CLINICAL & BASIC RESEARCH

Incidence of Optic Neuritis among Omani Patients with Multiple Sclerosis at the Sultan Qaboos University Hospital, Muscat, Oman

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abstract: *Objectives:* Multiple sclerosis (MS) is a chronic, multifaceted, heterogeneous autoimmune disease, with optic neuritis (ON) being a common early manifestation among those with MS. This study aimed to estimate the incidence of ON among Omani patients with MS. *Methods:* This retrospective cross-sectional study included all Omani patients diagnosed with MS at the Sultan Qaboos University Hospital, Muscat, Oman, between January 1991 and December 2019. The data were collected from the neurology registry and electronic medical records and analysed descriptively using univariant and multivariant statistical techniques. *Results:* Out of the 185 patients diagnosed with MS during the study period, 170 were included in the analysis. The male-to-female ratio was 1:2 and the mean age was 28 years. The incidence of ON in the population was 28.8%, with 83.7% of ON patients presenting with relapse-remitting MS (RRMS). Overall, 28.6% of patients presented with O N as an initial manifestation of MS, whereas 42.8% developed ON at a later stage. Most patients (49.4%) were from higher-latitude regions of Oman such as Muscat and Al Batinah. *Conclusions:* The incidence of both MS and ON increased over the study period. While the overall incidence was low in comparison with Western data, it was similar to the rates reported elsewhere in the Arabian Peninsula. Overall, ON was the most common manifestation of MS in the cohort, with younger female patients more frequently presenting with both MS and ON. A significant association was found between the RRMS subtype and ON presentation.

Keywords: Demyelinating Diseases; Optic Neuritis; Multiple Sclerosis; Relapsing-Remitting Multiple Sclerosis; Incidence; Epidemiology; Oman.

Advances in Knowledge
- *The overall incidence of optic neuritis (ON) among multiple sclerosis (MS) patients at a tertiary hospital in Oman over 29 years was 28.8%. While this is lower than the rates reported elsewhere globally, it is consistent with the findings of the other Arabian Gulf countries.*
- *Over the past decade, the incidence of both MS and ON showed a marked increase, likely as a result of more stringent diagnostic criteria. In particular, younger female patients were found to be more likely to present with both MS and ON, and a significant association was found between the relapse-remitting MS subtype and ON presentation.*
- *The number of cases originating from the Muscat and Al Batinah regions of Oman supports the hypothesis that latitude affects MS incidence.*

Application to Patient Care
- *As ON is a common early manifestation of MS in Omani patients, ophthalmologists and family physicians should ensure that they refer patients presenting with symptoms of vision loss for neurological assessment, especially young female patients who are at greater risk of developing both ON and MS.*
- *Further, considering that the incidence of both MS and ON increased notably over the study period, there is a need for enhanced suspicion of MS in the differential diagnosis process. Additionally, a national MS-specific registry should be established to more accurately monitor the number of cases recorded every year.*

Multiple sclerosis (ms) is a chronic, multifaceted, complicated and heterogeneous autoimmune disease that results in central nervous system inflammation, demyelination, gliosis and axonal degeneration.[1] Neurological deficits are common due to interrupted communication between neurons in the brain and the spinal cord as a result of the demyelination process. Clinically, MS takes a variety of forms that can be distinguished through disease activity and patterns of relapse and remission.[1] According to current international classifications, the following four MS subtypes are recognised: relapsing-remitting MS (RRMS), primary progressive MS, secondary progressive MS (SPMS) and progressive-relapsing MS.[2] Although the primary cause of MS is still unknown, both environmental and genetic factors are believed to play a role in triggering the disease. The epidemiology of MS varies according to demographic characteristics and latitude, a well-established risk factor. In addition, ethnicity/race has also been found to influence the global distribution of MS.[3]

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Optic neuritis (ON) is an acute, inflammatory and demyelinating disease of the optic nerve resulting from an autoimmune process, characterised by unilateral, painful and rapid loss of vision.[4,5] Typically, ON is recognised as an early clinical manifestation of MS in 20% of patients, but this condition can occur over the course of the disease in up to 50% of all MS patients.[6] In particular, female patients between the ages of 18 and 45 years have demonstrated an increased tendency towards developing ON compared to other MS patients.[7] Thus, the present study aimed to estimate the incidence of ON among Omani patients diagnosed with MS at a tertiary hospital over 29 years and compare the findings to internationally published data.

