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Review Article

Multiple sclerosis is prominent in the Gulf states: Review

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ABSTRACT

Introduction: Multiple sclerosis (MS) is an autoimmune disease that attacks the central nervous system, causing the appearance of focal areas of inflammation and demyelination. A detailed study of MS would offer a better understanding of the causes of increased number of MS cases in the Arab Gulf countries.
Materials and Methods: A comprehensive literature search was performed to extract data regarding MS in general and MS in Arabian Gulf countries in specific. Only peer-reviewed, full-text articles published in English were included.
Results: Data have shown a noticeable increase in cases of MS in the Arab Gulf countries. Although the underlying causes still remain elusive, many factors have been proposed to influence MS. This review will discuss the factors influencing MS, correlate their effects with disease pathology, their interaction in the context of disease development, and try to explain the increased number of MS in Arabian Gulf countries.
Conclusion: Understanding MS development could open new doors for the treatment of MS, as well as initiate novel target therapies for citizens of Arab Gulf countries.

1. Introduction

Neuroimmunological disorders present a spectrum of diseases that emerge from disrupted interactions between the nervous and the immune systems. Over the past few years, emerging data have consistently shown an increased number of Multiple Sclerosis (MS) cases in the Arabian Gulf countries. The Arabian Gulf countries include Kuwait, Bahrain, Oman, Qatar, Saudi Arabia and the United Arab Emirates (U.A.E.). Those countries share common culture, language, waters, atmosphere, and geographical area. An increase in the cases of MS in those countries could indicate the importance of targeted susceptibility factors. Therefore, the author has chosen to review this disease in particular and extensively review its susceptibility factors in Arabian Gulf countries.

2. Methods

A comprehensive literature search was conducted to extract data regarding MS. Only peer-reviewed, full-text articles published in English were included. Keywords and phrases entered onto database browsers include, but not exclusively, multiple sclerosis, multiple sclerosis reviews, multiple sclerosis in Arabian Gulf countries, multiple sclerosis pathogenesis, multiple sclerosis symptoms, multiple sclerosis clinical subtypes, multiple sclerosis incidence and prevalence, multiple sclerosis causes and multiple sclerosis aetiology, multiple sclerosis genetic, multiple sclerosis genome-wide study, multiple sclerosis genetic study, multiple sclerosis association study, multiple sclerosis genetic susceptibility factors, multiple sclerosis epigenetic factors, multiple sclerosis microRNA, multiple sclerosis mitochondrial genome, multiple sclerosis diagnosis, multiple sclerosis therapy, multiple sclerosis treatment, and multiple sclerosis future. Data were then subtracted according to their significance and thoroughly reviewed.

3. Multiple sclerosis (MS)

MS is a chronic, recurrent inflammatory disorder of the central nervous system (CNS) with presumed autoimmune aetiology. MS can be classically defined as a complex, multifactorial, and heterogeneous neuro-immunological disease. Symptoms depend on the anatomical

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locations of demyelinating plaques, though some plaques remain silent without clear measurable symptomatic manifestation. Fatigue and cognitive dysfunction may be poorly correlated to specific locations but can be caused by extensive cerebral distribution. MS is usually manifested by dysfunction of various neurological axes with paresthesia or numbness, motor weakness (particularly in the lower extremities, resulting in walking difficulties), monocular visual disturbances (optic neuritis), incoordination, Diplopia, dizziness, bladder and sexual dysfunction, sensory symptoms and ataxia [1] and vertigo [2].

