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The Prevalence, Epidemiology, Patient Well Being and Adherence to Therapy and Disease Burden of Multiple Sclerosis in Jordan

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ABSTRACT

Objectives: To estimate the clinical, demographical and epidemiological features of Multiple Sclerosis (MS) in Jordan in addition to patient adherence to therapy and disease burden.

Methods: Data for patients with clinically definite diagnosis of Multiple Sclerosis (MS) visiting major referral hospital for MS in Jordan were collected during the time June-December 2020.

Results: The prevalence of MS in Jordan is 24/100000. 870 patients (611 females, 70.2%; 259 males, 29.8%) agreed to disclose patient and history details. The Majority of patients were house-wives (214; 24.6%). The mean ($\pm$ SD) age at time of the study was 35 ($\pm$ 10.1) years, and mean ($\pm$ SD) duration of illness was 5 ($\pm$ 5.1) years. 125 (13.4%) newly diagnosed cases were reported during the time of the study. 537 (62%) were diagnosed immediately in less than one month after the first attack in comparison with 333 (38%) that were diagnosed after more than 6 months to years after the first attack. Family history of MS was found in 154 (18%) of the cases. Family members who have MS from the mother's side were slightly higher than that from the father's side (49 cases, 35.06% *vs* 54 cases, 31.82% with P value of 0.73). Patients who live in different countries/cities were 203 (23%). The majority of the patients live in Amman (696; 80%). 393 (45%) of the patients had Vitamin D deficiency at time of diagnosis. The Majority of patients were house-wives (214; 24.6%). The majority of patients suffered from optic neuritis and numbness during the early attacks, and was ignorant about MS prior to their illness making it psychologically harder to comprehend and adhere to therapy.

Conclusion: Initial symptoms typically occur between 23 and 43 years of age, and women have about twice increased likelihood of developing MS compared to men. The first presentation of the disease varies among patients. There is an increase in MS cases, and this might be due to different factors such as genetic and environmental and vitamin D deficiency. There is an increased awareness among medical staff in the last ten years. Lack of awareness of MS among patients and community renders negative impact and adherence to therapy.

Keywords: Pharmaco-epidemiology, Multiple sclerosis, Patient adherence, Interferon.

INTRODUCTION

Multiple sclerosis (MS) is a central nervous system disease with unknown etiology which is increasing noticeably in Jordan and affecting emotionally, economically and physically the most productive age group who are supposed to start new chapters in their lives; studying, marriage or starting their careers. It also affects their families and friends. Worldwide data shows an increase of MS prevalence. Many studies suggested different risk factors to develop MS; Vitamin D deficiency, genetics and family history, environmental factors, occupation, stress and being female.

The shortage of information related to Jordan since only a previous study conducted long time ago to assess MS epidemiology in Jordan, urged us to conduct this study for providing insights to the disease to improve the understanding of the disease and to help the healthcare providers to choose the best practice and medication to meet the different needs of people with MS. Also, the risk factors that trigger MS were covered and discussed in our study. Many studies suggest that the earlier the patient starts treatment, the better are the outcomes and the slower is the prognosis of the disease. However, diagnosing MS is not an easy task due to lack of precise tests; current diagnosis methods hardly include MS for potential diagnosis, and utilize Magnetic Resonance Imaging (MRI) to confirm the diagnosis. Therefore, there is a need to increase the awareness among public and healthcare providers to start treatment as soon as possible so as to minimize the disease burden and to slow the prognosis of the disease. Thus, the main symptoms and presentation that led the patient to visit the clinic for the first time were also covered in the study.

It is worth mentioning that the Ministry of Health in Jordan offers the treatment for all the patients in its hospitals across the country for free or with not more than 10 J.D (around 14 dollars) per month for the medication of any type, and it adopts the new generations and classes of the Disease Modifying Therapy (DMT) soon enough after its availability in the Jordanian market. Also, the tests and MRIs are for free.

MATERIALS AND METHODS

This is a center retrospective cohort study conducted in a major referral hospital for MS in Jordan; Al-Basheer Hospital, located in the capital city of Jordan, Amman. The former is the largest ministry of health hospital, to which people with MS are referred and is authorized to prescribe S1P modulators and Interferon medications to people with MS covered by governmental insurance. Thus, patients interviewed in this study were evaluated during their illness and considered subject to treatment of MS.

Consecutive Jordanian and non-Jordanian patients referring to the Hospital Pharmacy between the duration of June 2020 and December 2020 were interviewed and asked to fill a questionnaire. Verbal consent was requested from each patient or their guarding family member. The study was approved by the Jordanian Ministry of Health ethical committee. Information collected included patients' age, gender, nationality, place of birth, religion, job, residence, marital status, onset of primary symptom of MS, onset of diagnosis of MS, prescribed drug for MS, family history of MS, presenting symptoms, time of attacks and relapses before and after treatment, vitamin D sufficiency, disability status and capability to run chores, in addition to patients' response to diagnosis, family's response, patients' compliance and adherence, and patients' satisfaction and feedback to therapy. Number of interviewed patients visiting the hospital pharmacy was 870. Data were analyzed using SPSS program (IBM 25).

