6.88
<i>Kuwait</i> (Akhtar et al) [20]	2013	Multicenter hospital based	McDonald's criteria	1,035	1.9 :1	-	-	-
<i>Kuwait</i> (Alshubaili et al) [21]	1993-2000.	Single hospital- based center	Poser's criteria	338	1.39:1	26.0 ± 7.7	6.68 in 1993 to 14.77 in 2000.	1.05 in 1993 to 2.62 in 2000
<i>Kuwait</i> (Al-Din et al) [22]	1988	Multicenter hospital based	Poser's criteria	201	1.3: 1	25.2 ± 7.97	10.2	-
<i>Kuwait</i> (Al-Din) [23]	1981-1983	Multicenter hospital based	Poser's criteria	95	1.11:1	27.5	8.33	-
UAE (Inshasi and Thakre) [24]	2000-2007	Single hospital- based center	McDonald's criteria	284	2.85:1	26.66 ± 6.6	54.77	6.8

UAE (Schiess et al) [25]	2010 - 2014	Multicenter hospital based	McDonald's criteria	510	1.77:1	-	18	6
<i>Qatar</i> (Akhtar et al) [26]	2005-2010	Single hospital- based center	McDonald's criteria	142	1.73: 1	31	-	-
<i>Qatar</i> (Deleu et al) [27]	2010	Single hospital- based center	McDonald's criteria	154	1.33:1	27.0 ± 8.6	64.57	-
Oman (Tharakan et al) [28]	1990- 2000	Single hospital- based center	Poser's criteria	30	1.1:1	27	4	-

A brief description of the epidemiology and natural history of MS in each country is presented here:

Kuwait:

Alshubaili et al. reported an increase in MS incidence from 1.05/100,000 in 1993 to 2.62/100,000 in 2000 in Kuwait. Similarly, increase in the prevalence from 6.68/100,000 in 1993 to 14.77/100,000 in 2000. The prevalence was much markedly higher for Kuwaitis 31.15/100,000, as compared to non-Kuwaitis 5.55/ 100,000. The average age of disease onset 26.0 ± 7.7 years. The crude female to male ratio was 1.39:1. The clinical course was relapsing-remitting MS (RRMS) in 78.4%, followed by secondary progressive MS (SPMS) in 14.8% and the primary progressive MS (PPMS) in 6.5%. The most common symptoms presenting at diagnosis were sensory in 52.4% and motor weakness in 50.0% followed by unilateral optic neuritis in 32.5%, ocular palsy in 25.7% and cerebellar signs in 24.6%. Less common symptoms included sphincter disturbances in 22.5% [21]. The latest MS epidemiology study in Kuwait was multicenter hospital-based study done by Alroughani et al. reported MS prevalence in 2011 was 85.05/100,000 with incidence 6.88/100000, which is considered the highest prevalence and incidence had been recorded among all AGCs. The prevalence rate was higher in women (108.92//100,000 versus 60.82/100,000), with female to male ratio was 1.8:1.

Qatar:

Qatar considered as medium-to-high risk area for MS according to Deleu et al. reported the first MS epidemiological study done in Qatar which showed a

high prevalence of 64.57/100,000 in 2010. The crude female- to-male ratio was 1.33:1 which is obviously lower than that observed in the remaining AGCs. The average age of disease onset 27.0 ± 8.6 years. A positive family history was found in 10.4% of included MS patients. The most common symptom at presentation was sensory symptoms in 33.3%, followed by optic neuritis in 20.8% or pyramidal symptoms in 20.8%, brainstem in17.7%, cerebellar in 4.4% and less commonly spinal cord in 3%. The clinical course was RRMS in 68.2 %, SPMS in 7.2 %, relapsing progressive multiple sclerosis (RPMS) 3.9%, PPMS in 0.6 %, and Clinically Isolated Syndrome (CIS) in 14.2% [27]. In another study done by Akhtar et al. the most common presenting symptoms Sensory symptoms in 63% followed by visual in 45%, motor in 43%, cerebellar in 32%, brainstem in 27%, spinal cord in 14%, and bladder/bowel symptoms in 10%. The clinical course was RRMS in 58.5% patients, SPMS in 4.5%, PPMS in 2%, and CIS in 7% [26].

