

# Demographic and disease characteristics of multiple sclerosis in the Southwest Region of Saudi Arabia

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## ABSTRACT

**الأهداف:** توضيح الخصائص الديموغرافية والمرضية الأساسية لمرض التصلب المتعدد في جنوب غرب المملكة العربية السعودية.

**الطريقة:** شملت هذه الدراسة 82 مريضا مسجلا من مرض التصلب العصبي المتعدد، الذين أجريت مقابلات معهم لجمع الخصائص الديموغرافية والمرضية الأساسية. تم استخدام التردد والنسبة المثوية والمتوسط والانحراف المعياري لوصف المعلومات. تم استخدام (مربع كاي) واختبار (فيشر) الدقيق لدراسة الاختلافات بين المرضى الذكور والإناث في فترات الثقة 95%. اعتبرت الاختلافات ذات دلالة إحصائية عند  $p < 0.05$ .

**النتائج:** من بين ما مجموعه 82 مريضا مسجلا، كان هناك 50 من الإناث، مما أسفر عن نسبة من الإناث إلى الذكور تبلغ 1.56:1. كان متوسط عمر تشخيص المرض  $30.50 \pm 9.29$  سنة. ولوحظ وجود فروق ذات دلالة إحصائية بين الذكور والإناث ( $p = 0.003$ , 78.1%) فيما يتعلق بالعمر عند التشخيص. كان متوسط مدة المرض  $4.07 \pm 3.65$  سنة. كان النوع الأكثر شيوعا من المرض نوع RRMS (64.6%). كانت الأعراض البصرية (37.8%) هي الأعراض السائدة الأكثر شيوعا عند التشخيص.

**الخاتمة:** قدمت هذه الدراسة معلومات أساسية عن مرضى التصلب المتعدد في جنوب غرب المملكة العربية السعودية وقدمت معلومات مفيدة حول الاختلافات بين الذكور والإناث في مظهر هذا المرض. ينصح المزيد من الدراسات المستقبلية.

**Objectives:** To study the basic demographic and disease characteristics of multiple sclerosis (MS) in the Southwest Region of the Kingdom of Saudi Arabia.

**Methods:** This is a retrospective study on demographics and risk factors of 82 MS cases registered in the Armed Forces Hospital, Khamis Mushayt, and the Aseer Central Hospital, Abha, Kingdom of Saudi Arabia. The study was conducted from April 2017 to April 2018. Data was gathered through interview questionnaires and review of medical records. Frequencies, percentages, means, and standard deviations (SD) were used for descriptive

statistics. Chi-square and Fisher exact tests were used to investigate differences between male and female patients at 95% confidence intervals (CI). Differences were considered statistically significant at  $p < 0.05$ .

**Results:** Out of the total of 82 patients, 50 were female, yielding a female-to-male ratio of 1.56:1. The mean age at disease diagnosis was  $30.50 \pm 9.29$  years. As compared to females, the proportion of male patients in the younger age group at disease diagnosis was significantly higher (78.1%,  $p = 0.003$ ) than that in the older age group. Mean disease duration was  $4.07 \pm 3.65$  years. The most common variant of the disease was the remitting-relapsing type (64.6%). Optic symptoms (37.8%) were the most common predominant symptom at diagnosis.

**Conclusion:** This study provides the baseline information about patients with MS in the Aseer region in the Kingdom of Saudi Arabia, and offers useful insights into male-female differences in the manifestation of this disease. Further prospective studies are needed.

