International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2013): 6.14 | Impact Factor (2014): 5.611

The Pattern of First Multiple Sclerosis Presentation in Patients Attending King Khalid University Hospital (2000-2012)

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Abstract: ***Background: Multiple sclerosis is an autoimmune disease characterized by destruction of myelin in the central nervous system. In Saudi Arabia, there are no recent studies describing the pattern of the disease. Therefore, this study aims to describe the epidemiological pattern of multiple sclerosis and the most frequently encountered clinical manifestations of the disease. Methodology: All data were extracted by using questionnaires completed through reviewing all patients' medical record of all cases of MS that were admitted to KKUH between 2000 and 2012. Mean, standard deviation and Chi square were used for results presentation. Results: Among all patients, females were much more affected than males as they comprised 75.5% while males were 24.5%.The majority of patients were in their twenties and the mean age was 27.16 ±7.74 years. Most of the patients presented complaining of limb weakness (69.6%) followed by numbness (56.9%) then visual manifestations (47.5%). Conclusion: The majority of patients were females and the most frequently diagnosed age group was between 20 and 29 years old. Limb weakness was the most commonly experienced symptom among the patients followed by numbness then visual manifestations.***

Keywords: Multiple Sclerosis, patients, presentation, pattern

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory disorder that usually affects young adults. It is characterized by demyelination in the central nervous system and the appearance of subsequent symptoms. There are some proposed causes for multiple sclerosis; yet, the exact etiology has not been identified. However, epidemiological studies provided possible risk factors for the disease. It is thought to be a combination of genetic predisposition, environmental and infectious agents. The usual pattern is recurrent attacks followed by partial recovery (relapsing-remitting form). [1]

Females are mainly more affected than males. [2,3]From 1955 to 2000, it was observed that multiple sclerosis female to male ratio increased from 1.4 to 2.3 through a systematic review of 28 epidemiological studies. The median and mean ages of MS onset were 23.5 and 30 years of age, respectively. It was also noted that the relapsing-remitting form of the disease tends to have an earlier onset compared with other forms with an average that ranges between 25 and 29 years old. [2] A global study done by the World Health Organization and Multiple Sclerosis Federation in 2008 showed that the range for age of onset of MS symptoms was between 25.3 and 31.8 years with an average age of onset of 29.2 years. Regionally, the average age of onset was lowest in the Eastern Mediterranean (26.9) and the female to male ratio was 2:1. [3]

A study was conducted in Saudi Arabia in 1997including 89 MS patients (38 males and 51 females) in which 73% of them were Saudis. The disease onset appeared to be earlier in Saudis with a mean age of onset that was 25.9 compared to 29.4 in non-Saudi patients. The clinical course was relapsing-remitting in 60.7% of the cases. [4]

The aim of our study is to describe the pattern of first presentation of Multiple Sclerosis patients attending King Khalid University Hospital and to display the age of onset and gender distribution among them (2000-2012). There is a need to know the recent pattern of the disease since the last available local study regarding Multiple Sclerosis was done about 17 years ago.[4]

2. Materials and Methods

The study took place in the medical records department at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia, between the years 2012 and 2013. We reviewed all recorded multiple sclerosis related visits during this period.

Data collection was done in the hospital's medical records department by revising patients' medical records and extracting the required data through completing questionnaires designed specifically for the study. The questionnaire was first designed based on an intense literature review of multiple sclerosis. A pilot study was then done to make the proper modification and to include all the needed data. The questionnaire was composed of two main parts. The first part was patient's personal demographic data which included age, gender, occupation, nationality, education and marital status. The second part of the questionnaire was mainly concerned with the clinical data of the disease, which included family history, age when first diagnosed with MS, date of diagnosis, symptoms of the first attack, duration of the first attack, duration of the whole disease, department of admission, investigations, medications and concomitant diseases.