Saudi Arabia:

In compression with other AGCs, Saudi Arabia MS prevalence is low 25/100,000 reported in 1995. However, the prevalence of MS in Saudi Arabia can't be relayed on according the latest study done in 1995 because no more reports have been published since then. Additionally, no study reported the incidence of MS in Saudi Arabia. The mean age at onset in Saudi patients 25.9 years was lower than that of the non-Saudis 29.4 years. The crude female to male ratio was

1.34:1. In Saudi subjects, there was an increase in female: male ratio 1.32:1. In other Hand, in non-Saudis subjects the ratio 1.4:1. The clinical course was RRMS in 60.7%, RPMS in 20.2% and PPMS in 19.1%. Limb weakness was the commonest presenting symptom in both the Saudi and non-Saudi patients. There were some variations between both groups, brain stem symptoms were more frequent in the Saudi group whereas the non-Saudis had a higher frequency of motor, sensory and sphincteric symptoms [17].

UAE:

Inshasi and Thakre reported the first crude prevalence rate was 19.2/100.000 in the whole group, while in the Dubai Native population was 54.777/100,000 in 2007. The annual Incidence rate for MS cases in Dubai Native population was 6.8/100,000 during 2000-2007. In the whole group with a female to male ratio of 2.02:1 while in the Dubai Native population, higher female to male ratio of 2.85:1. The most common presenting symptoms in the whole group was motor manifestations in 72.78% followed by sensory symptoms in 48.41%, cerebellar manifestations in 19.96%, ocular manifestations in 16.13%, and brainstem manifestations in 5.3%. There was no difference between the Dubai Natives and the Immigrants presenting symptoms. The clinical course was RRMS in 76.9% of the Dubai Natives and 66.6% of the Immigrants group. RPMS and SPMS were 4.4% and 10.6%, respectively, in the Dubai Natives and 7.9% and 13%, respectively, in the Immigrants [24]. Similar epidemiological result reported by Schiess et al. the crude prevalence rate was 18/100,000 and crude prevalence rate in Emiratis was 57.09/100,000 in 2014 which is higher than the earlier study. The Agestandardized incidence rate in Emiratis was 6.0/100,000. The whole group female/male ratio was 1.77:1. While in Emiratis female/male ratio of 1.70:1. The most common presenting symptoms was Visual in 40%, Sensory in 26% then motor in 20%. The clinical course was RRMS in 77.8%, SPMS in 8.2%, PPMS in 1.1% and CIS in 12.3% [25].

Oman:

Oman has the lowest reported MS occurrence in the AGCs; however, the MS prevalence has increased from 1.2/100,000 in 1996 to 4/100,000 in 2000. Mean age at onset was 27 and male to female ratio was 1.1:1. Among 30 patients with MS diagnosis, 23 patients had the RRMS, 4 were SPMS, and 3 were PPMS. The most common presenting symptoms blurred vision in 12 patients, sensory symptoms in 6 patients, ataxia in 5 patients, diplopia in 3 patients, and hemiplegia in 2 patients [28].

DISCUSSION:

Our systematic review yielded 13 studies on epidemiology of MS in the AGCs. McDonald's criteria were the most commonly used diagnostic criteria 53.84%, Poser et al. criteria were used in 46.15% of studies. Single hospital-based studies accounted in 61.53 % of studies [16-18, 21, 24, 26-28], while 38.46% of studies were conducted in a multicenter hospital-based setting [19&20, 22&23, 25].

The female/male sex ratio varied among studies in the region, ranging from 0.8 in Oman [28] to 4.3 in Saudi Arabia [16]. The mean age at disease onset ranged from 25.2 years Kuwait to 32 years Saudi Arabia.

Prevalence rates range from 6.68/100,000 in 1993 to 14.77/100,000 in 2000 [21] to 85.05/100,000 in 2013 in Kuwait, [19] which is considered as the highest prevalence rate among all AGCs. In addition, Qatar is the second highest prevalence with 64.57 /100,000 cases reported in 2010 [27]. Oman considered to be the lowest prevalence rates with 4/100000 reported in 2000.