*Neurosciences 2018; Vol. 23 (4): 320-325  
doi: 10.17712/nsj.2018.4.20180235*

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*Received 5th June 2018. Accepted 8th August 2018.*

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Multiple sclerosis (MS) is one of the world's most common neurological disorders. It affects millions of people worldwide, and the number of MS diagnoses is increasing each year.<sup>1</sup> Looking at the

regional distribution, Middle Eastern and North African countries are located in a low-moderate risk zone for MS based on the 2013 MS Atlas.<sup>1</sup> However, recent studies suggest a moderate-high prevalence in areas within this region, with an increase in the incidence and prevalence especially among women.<sup>2-4</sup>

According to a recent review, there is a wide variation in the reported prevalence across countries in the region. Prevalence has been reported ranging from 5.1 per 100,000 in Israel to 240 in Cyprus. No recent prevalence studies could be identified in several Middle Eastern countries such as Kingdom of Saudi Arabia, Iraq, Bahrain, Oman and Yemen.<sup>5</sup> In the Kingdom of Saudi Arabia, there is no national study that has reported the prevalence of MS, however, a hospital-based study from Riyadh revealed a prevalence rate of 40 cases per 100,000 of the population.<sup>6</sup>

Global survey findings have reinforced that females are affected with MS more commonly than males, with a female-male ratio around 2:1.<sup>1</sup> Multiple sclerosis is an adult-onset disease, with a mean age at onset of above 20 years, but 3-10% of people with MS are diagnosed under the age of 16.<sup>7,8</sup> It most often hits people at the most productive years of their lives, at a time when they are building their career, finding a life partner, or having children. Consequently, MS impacts the social and economic wellbeing of the individual as well as their families. Clinically, there are 4 types of MS, with relapsing-relapsing MS (RRMS) being the most commonly diagnosed form. The world atlas of MS reports that 85% of people have the relapsing-relapsing form of MS.<sup>1,9</sup> The world atlas reports no variation in the prevalence of the different types of MS at diagnosis between regions or income groups.<sup>1</sup> Sensory and motor symptoms are the most commonly presenting symptoms.<sup>10</sup> The most important DMTs for MS are the disease-modifying therapies (DMT) that are interferon-based.<sup>11</sup>

Extensive literature search over internet revealed that research on MS in Saudi Arabia has been limited. Single-hospital based studies covering the capital city Riyadh are the predominant source of information on MS epidemiology in the Kingdom of Saudi Arabia. A study conducted in Riyadh, Kingdom of Saudi Arabia, reported a prevalence of 25 cases per 100,000 of the population, with a female-male ratio of 1.34:1 and a mean age at onset of  $27.7 \pm 7.8$ .<sup>12</sup> However, this study

was conducted about two decades back. As regards the Southwest region of Saudi Arabia, there is lack of studies describing the demographics and disease characteristics or addressing the risk factors of MS. Hence, this study was designed to address this existing gap. The current paper addresses the primary objective of this study, that is, to characterize patients with MS in the southwest region of Saudi Arabia in terms of demographics and clinical features. The risk factors of MS revealed in this study population will be described elsewhere.

**Methods.** This paper presents preliminary data from a case-control study focusing on cases of MS registered in the 2 major government-run tertiary hospitals in the Aseer region, Southwest Kingdom of Saudi Arabia, from April 2017 to April 2018. The Armed Forces Hospital, Southern Region (AFHSR), Khamis Mushayt, Kingdom of Saudi Arabia runs under the aegis of the Saudi National Guard, and the Aseer Central Hospital (ACH), Abha, Kingdom of Saudi Arabia, runs under the Ministry of Health of Saudi Arabia. All medical services in these centers are free of cost for Saudi citizens. These 2 hospitals are the only referral centers for MS cases in this region. We identified 58 registered cases of MS at the AFHSR neurology clinic and 47 cases at ACH who matched the inclusion criteria. A total of 82 cases were thus enrolled in the current study. For the purpose of this study, cases that matched the criteria were defined as the patients aged 18 years or older, diagnosed previously for MS or clinically isolated syndrome (CIS) by a neurologist, and attending the neurology clinic of the AFHSR or the ACH regularly for last one year. Patients aged <18 or not meeting the other inclusion criteria were excluded from the study. Data was collected from patients by using an interview questionnaire. The interview took place in the Neurology Clinics on the patients' scheduled day of attendance. Medical records were used to gather any missing responses or data that the patient could not provide (namely, drug names, type of disease). Ethics approval for the study was obtained from the Institutional Ethics Committees of both hospitals. In accordance with the principles of Helsinki declaration, all participants were given detailed information about the study before enrolment. Anonymity and confidentiality of information was assured and consent was obtained from all participants.