Methods

This retrospective cross-sectional study was conducted at the Sultan Qaboos University Hospital (SQUH), a tertiary hospital in Muscat, Oman, from January 1991 until December 2019. This study included all Omani patients at SQUH with confirmed MS diagnoses according to the 2017 McDonald diagnostic criteria.[8] The patients without confirmed MS diagnoses were excluded from the study. The data were collected from the SQUH neuro-ophthalmology clinic registry, the patients' electronic medical records and the hospital information system database.

The electronic medical records were established at SQUH in 2006; as such, the data pertaining to
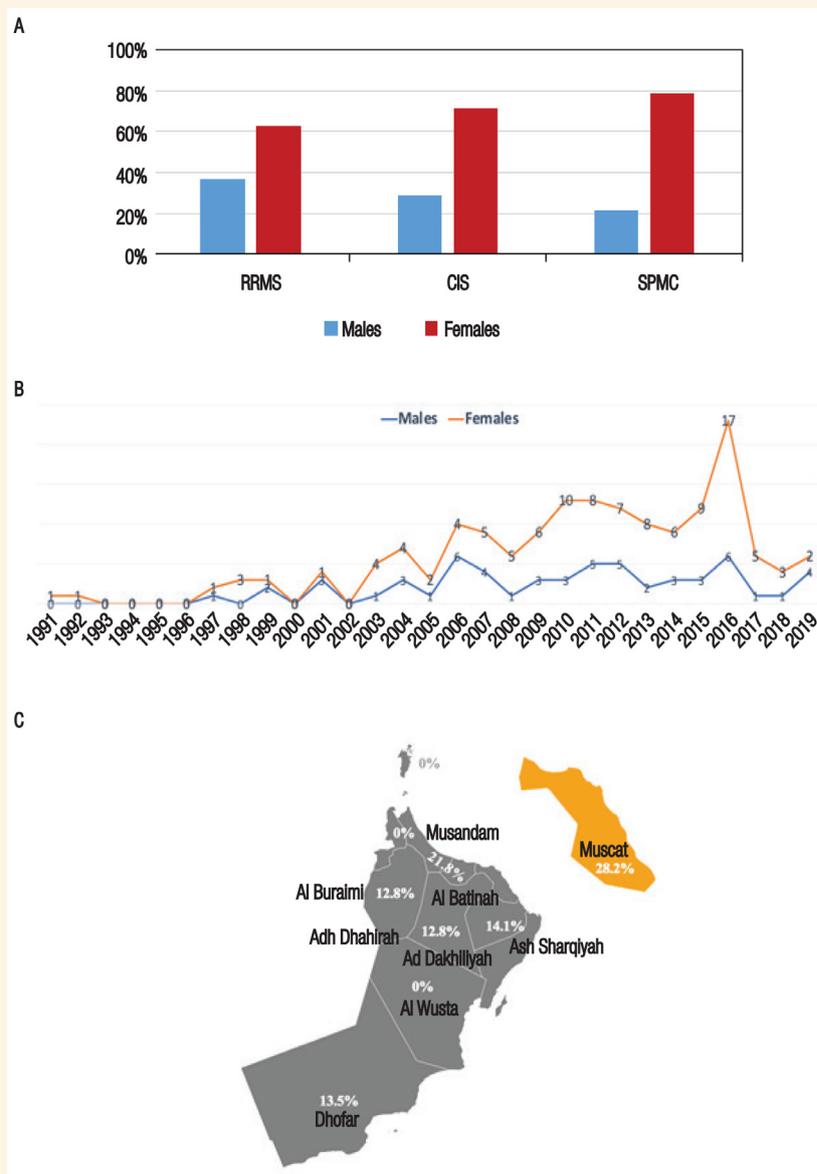
Figure 1: Distribution of multiple sclerosis cases according to gender (**A**) by subtype, (**B**) over time at the Sultan Qaboos University Hospital, Muscat, Oman, from 1991 to 2019 (N = 170) and (**C**) among governorates.
RRMS = relapse-remitting multiple sclerosis; CIS = clinically isolated syndrome; SPMS = secondary progressive multiple sclerosis.