The annual MS incidence rate in the AGCs was only reported in few studies ranging from 1.05/100,000 in 1993 to 2.62/100,000 in 2000 in Kuwait [21]. The 3-year incidence rate in Kuwait was reported to be 6.88/100,000 in a later study 2013 [19]. In UAE annual incidence rate of 6.8/100,000 during 2000-2007 [24], While the age-standardized incidence rate in UAE during 2010 - 2014 was 6.0/100,000 person-years.

As we do not have any previous studies suitable for comparison to show any increase in the incidence and prevalence of MS in the AGCs, a high rate could be explained partly by the general increase in MS in the region, genetic susceptibility, closed community, consanguineous marriages, and rapid rate of change in socioeconomic life in AGCs. Another factor is the availability of modern diagnostic techniques and facilities, particularly the MRI [24]

The geographical distribution of MS patients has been the point of care in many studies worldwide. In recent systematic reviews on the prevalence of MS in different countries or regions in the world show the changing in epidemiology of disease due to genetic and environmental differences among these societies, contributing to a global increase in the rate of MS. Reports from regions lacking sufficient epidemiological studies could be of significantly importance in this regard [29].

Diagnosis of MS in the AGCs was similar to the international figures in regard to RRMS clinical subtype; however, in contrast to the international figures, PPMS was less prominent in Qatar, Dubai and Kuwait and was second to PRMS and SPMS in Saudi Arabia and Oman, respectively. The SPMS cases were the second most dominant diagnosis in Dubai and Oman, whilst in Oatar, SPMS cases were the third most dominant diagnosis clinically. The CIS constituted the second diagnosis in Kuwait, Qatar, and the Dubai. Those data indicate that internationally and locally, in AGCs, RRMS is considered the most diagnosed clinically; however, data regarding the remaining clinical subtypes show regional differences. Those data may indicate patients' needs to be diagnosed early however, AGCs citizens do not seek medical help in early disease stages, instead, they seek for help in late stages of the disease. The late stage of disease presentation or late diagnosis caused by many factors such as: (1) Low physician availability, (2) Late appointments, as a consequence, could take more than a month and patients, as a result, may develop additional brain lesions, and (3) Availability of MRI, in governmental hospitals patients may wait for few months to get MRI as a result of the increasing number of patients and low numbers of MRI machine available [30].

In the end, even though the awareness of patients and physicians has increased through the last decades and although the clinical diagnostic criteria are available for MS patients, new specialized hospitals for neurological disease, especially MS disease, must be built to keep up with the increasing numbers of MS cases.

This review has some limitations. The included studies are limited to publications in English. The lack of standardized age- and sex-specific estimates of prevalence data is an obstacle in combining studies from the same regions and comparing the changes over time.

CONCLUSION:

There is an increase in the prevalence and incidence that were reported in some AGCs such as Kuwait over the years. However, the prevalence and incidence of MS overall in are not well-documented in many countries of Arabian Gulf Region. Although most prevalence estimates are derived from single hospitalbased centers within a country, recent advances in MS registries will allow nation-wide studies.

REFERENCES:

- 1. Hafler DA. Multiple sclerosis. J Clin Invest. 2004 Mar;113(6):788-94.
- 2. Nylander A, Hafler DA. Multiple sclerosis. J Clin Invest. 2004 Mar;113(6):788-94.
- Korn T. Pathophysiology of multiple sclerosis. J Neurol. 2008 Dec;255 Suppl 6:2-6.
- Wu GF, Alvarez E. The immuno-pathophysiology of multiple sclerosis. Neurol Clin. 2011 May; 29(2): 257–278.