A structured questionnaire was constructed after thorough review of previous similar research studies on MS and its risk factors.<sup>13-16</sup> Content validity was established by a team of experts in the neurology department of the concerned hospitals. The questionnaire was designed to extract detailed information related

**Disclosure.** Authors have no conflict of interests, and the work was not supported or funded by any drug company.

to the following areas: (A) Demographic and baseline characteristics: age, gender, education, occupation, residence, monthly income, body mass index, family history of MS. (B) Disease characteristics: age at disease diagnosis, disease type, signs and symptoms at onset, disease duration, current medication. The study was conducted from April 2017 to April 2018. Data was analyzed using SPSS version 23 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to illustrate the socio-demographic and disease characteristics of the cases. For demographic and disease description, frequencies, percentages, means, SD, and ranges were calculated. To study differences between male and female patients, univariate analysis using chi-square tests and Fisher's exact test was used. The odds ratio (OR) associated with each potential risk factor and the 95% CI were calculated.

**Results.** This study identified 82 patients with MS registered for treatment in 2 major hospitals of the covered region. With age ranging from 18-56 years, the mean age of the cases was  $34.57 \pm 9.48$  years. There were 50 female patients and 32 male patients, yielding a female-male OR of 1.56:1. The basic information of the patients is described in Table 1.

Table 2 presents the demographic characteristics of the patients. Mean age at diagnosis was  $30.50 \pm 9.29$  years. Age at disease diagnosis was reported as below 18 years in 2 cases, which amounts to 2.4% of all cases. Both of these cases were male patients. The minimum age at diagnosis was 10 years. The proportion of male patients in the younger age group (namely, age at disease diagnosis) was significantly higher (78.1%,  $p=0.003$ ) than that in the older age group; this was however not true for female patients. A significantly higher proportion of male patients (78.1%,  $p=0.003$ ) had a younger age of onset as compared to female patients. The disease duration ranged from less than 1-11 years. The mean disease duration was  $4.07 \pm 3.65$  years. Most of the patients, both male and female, had a disease duration between 1-5 years. There was no significant difference between male and female patients regarding disease duration, type of disease, and predominant symptom at disease onset. Almost two third of the cases (64.63%) were of the relapsing-remitting type, and 10 cases represented clinically isolated syndrome (CIS). The predominant symptoms at disease onset could be optic, sensory, cerebellar, brain stem, and spinal cord symptoms. The most common presentations were blurred vision, numbness and tingling, bladder/bowel problems, difficulty in balance, and trouble in walking. Treatment information was obtained from the medical

records. The disease-modifying drugs that were most commonly used were interferon beta-1a and interferon beta-1b (Rebif) (Table 3).

**Discussion.** This study describes the epidemiological data on MS originating from the Aseer region of the Kingdom of Saudi Arabia. There is an increase in the prevalence of MS in the Gulf region, and this trend has been explained by an increase in the prevalence of MS worldwide, genetic susceptibility, an increase in public awareness, the practice of consanguineous marriages, or the rapid rate of change in socioeconomic life.<sup>1,17</sup> The health service-related factors that could influence the prevalence of MS are the readily available modern diagnostic techniques (such as magnetic resonance imaging (MRI) and localized facilities made available to the general public, as well as improvements in health care systems over the past few decades. Despite these factors, we found a low number of cases in the covered region. Although our study did not aim to estimate the prevalence of MS, we did make a crude estimate, considering that the hospitals where our study was based are the only 2 tertiary hospitals in the region, and the only referral centers for neurological diseases in Southern Saudi Arabia. According to the national demography survey of 2016, the Saudi population in the Aseer region, Kingdom of Saudi Arabia, is approximately 17,19950.<sup>18</sup> With 82 cases at the 2 centers, a crude prevalence of 4.7/100,000 is obtained. This is low compared to previously reported rates from the Kingdom of Saudi Arabia.<sup>6,12,17</sup> This low rate could be due to gaps in knowledge regarding the signs and symptoms of MS. It could also point towards poor referral practices in the region. Another reason could be the wide topographical differences in the Aseer region, Kingdom of Saudi Arabia. Some areas of this region are in the plains, and thus their residents have easier access to medical facilities in larger cities in other provinces. In contrast the hilly areas of the region that are sparsely populated may be catered to by these 2 hospitals included in the study.