Table 1: Regional distribution of multiple sclerosis cases according to gender at the Sultan Qaboos University Hospital, Muscat, Oman, from 1991–2019 (N = 170)

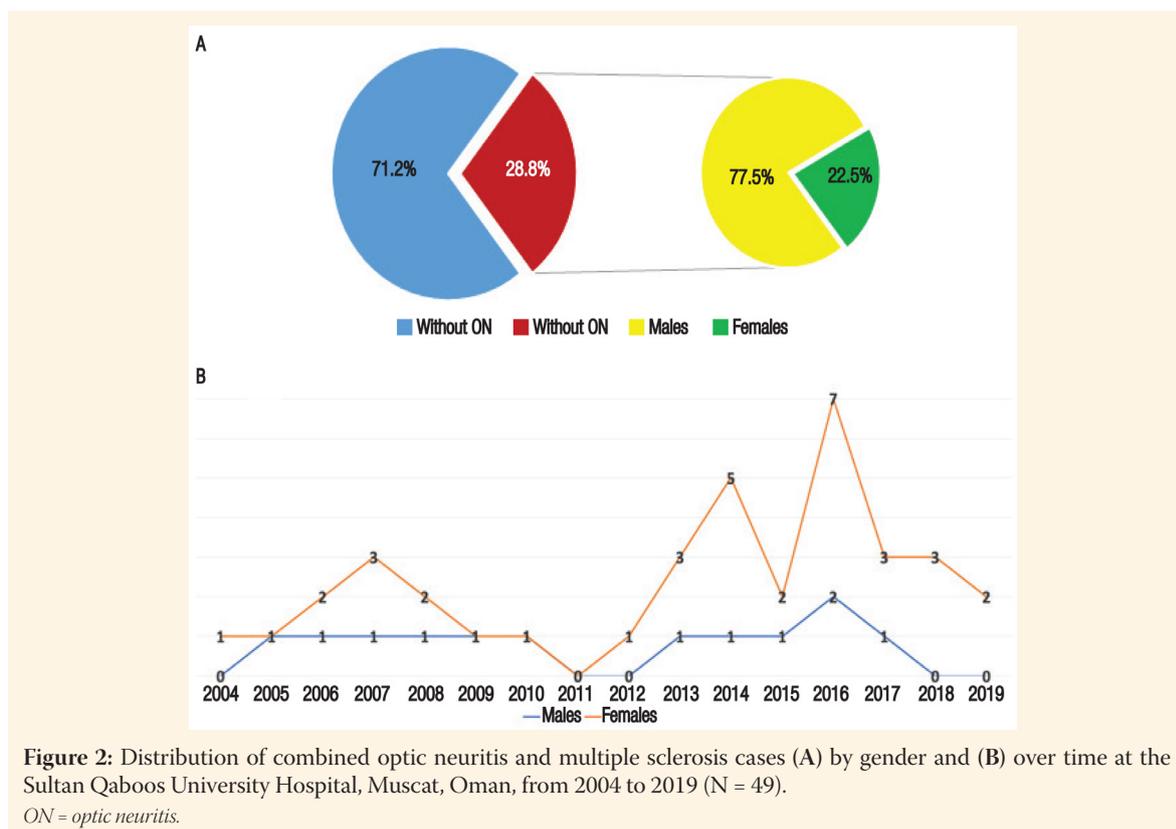| Governorate	n (%)		
	Gender		
	Male	Female	Total
Muscat	16 (33.3)	32 (66.7)	48 (28.2)
Al Batinah (North and South)	7 (19.4)	29 (80.6)	36 (21.2)
Dhofar	12 (48)	13 (52)	25 (14.7)
Ash Sharqiyah (North and South)	8 (33.3)	16 (66.7)	24 (14.1)
Ad Dhahirah	10 (47.6)	11 (52.4)	21 (12.4)
Ad Dhakhiliyah	6 (37.5)	10 (62.5)	16 (9.4)
Musandam	0 (0)	0 (0)	0 (0)
Al Buraimi	0 (0)	0 (0)	0 (0)
Al Wusta	0 (0)	0 (0)	0 (0)
Total	**59 (34.7)**	**111 (65.3)**	**170 (100)**