4. MS clinical subtypes

Four different subtypes of MS are clinically distinguishable: relapsing remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), and progressive relapsing MS (PRMS). RRMS represents 85% of MS cases; it is characterised by unpredictable relapsing episodes, alternating with periods of remission. Moreover, cranial focal areas of inflammation and demyelination can be resolved overtime, as the damage is reversible. PPMS comprises around 10 to 15% of MS cases, in which steady accumulation of neurological disability, mainly progressive myelopathy, appears from disease onset. Some patients develop superimposed relapses. These amount to nearly 5% of MS cases, and are said to display PRMS, which, similarly to PPMS patients, have progressive disability from the onset of symptoms, but with acute attacks or relapses. SPMS represents a stage subsequent to RRMS, wherein patients convert from RRMS to SPMS with time and show progressive neurological decline, either with or without relapses after the initial relapsing remitting pattern. Despite many prognostic indicators for progression that have been well studied, expectations for patients conversing into SPMS remain difficult without a definitive biomarker. A recent study done locally by Alroughani et al. has pointed to few disease progression predictors, of those: patients' age at disease onset ≥ 40, male gender, spinal cord symptoms at disease onset, and ≥3 relapses [3]. The neurological disabilities in SPMS are initially reversible, but intriguingly and for an unknown reason, axonal degeneration occurs with irreversible damages [2,4,5]. The clinical manifestations of MS subtypes may vary between patients, even between those that settle in the same MS clinical subtype. For example, some patients with RRMS may have mild symptoms and low Expanded Disability Status Scale (EDSS) score and have developed the disease over a period of more than 20 years, benign MS; others may progress in few years and even develop to SPMS, malignant MS. Reasons for such variation remain elusive, and long-term clinical results of MS remain challengeable [6].

Neurologists usually assess patient disability by Expanded Disability Status Scale (EDSS). The EDSS was first assigned in 1983 by John F. Kurtzke. The disability is measured in eight functional systems (FS): pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral and others. Score values range from 1.0 to 10.0, with 10.0 equating to death due to MS. Neurologists usually refer EDSS scores of 1.0 to 4.5 to fully ambulatory patients, whereas scores of 5 to 9.5 are assigned to patients with impaired ambulation [7].

5. MS epidemiology

A consideration of MS epidemiology in Arabian Gulf countries must be related to the worldwide number of MS. As for that, the worldwide epidemiology will be discussed and followed with Arabian Gulf epidemiology.

5.1. MS female to male ratio in general

As it is with other autoimmune diseases, affliction with MS shows a female over male preponderance. The ratio of female:male patients varies according to each country. In East Asia, for example, this ratio was found to be 3.0, whereas in the United States it equates to 2.6 [2,8]. MS commonly affects adults in their twenties to fifties, peaking at thirty years of age. Sometimes, symptoms first present before the age of 10 or after 60, and in rare cases, on the eighth decade of one's life [2,8].

5.2. MS incidence and prevalence in general

MS is afflicting more people every day. According to the Atlas of MS for 2013, the number of MS diagnoses has increased from 2.1 million in 2008 to 2.3 million in 2013. Moreover, the global median prevalence of MS has increased from 30 to 33 per 100,000 between 2008 and 2013 [8]. However, those numbers may not reflect the real number of MS patients as some are not yet diagnosed with MS. This could be a consequence of either patients being treated for specific symptoms without exploring the remaining signs of the disease or the difficulty of reaching neurologists.

Ethnicity plays an important role in disease development, seeing that Caucasian populations have 10 times higher prevalence of MS than do African or Asian counterparts. The highest prevalence has been found in North American and European countries, with a prevalence of 140 and 108 per 100,000, respectively; the lowest prevalence, in contrast, has been found in Sub-Saharan Africa and East Asia, at 2.1 and 2.2 per 100,000, respectively [8–11]. Moreover, within the same population the prevalence could vary according to each country. In the European population, Sweden harbours the highest prevalence of MS (189/100,000), whereas Albania shows the lowest prevalence (22/100,000) [8].

Another element impacting on variation in MS prevalence is regional latitude. In South America, for instance, Argentina, a medium-risk country for MS, has a prevalence of about 18/100,000. This is six times higher than is the prevalence recorded for Ecuador (3.2/100,000), a low-risk country for MS [8–12]. Furthermore, in isolated countries, the prevalence of MS could vary between different regions, as some may provide resistance to MS whilst others do not [13].

5.3. MS incidence, prevalence and regional differences in Arabian Gulf countries

Recent data from the last few years have shown increased cases of MS in the Arabian Gulf countries. Reports from the U.A.E, Dubai in specific, indicate an MS prevalence of 54.77/100,000 [95% confidence interval (95% C.I.) = 46.99–62.55] in 2007, with an annual incidence rate of 6.8/100,000 (95% C.I. = 3.8–9.87) between 2000 and 2007. The female:male ratio was 2.85:1 in Dubai's native population and the mean age of onset was 26.66 ± 6.6 years. Patients' main symptoms were related to motor, sensory, cerebellar and ocular manifestations (72.78%, 48.41%, 19.96%, 16.13%, respectively), with EDSS median and mean of 1.5 and 2.38, respectively. Patients were diagnosed with