The average age of the development of MS has been estimated to be 25-33 years.<sup>1</sup> This study found that the age at disease diagnosis is similar to that reported from other countries, particularly the region.<sup>1,3,5,6</sup> Our study also confirmed the female preponderance in MS, as has been found in other studies.<sup>1,19</sup> The female-to-male ratio of 1.56:1 found in this study is similar to that reported in a nationwide study from Qatar.<sup>3</sup> In our study, we found a family history of MS in 4.8% of our patients, which is much lower than what other regional studies have found.<sup>3</sup> In view of similarities in social

**Table 1** - Baseline information of multiple sclerosis patients of both genders.

Characteristic	Male n (%)	Female n (%)	OR (CI)	P-value
<i>Age</i>				
18- 30 years	21 (65.6)	20 (40.0)	2.86 (1.13-7.20)	0.02
More than 30 years	11 (34.4)	30 (60.0)		
<i>Marital status</i>				
Married	20 (62.5)	38 (76)	0.5 (0.20-1.3)	0.22
Single	12 (37.5)	12 (24)		
<i>Education</i>				
Illiterate	0 (0.0)	14 (28.0)	0.004	
School	18 (56.2)	23 (46.0)		
University	14 (43.8)	13 (26.0)		
<i>Occupation</i>				
Non-working	2 (6.3)	43 (86.0)	<0.001	
Military	13 (40.5)	0		
Other jobs	17 (53.2)	7 (14.0)		
<i>Residence</i>				
Urban	26 (81.2)	35 (70.0)	1.85 (0.63-5.43)	0.30
Rural	6 (18.8)	15 (30.0)		
<i>Income /month</i>				
<5000 SR	0 (0.0)	11 (22.0)	0.001	
5000-10000SR	14 (43.8)	30 (60.0)		
10000-20000SR	13 (40.6)	8 (16.0)		
≥20000 SR	5 (15.6)	1 (2.0)		
<i>BMI</i>				
Normal	18 (56.2)	21 (42.0)	0.02	
Overweight	14 (43.8)	19 (38.0)		
Obese	0 (0.0)	10 (20.0)		
<i>Family history of MS</i>				
Yes	2 (6.3)	2 (4)	1.61 (0.214-11.96)	0.64
No	30 (93.7)	48 (96)		

OR - Odds ratio, CI - confidence interval, SR - Saudi Riyals, BMI - body mass index, MS - multiple sclerosis.

**Table 2** - Demographic characteristics of patients with multiple sclerosis.

Characteristic	Ratio	Mean±SD	Range
<i>Gender Ratio</i>			
Female	1.56		
Male	1		
<i>Current age in years</i>			
Total MS patients		34.57±9.48	18-56
<i>Age at diagnosis</i>			
Total MS patients		30.50±9.29	10-54
Male		26.90±7.7	10-44
Female		32.8±9.8	18-56
Disease duration (years)		4.07±3.65	<1-11

SD - standard deviation, MS - multiple sclerosis

structure, culture, and tradition in the Arab gulf, the likely reason for this finding could be underreporting by the participants.

The pattern of disease type in the current study, with the majority of cases being of the relapsing-remitting

type, resonates with that from other studies.<sup>3-5</sup> A primary progressive course was rare in both male and female patients. Another important finding of this study is the frequency of CIS in our patients (12.19%), which is similar to that reported in Qatar.<sup>3</sup> The most common symptom at presentation was found to be optic manifestations, followed by cerebellar and spinal symptoms. In this study we have only focused on the predominant symptom at diagnosis, although multiple symptoms were experienced by the patients.