The study was approved by Institutional Review Board as well as all the relevant departments including community

medicine department and medical records department. All patients' information were kept strictly confidential and only used for research purpose.

SPSS software (version 21) was used for data analysis. Quantitative variables were presented by mean and standard deviation. The gender was demonstrated in the form of proportion. The association between the gender and the pattern of the first attack of multiple sclerosis was tested using Chi square test. The level of significance in the study was 0.05.

3. Results

Although the study aimed to include 310 MS patients, 204 (65.8%) of the patients' medical files were found to be complete. Among MS patients attending KKUH between 2000 and 2012, the majority were females as the study included 154 female patients (75.5%) compared to 50 male patients (24.5%) as presented in table 1 which shows the age of patients at diagnosis. The majority of patients were diagnosed with MS between the age of 20 and 29 (45.6%) followed by age group between 30 and 39 (28.9%). The mean age at diagnosis of MS was 27.16 ±7.74 years. The youngest MS patient was diagnosed at the age of 11 while the oldest was 48 years old. It also shows the distribution of the age groups by gender. Females are more than three times the males in all age groups except in patients aged 30-39 where the females are only about two times the males.

The neurological manifestations of MS patients are shown in table 2. One hundred and forty-two (69.6%) patients presented with weakness as the highest frequency among neurological manifestations at all age groups with percentages between 20-26% of cases within specific age groups. It was followed by 116 (56.9%) patients presenting with numbness. However, it seems that the percentage of numbness increases as the age of patients at diagnosis increases. Visual manifestations had the third highest frequency as 97 (47.5%) patients had visual problems. Other manifestations including gait problems (37.3%), pain (23.5%), imbalance (15.7%) and dizziness (12.7%), depression (4.9%) were also present. It is also noted that 5 out of 10 patients presenting with depression are aged between 40 and 50 at the time of diagnosis.

Table 3 shows that among 204 MS patients, 51 (25%) patients are not on any disease modifying drugs whereas 136 (66.7%) are on Interferon beta 1a. Other patients are on Mitoxantrone (3.4%), Natalizumab (2%), Azathioprine (1.5%) and Baclofen (1.5%).

4. Discussion

This study covered 12 years of cases admitted to KKUH. It was found that the age of onset was similar to that obtained in the latest study conducted in Saudi Arabia. [4] Most patients diagnosed with the disease were in their twenties comprising 45.6 % and the mean age of diagnosis was 27.16 ±7.74 years while the previous study reported a mean age of 27.7 ±7.8 years. [4] Therefore, it is clear that there hasn't been a noticeable change in the age at presentation of multiple sclerosis patients in Saudi Arabia over the period from 1998 until 2012. The age at symptoms' onset is considered relatively early when compared to results found in similar European studies. [5,6] In the United Kingdom, the mean age at symptoms' onset was 34 years old in a study that was conducted in Leeds. [5] The earlier age of disease onset could be attributed to the finding in the previous study that most cases of multiple sclerosis in Saudi Arabia have a relapsing remitting disease (60.7%) which tends to have an earlier onset than other forms of multiple sclerosis while in Leeds study most of the patients were diagnosed with a secondary progressive disease (47%) and only 19% of them with a relapsing remitting disease. [5]

In the study of 1998 in Saudi Arabia, it was found that Saudi patients with multiple sclerosis have an earlier onset of the disease with a mean age of 25.9 years compared to 29.4 for the non-Saudis. [4] In our study, the number of non-Saudi patients was very limited as they were 9 out of the total 204 patients which only represent 4.4% of the study population while in the previous study the percentage of non-Saudis was considerably higher (27%). [4]

Many facts regarding multiple sclerosis are not fully understood and many studies had been done which, in most of the cases, yielded different results. However, one of the few facts that could be agreed upon is the gender distribution of the disease. It is well known that both the incidence and the prevalence of multiple sclerosis are higher in females than in males. Nonetheless, these measures vary from one study to another. We compared our results about gender distribution among MS patients attending KKUH with previous studies done globally and locally.[3,4, 6, 10, 11]