patients diagnosed with MS before 2006 were retrieved from the hospital's neurology clinic registry, whereas the data from 2006 onwards were collected from the patients' electronic medical records (TrakCare®, InterSystems Corp., Cambridge, Massachusetts, USA). The information recorded included sociodemographic characteristics (i.e. age, gender and location of residence), year of diagnosis, subtype of MS and the presence of ON. Further, additional data were collected and reported for patients with ON, including age at presentation, number of attacks during the follow-up period and progression of the disease. The patients were directly contacted to confirm their location of residence to estimate the geographic distribution of the disease.

Afterwards, the collected data were analysed using the Statistical Package for the Social Sciences (SPSS), Version 23.0 (IBM Corp., Armonk, New York, USA). Ethical approval for this study was obtained from the Medical Research & Ethics Committee of the College of Medicine and Health Sciences at Sultan Qaboos University (MREC #1951). Furthermore, additional authorisation was obtained from the relevant hospital authorities to access the patients' electronic medical records and the hospital information system database.

Results

A total of 185 patients were diagnosed with MS at SQUH between January 1991 and December 2019, out of which 15 patients (8.1%) were excluded due to diagnostic uncertainty, resulting in 170 patients (85.4%) being ultimately included in the analysis. Overall, 59 (34.7%) patients were male and 111 (65.3%) were female, with a male-to-female ratio of 1:2 and

Figure 2: Distribution of combined optic neuritis and multiple sclerosis cases **(A)** by gender and **(B)** over time at the Sultan Qaboos University Hospital, Muscat, Oman, from 2004 to 2019 (N = 49).
ON = optic neuritis.

Table 2: Initial presentation of combined optic neuritis and multiple sclerosis cases according to gender at the Sultan Qaboos University Hospital, Muscat, Oman, from 1991 to 2019 (N = 49)

Gender	n (%)			
	Initial presentation			
	ON	Other MS manifestations	Both	Total
Male	2 (18.2)	3 (27.4)	6 (54.5)	11 (22.4)
Female	12 (31.6)	18 (47.4)	8 (21.1)	38 (77.6)
Total	14 (28.6)	21 (42.8)	14 (28.6)	49 (100)

ON = optic neuritis; MS = multiple sclerosis.

Table 3: Incidence of combined optic neuritis and multiple sclerosis cases according to gender and multiple sclerosis subtype at the Sultan Qaboos University Hospital, Muscat, Oman, from 2004 to 2019 (N = 49)

Gender	n (%)			
	MS subtype			
	RRMS	CIS	SPMS	Total
Male	10 (90.9)	1 (9.1)	0 (0)	11 (22.4)
Female	31 (81.6)	4 (10.5)	3 (7.9)	38 (77.6)
Total	41 (83.7)	5 (10.2)	3 (6.1)	49 (100)

MS = multiple sclerosis; RRMS = relapse-remitting multiple sclerosis; CIS = clinically isolated syndrome; SPMS = secondary progressive multiple sclerosis.

a mean age of 28 years. The youngest patient began showing signs of MS at the age of nine years, whereas the eldest was 60 years old. In terms of subtype, most patients had RRMS (n = 135, 79.4%), followed by clinically isolated syndrome (CIS; n = 21, 12.4%) and SPMS (n = 14, 8.2%). Other MS subtypes were not detected or diagnosed during the study period.

Out of the 135 patients with RRMS, 50 (37%) were male and 85 (63%) were female, while out of the 21 patients with CIS, six (28.6%) were male and 15 (71.4%) were female. Finally, out of the 14 patients with SPMS, three (21.4%) were male and 11 (78.6%) were female [Figure 1A]. The association between gender and MS subtype was not found to be significant (P >0.050).

The first documented case of MS in the neurology registry was recorded in 1991. Subsequently, the number of MS diagnoses per year began to increase, particularly from 2010 onwards. The greatest number of cases per year was recorded in 2016 (n = 23), comprising six (26.1%) male and 17 (73.9%) female patients [Figure 1B].