- Costello K. Multiple sclerosis research: diagnostics, disease-modifying treatments, and emerging therapies. J Neurosci Nurs. 2013 Dec;45(6 Suppl 1):S14-23.
- Mayr W, Pittock S, McClelland R, et al. Incidence and prevalence of multiple sclerosis in Olmsted County, Minnesota, 1985-2000. Neurology. 2003 Nov 25;61(10):1373-7
- Alonso A, Hernán MA. Temporal trends in the incidence of multiple sclerosis: a systematic review. Neurology. 2008 Jul 8;71(2):129-35.
- Kamm CP, Uitdehaag BM, Polman CH. Multiple sclerosis: current knowledge and future outlook. Eur Neurol. 2014;72(3-4):132-41.
- 9. Kantarci O1, Wingerchuk D. Epidemiology and natural history of multiple sclerosis: new insights. Curr Opin Neurol. 2006 Jun;19(3):248-54.
- World Health Organization: Atlas multiple sclerosis resources in the world 2008. Geneva: WHO Press; 2008.
- Bohlega S, Inshasi J, Al Tahan AR, et al. Multiple sclerosis in the Arabian Gulf countries: a consensus statement. J Neurol. 2013 Dec;260(12):2959-63. doi: 10.1007/s00415-013-6876-4. Epub 2013 Mar 17.
- 12. Ghamari ZT. A Review of Geoepidemiological Differences of Multiple Sclerosis in Iran and Other Middle East Countries. Arch Neurosci. 2015 July; 2(3): e22028.
- 13. Khalil AB, Beshyah SA, Abdella N, et al. Diabesity in the Arabian Gulf: Challenges and Opportunities. Oman Med J. 2018 Jul; 33(4): 273–282.
- 14. McDonald WI, Compston A, Edan G, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. Ann Neurol. 2001 Jul;50(1):121-7.
- 15. Poser CM, Paty DW, Scheinberg L, et al. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol. 1983 Mar;13(3):227-31.
- 16. Yaqub BA and Daif AK. Multiple sclerosis in Saudi Arabia. Neurology. 1988 Apr;38(4):621-3.
- Daif AK1, Al-Rajeh S, Awada A, et al. Pattern of presentation of multiple sclerosis in Saudi Arabia: analysis based on clinical and paraclinical features. Eur Neurol. 1998;39(3):182-6.
- Halawani AT, Zeidan ZA, Kareem AM, et al. Sociodemographic, environmental and lifestyle risk factors for multiple sclerosis development in the Western region of Saudi Arabia. A matched case control study. Saudi Med J. 2018 Aug;39(8):808-814.

- Alroughani R, Ahmed SF, Behbahani R, et al. Increasing prevalence and incidence rates of multiple sclerosis in Kuwait. Mult Scler. 2014 Apr;20(5):543-7.
- Akhtar S, Alroughani R, Ahmed SF, et al. Retrospective Cohort Study of Gender Differential in Risk of Multiple Sclerosis in Kuwait. Neuroepidemiology. 2016;46(3):203-8.
- 21. Alshubaili AF, Alramzy K, Ayyad YM, et al. Epidemiology of multiple sclerosis in Kuwait: new trends in incidence and prevalence. Eur Neurol. 2005;53(3):125-31. Epub 2005 Apr 28.
- 22. al-Din AS, Khogali M, Poser CM. Epidemiology of multiple sclerosis in Arabs in Kuwait: a comparative study between Kuwaitis and Palestinians. J Neurol Sci. 1990 Dec;100(1-2):137-41.
- 23. Al-Din AS. Multiple sclerosis in Kuwait: clinical and epidemiological study. J Neurol Neurosurg Psychiatry. 1986 Aug;49(8):928-31.
- 24. Inshasi J, Thakre M. Prevalence of multiple sclerosis in Dubai, United Arab Emirates. Int J Neurosci. 2011 Jul;121(7):393-8.

- 25. Schiess N, Huether K, Fatafta T, et al. How global MS prevalence is changing: A retrospective chart review in the United Arab Emirates. Mult Scler Relat Disord. 2016 Sep;9:73-9.
- 26. Akhtar N, Elsetouhy A, Deleu D, et al. Newly diagnosed multiple sclerosis in state of Qatar. Clin Neurol Neurosurg. 2013 Aug;115(8):1333-7.
- 27. Deleu D, Mir D, Al Tabouki A,et al. Prevalence, demographics and clinical characteristics of multiple sclerosis in Qatar. Mult Scler. 2013 May;19(6):816-9.
- Tharakan JJ, Chand RP, Jacob PC. Multiple sclerosis in Oman. Neurosciences (Riyadh). 2005 Jul;10(3):223-5.
- 29. Heydarpour P, Khoshkish S, Abtahi S, et al. Multiple Sclerosis Epidemiology in Middle East and North Africa: A Systematic Review and Meta-Analysis. Neuroepidemiology. 2015;44(4):232-44.
- Mohammed EM. Multiple sclerosis is prominent in the Gulf states: Review. Pathogenesis. 2016 May;3(2):19–38