Among the MS population attending KKUH, we found that the vast majority of the patients were females. Similarly to almost all the studies that had been conducted. In fact, in most of the previous studies, it was found that female patients were almost 3 times the male patients. In our study, the female to male ratio was 3.08:1. As many other auto-immune diseases, the exact reason behind the tendency of these diseases to affect women more frequently than men is not known. [7]

However, a large study was conducted in Canada which included 27,074 MS patients showed that female to male ratio have been steadily increasing over the last 50 years to exceed 3.2:1. It was suggested that this increase is a result of a gene-environment interaction which could be preventable in situ. [8] A possible cause for the higher female to male ratio in Canadians is thought to be the lifestyle. As a result of their lifestyle, women in Canada are more exposed to some of the suggested risk factors such as stress, certain infections, living in high altitude and exposure to ultraviolet sun rays. [8,9]

The results about female to male ratio and its similarity to the previously conducted studies is most likely due to the nature of the disease which is known to have an inflammatory auto-immune process. However, some variation in the ratio between our study and other studies is most likely due to the small number of MS patients in KKUH compared to other studies in other countries. [7]

The disease's most frequent clinical manifestation represented in our sample was weakness which affected 70 % of the patients. Similar results globally and regionally corresponded to our results. A very close numbers were reported in a study conducted in Dubai, UAE where 72% of the native subjects included in the study presented with weakness. [10] In another study that was done in Jordan, with a sample size of 224 subjects, 30.8 % presented with weakness as the most frequent finding. This shows that weakness is more prevalent as a manifestation of MS in the region. [11]

The second most frequent manifestation was numbness comprising 57% of the sample. After reviewing literature, recent studies reported similar numbers regarding sensory impairment both in Saudi Arabia and Jordan. However, global studies did not report numbness as a manifestation either due to its minimal effect on the quality of daily life or its very early appearance in the course of the disease. [4,10]

Visual impairment, on the other hand, was reported as the third most common manifestation affecting 48 % of the sample. Similarly, studies conducted in South Wales and Taiwan reported 40% and 38%, respectively. [13] However, in Japan, visual impairment was reported as the most common clinical feature starting with optic nerve involvement then progressing to severe bilateral visual impairment. [12] When we compare our results with most recent study in Saudi Arabia, with a sample of 89 patients, the resemblance in numbers of results was observable only in frequency of weakness and dizziness, where this study reported much lower results regarding visual manifestations, which could be explained by either the increase of cases over the years or the early diagnosis. [4]

Regarding the treatment of Multiple sclerosis (MS), there is no known cure. Treatment usually focuses on strategies to treat MS attacks, manage symptoms and reduce the progression of the disease. Some people have such mild symptoms that no treatment is necessary.[16] In our research, among 204 patients from 2000-2012, there were 51 patients (25%) with no disease modifying drugs which indicate that the attacks they had were mild and not requiring any medication.

According to literature, there are 6 main disease modifying drugs for treating multiple sclerosis prescribed according to the patient's situation based on physician's assessment and lab investigations. In our sample, 4 drugs have been prescribed. The most often drug used in our sample is *Interferon beta 1a* as it was prescribed to 163 patients (66.7 %). This type of drug — such as *Avonex*, *Betaseron*, *Extavia* and *Rebif*— appears to slow the progression of the disease, reduces the number and the severity of attacks. Other patients are on *Mitoxantrone* (3.4%). This drug is rarely used because of the serious side effects. However, it is usually used to treat severe advanced multiple sclerosis based on both clinical assessment and MRI studies. Other patients were on *Natalizumab* (2%). This type of drug like *Tysabri* is generally prescribed to patients who do not respond to or can't tolerate other types of treatment and it mainly reduces the progression of the disease. [14, 15]

A study which included 10,000 MS patients in the United States in 2010showed that 55% of the sample were using disease modifying drugs and the most prescribed drug was Interferon beta 1a (57%) followed by Copaxone (43%).[17]

5. Conclusion

In conclusion, multiple sclerosis in King Khalid University Hospital was far more common in females than in males and the most frequently diagnosed age group was between 20 and 29 years old with a mean age of 27.16 ±7.74years.Limb weakness was the most commonly experienced symptom among the patients followed by numbness then visual manifestations. The majority of the patients were prescribed Interferon beta 1a whereas 25% received no treatment.