In terms of geographic distribution, the majority of MS patients originated from Muscat (n = 48, 28.2%), with 16 (33.3%) male and 32 (66.7%) female patients [Figure 1C]. This was followed by Al Batinah (n = 36, 21.2%), with seven (19.4%) male and 29 (80.6%) female patients. The region where the fewest cases were reported was Ad Dhakhiliyah, with 16 (9.4%) patients in total, out of which six (37.5%) were male and 10 (62.5%) were female. No cases were reported from the three governorates of Oman (i.e. Musandam, Al Buraimi and Al Wusta) [Table 1]. Furthermore, the association between disease incidence and areas of high latitude was not found to be significant (P >0.050).

Over the 29-year study period, 49 MS patients developed ON, resulting in an incidence of 28.8%; out of these, 11 (22.5%) patients were male and 38 (77.5%) were female [Figure 2A]. The first case of ON at SQUH appeared in the registry in 2004, with the number of diagnoses per year increasing considerably from 2012 onwards. The highest number of cases was reported in 2016 for male patients (n = 2) and in 2017 for female patients (n = 7) [Figure 2B]. Overall, 28.6% of patients with both MS and ON presented with ON as an initial presentation of MS, whereas 42.8% developed ON over the course of the disease [Table 2]. The association between gender and the development of ON was not found to be significant (P = 0.050), although a significant association was found between ON presentation and MS subtype (P <0.050), with the majority of ON cases occurring in patients with the RRMS subtype (83.7%) [Table 3].

Discussion

The incidence of ON among MS patients at SQUH over the 29-year study period was 28.8%, which is lower than the rates reported elsewhere globally. According to a prospective study conducted in India, the incidence of ON among MS patients was 70% (n = 20/30).[9] Another study reported an incidence of 50% at a tertiary care unit in Turkey, with ON often reported as an initial presenting feature of MS.[10] The low incidence rate of ON noted in the current study could be due to several reasons, including methodological differences in sample size and study design, as well as genetic variations between different populations.

However, it is also possible that this finding is due to the generally low incidence of MS in Oman, given the previously reported prevalence rate of 4 in 100,000 individuals.[11] Other Arabian Gulf countries have reported similarly low rates of MS, although there are methodological concerns to such studies that may hinder definitive conclusions regarding regional prevalence.[12] A more recent study indicated that the rate of MS in Oman may be much higher

than previously believed, with a crude estimated prevalence of 15.9 per 100,000 individuals, designating the country as a medium-risk zone.[13]

In the present study, the incidence of both MS and ON at SQUH was found to increase considerably over time, beginning from 2010–2012 onwards. This increase over the past decade may be due to the application of the McDonald criteria to support the diagnosis of suspected cases of MS at SQUH, resulting in fewer cases going undiagnosed.[8] In the present study, ON represented the first clinical manifestation of MS in 28.6% of the patients who developed ON. This finding is in parallel with other studies conducted elsewhere globally. For instance, in Bosnia and Herzegovina, 10 (11.2%) out of 89 MS patients demonstrated clinical signs of ON as the first sign of disease, a finding that was statistically significant compared to other disease manifestations (P = 0.01).[7] In addition, a previous review of the literature suggested that ON is the initial presentation in approximately 20% of MS patients.[14]

Overall, 79.4% of MS patients in the present study were reported to have the RRMS subtype, whereas the remaining 12.4% and 8.2% of patients were reported to have CIS and SPMS, respectively. A retrospective study conducted in the United Arab Emirates (UAE) reported a comparable distribution of these subtypes among Emirati MS patients (i.e. 77.8%, 12.3% and 8.2%, respectively).[15] Moreover, there was a significant association between the RRMS subtype and ON presentation in the current Omani cohort, with 83.7% of patients with both ON and MS having the RRMS subtype. This result was found to be slightly higher in comparison to that reported by other research, which found that 70% of MS patients with ON demonstrated relapsing-remitting disease activity.[16] In addition, in the present study, female patients were found to be more frequently diagnosed with MS compared to male patients (i.e. at a ratio of 1.9). The gender ratio of MS cases varies depending on country and region, with higher ratios of 2.6 and 3.0 reported in the USA and East Asia, respectively.[17] In turn, the female preponderance of MS is lower in Arabian Gulf countries, with ratios of 1.8 and 1.3 reported in Kuwait and Saudi Arabia, respectively.[17,18] In the present study, 34.2% of female patients with MS developed ON compared to 18.6% of male patients, with a female-to-male ratio of 3.5. The female predominance of ON is well-established in the existing literature at a ratio of 3 or higher.[19]