In this study, the incidence of first symptoms under the age of 18 years was 2.2%, which is consistent with previous reports.<sup>8</sup> Our estimate of the proportion of patients with first symptoms under the age of 18 years provides, at the least, a rough estimate of the actual prevalence of early onset MS in this region, because the centers where the study was conducted are the prominent tertiary care centers in this area. Pediatric-onset MS is not a well-recognized disease, which potentially results

**Table 3** - Disease characteristics of multiple sclerosis in the study group.

Characteristic	Males n (%)	Females n (%)	P-value
<i>Age at disease diagnosis</i>			
Less than 18	2 (6.3)	0 (0.0)	0.003
18-30years	25 (78.1)	25 (50.0)	
More than 30 years	5 (15.6)	25 (50.0)	
<i>Duration of disease</i>			
Less than 1 year	4 (12.5)	9 (18.0)	0.89
1-5years	17 (53.1)	25 (50.0)	
5-10 years	9 (28.1)	12 (24.0)	
More than 10 years	2 (6.3)	4 (8.0)	
<i>Type of disease</i>			
RRMS	22 (68.8)	31 (62.0)	0.889
RPMS	4 (12.5)	6 (12.0)	
SPMS	3 (9.4)	5 (10.0)	
PPMS	0	1 (2.0)	
CIS	3 (9.4)	7 (14.0)	
<i>Symptoms at disease onset</i>			
Optic	10 (31.3)	21 (42.0)	0.774
Spinal cord	9 (28.1)	11 (22.0)	
Cerebellar	8 (25.0)	10 (20.0)	
Sensory	5 (15.6)	7 (14.0)	
Brain stem	0 (0.0)	1 (2.0)	
<i>Medication Used</i>			
Betaferon (interferon beta-1b)	19 (59.3)	19 (36.0)	0.25
Rebif (interferon beta 1-a)	11 (34.4)	26 (52.0)	
Rebif+beta	2 (6.3)	2 (4.0)	
Rebif+Vit. D	0	2 (4.0)	
Tecfidera	0	1 (2.0)	

RRMS - relapsing remitting multiple sclerosis, RPMS - relapsing progressive multiple sclerosis, SPMS - secondary progressive multiple sclerosis, PPMS - primary progressive multiple sclerosis, CIS - clinically isolated syndrome.

in delayed diagnosis. In addition, not all children with MS may be referred to specialized care centers.

**Limitations and strengths.** One of the limitations of this study may be an underestimation of the number of patients with MS, due to the inability of some of these patients to attend the regional centers. The accuracy of the recall and record of date and nature of first-symptom onset is another limitation in our study, common to studies with such a retrospective design. Prospective studies with concurrent neurological examinations or those using additional validating methods such as MRI may enhance the accuracy of these findings. Multiple sclerosis has long-term physical and cognitive effects; although this was not the focus of our present study, future studies may be able to address long-term physical and cognitive outcomes in these populations. Despite the limitations of our sample, this study derives its strength from the fact that it offers the demographic and disease characteristics of people with MS in this region of the Kingdom of Saudi Arabia. It offers unique insights into gender differences

in how MS manifests. These results may help to gauge the prevalence and demographic characteristics of MS in the country and, thus, may assist in the effective targeting of resources to identify and treat individuals with MS. Increased awareness on MS will hopefully enhance care and long-term follow-up management of these patients. These findings are expected to stimulate additional research studies that can help us confirm, understand, and better explain the current findings and their implications for MS care. Prospective studies using standardized diagnostic criteria and standardized follow-ups with frequent MRI assessments are thus strongly recommended.

In conclusion, this study provided the baseline information of multiple sclerosis patients in Aseer region, Kingdom of Saudi Arabia, and offered useful insights into differences in the manifestation of this disease across genders.

**Acknowledgment.** *The authors would like to thank the staff of Neurology Department, Armed Forces Hospital, Khamis Mushayt and*

*Aseer Central Hospital, Abha, Kingdom of Saudi Arabia for facilitating access to patients and records. We would like to thank Editage english editing services (www.editage.com) for English language editing of this manuscript.*

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