6. Recommendations

Accordingly, the clinical suspicion should be raised in female patients aging 20 to 29 years old presenting with the main symptoms mentioned earlier especially those with limb weakness.

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Tables and Figures

Table 1: Distribution of MS patients attending KKUH (2000-2012) by age and sex

Variable	Frequency (%)		
Age at Diagnosis	M	F	Total
<20	8 (16%)	27(17.5%)	35 (17.2%)
20-29	20 (40%)	73(47.4%)	93 (45.6%)
30-39	18 (36%)	41(26.6%)	59 (28.9%)
40-50	4 (8%)	13(8.4%)	17 (8.3%)

Table 2: Distribution of manifestations and age at diagnosis among MS patients attending KKUH (2000-2012)

Age in year Manifestations	**<20 (%)**	**20-29 (%)**	**30-39 (%)**	**40-50 (%)**	**Total (%)**
Weakness	24 (22.6%)	63 (20.9%)	41 (21.9%)	14 (25.9%)	142 (69.6%)
Numbness	14 (13.2%)	53 (17.6%)	37 (19.8%)	12 (22.2%)	116 (56.9%)
Visual	18(17.0%)	40 (13.3%)	34 (18.2%)	5 (9.3%)	97 (47.5%)
Gait	13 (12.3%)	41 (13.6%)	18 (9.6%)	4 (7.4%)	76 (37.3%)
Pain	9 (8.5%)	23 (7.6%)	9 (4.8%)	7 (13.0%)	48 (23.5%)
Balance	9 (8.5%)	13 (4.3%)	10 (5.3%)	0 (0.0%)	32 (15.7%)
Dizziness	3 (2.8%)	16 (5.3%)	7 (3.7%)	0 (0.0%)	26 (12.7%)
Speech	6 (5.7%)	12 (4.0%)	3 (1.6%)	2 (3.7%)	23 (11.3%)
Bladder	2 (1.9%)	11 (3.7%)	7 (3.7%)	2 (3.7%)	22 (10.8%)
Fatigue	2 (1.9%)	10(3.3%)	7 (3.7%)	1 (1.9%)	20 (-9.8%)
Depression	1 (0.9%)	1 (0.3%)	3 (1.6%)	5 (9.3%)	10 (-4.9%)
Coordination	2 (1.9%)	4 (1.3%)	3 (1.6%)	1(1.9%)	10 (-4.9%)
Muscle Spasm	0 (0.0%)	3 (1.0%)	3 (1.6%)	1(1.9%)	7 (-3.4%)
Tremors	0 (0.0%)	6 (2.0%)	1 (0.5%)	0 (0.0%)	7 (-3.4%)
Bowel	2 (1.9%)	2 (0.7%)	2 (1.1%)	0 (0.0%)	6 (-2.9%)
Headache	1 (0.9%)	3 (1.0%)	0 (0.0%)	0 (0.0%)	4 (-2%)
Heat Sensitivity	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (-0.5%)
Sexual Dysfunction	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (-0.5%)

Table 3: Disease Modifying Drugs of MS patients attending KKUH (2000-2012)

Patients on Drugs	Frequency	%
None	51	25%
Interferon Beta 1a	136	66.70%
Mitoxantrone	7	3.40%
Natalizumab	4	2.00%
Azathioprine	3	1.50%
Baclofen	3	1.50%
Total	204	100