Furthermore, in the present study, the mean age of the enrolled population was 28 years, with similar mean ages observed for both males and females at 29 and 28 years, respectively. Corresponding findings have been reported from Iran (mean age = 25 years). Conversely, MS patients in the UAE are reportedly somewhat older (mean age = 34 years).[15,20] In regards to the ON patients in the present study, the mean age was found to be 26 years, with a mean age of 24 and 27 years for male and female patients, respectively. Overall, the majority of ON patients (59.2%) were between 21 and 30 years of age. This finding was lower in comparison with the data originating from Hong Kong that showed the mean age of ON patients to be 40 years; however, 90% of MS patients presenting with ON in Bosnia and Herzegovina were found to be between 18 and 30 years of age.[7,21] Such results suggest that the demographic epidemiology for MS-associated ON may be similar to that of MS in general.

Latitude is a well-established factor affecting the incidence of both MS and ON; for instance, previous research has indicated that the incidence of MS in Argentina is six times higher than that recorded in Ecuador.[22] It is, therefore, unsurprising that Oman, a country located in the East Mediterranean region, should demonstrate a lower incidence of MS compared with Western countries of higher latitude.[23] Moreover, according to the geographical distribution of patients in the present study, certain regions of Oman at higher latitudes, such as Muscat and Al Batinah, accounted for the greatest number of patients, with fewer cases originating from lower-latitude regions such as Dhofar, Ash Sharqiyah, Ad Dhakhiliyah, Ad Dhahirah and Al Wusta.

Nonetheless, the association between latitude and disease incidence was not statistically significant in the present study, which may have been due to several reasons. First, no cases were reported from the highest-latitude areas in Oman (Musandam and Al Buraimi). Second, such associations are difficult to ascertain in a single country that does not span a considerable latitude or longitude. Finally, as the capital city of Oman, Muscat is home to a large proportion of the national population, followed by the surrounding region of Al Batinah, which may account for the large number of cases from these areas. However, it was found that male patients more frequently originated from areas of lower latitude such as Dhofar compared with other governorates. The idea that the gender ratio for MS may vary with changes in latitude might be another possible explanation for these findings.[24]

The interpretation of this study's findings is contingent upon certain limitations. For instance, generalisation of results is difficult as the study was conducted using a retrospective cross-sectional design and was limited to a single institution. While SQUH is a tertiary care institution that accepts referrals from all over the country, the catchment area remains limited; moreover, the presence of other tertiary institutions in Muscat that might also receive MS and ON patients

prohibits the generalisation of the incidence of these conditions to the whole of Oman. Additionally, as a partially heritable disease, genetic factors play a considerable role in the epidemiology and incidence of MS. Unfortunately, data concerning such genetic factors were missing for the majority of patients in the present study. Therefore, further prospective research is recommended to counteract these limitations using a larger sample size.

Conclusion

Over the 29-year study period, the incidence of ON among MS patients at SQUH was low (28.8%), which was in keeping with other Arabian Gulf countries. Nonetheless, ON remained the most common early manifestation of MS among the enrolled patients, with almost one-third of MS patients presenting with ON as their first symptom. Moreover, the incidence of both MS and ON appeared to increase over time, particularly over the last decade, thus supporting the need for further research on this topic. Finally, more MS cases were reported from higher-latitude areas of Oman, a result in line with previous research supporting latitude as a well-established risk factor for MS.

Further research is needed that can focus on more in-depth analysis, such as comparing the difference between the initial presentation (ON versus other MS) and gender, governorate and year and whether sub-types (RRMS versus other sub-types) are significantly different by gender, governorate and year.

AUTHORS' CONTRIBUTION

AM designed the study, and FK and BS collected the data. FK performed the statistical analysis, while FK and BS drafted the manuscript. Additionally, AM critically reviewed and revised the manuscript. All authors approved the final version of the manuscript.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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