RESULTS

The prevalence of MS in Jordan is 24 per 100000. 931 patients registered in the out-patient pharmacy in Al-Bashir Hospital (660 females, 70.9%; 271 males, 29.1%). Out of those, 870 patients (611 females, 70.2%; 259 males, 29.8%) were interviewed.

The mean (± SD) age at the time of study was 35 (± 10.1) years, and mean (± SD) duration of illness was 5 (± 5.1) years.

Most of the interviewed patients were diagnosed within the last 5 years. However, despite the time of diagnosis, patients reported that they have been suffering for long with their symptoms and two-thirds of them were unlucky to have prompt diagnosis.

154 (18%) of the patients confirmed having relatives with MS. Most

of who had first degree relatives diagnosed with MS also had second degree relatives as well. Family members who have MS from the mother's side were slightly higher than that from the father's side (49 cases, 35.06% *vs* 54 cases, 31.82% with P value of 0.73). An MS child for a parent with MS was 5 (0.6%), while a sibling for an MS patient was 46 (5.3%). Parents from the same city were found in 540 (62.1%). The majority of the cases had origins from Palestine (619 father's side, 71.15%; 589 mother's side, 67.7%), followed by the Central of Jordan (99 father's side, 11.83%; 93 mother's side, 10.69%), North (69 father's side, 7.93%; 68 mother's side, 7.82%), South (50 father's side, 5.75%; 48 mother's side, 5.52%) and those from other nationalities (33 father's side, 3.79%; 72 mother's side, 8.28%). Christians were 41 (5.05%) and Muslims were 829 (94.95%).

Patients who lived in different countries/cities were 203 (23%). Most of them lived in the gulf area in their childhood, and then moved to Jordan. The majority of patients live in Amman 696 (80%), followed by Zarqa 85 (9.77%), Balqa 33 (3.79%), South of Jordan (22, 2.53%), North of Jordan 17 (1.95%), Madaba 13 (1.49%) and outside Jordan 4 (0.47%).

The majority of patients were born in Amman, followed by Gulf as shown in Figure 1.

393 (45%) of the patients had vitamin D deficiency at time of diagnosis. 235 (27%) of the patients didn't check vitamin D levels. 123 (14%) didn't remember whether they checked it or not. 70 (8%) was normal. 49 (6%) was insufficient.

The majority of patients were housewives as it is shown in Figure 2. It is important to mention that 24 (3%) of the patients retired earlier due to the illness, and some mentioned that they left their work or were dismissed by their worker due to the disease.

34% of the patients reported having two primary symptoms and 5% had three or four symptoms. 352 (41%) of patients reported symptoms of vision problems that varied between double-vision, blurred vision, involuntary movement of the eyes, and other symptoms. Almost third of the patients reported experiencing numbness of either limbs or all limbs, which in some had diffused to other parts of the body, specifically from the toes to the lower body and abdomen. Some patients had experienced partial paralysis and mobility movement. Few patients had reported uncontrolled bowel and bladder problems. Other general symptoms included fatigue and pain which differed between the patients, included but not limited to back-pain, headaches and sore muscles. Muscle spasm, stiffness or weakness was often observed accompanied with other symptoms such as mobility problems.

The first reaction after diagnosis varied. 325 (37.4%) patients expressed acceptance, 322 (37%) patients expressed frustration, despair, depression, isolation, worry, sadness, fear and they cried.
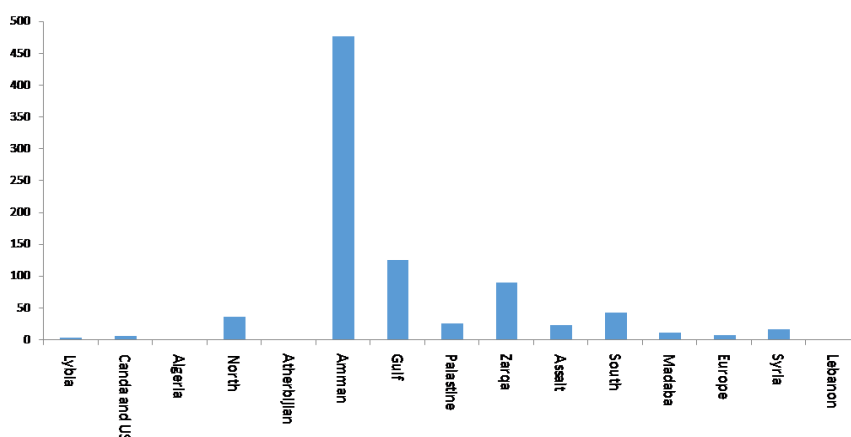

Figure 1: The place of birth.

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111 (12.8%) patients were shocked and surprised as they never heard about the disease. 81 (9.3%) patients felt distress and nervousness. 24 (2.8%) patients changed from acceptance to fear and worry after reading about the disease on the net, or the physician explained the disease. 23 (2.6%) patients didn't accept the diagnosis and lived in denial. 11 (1.3%) patients were relieved after the diagnosis after what they suffered for years. 6 (0.7%) patients lived with bitterness, blaming and angry feelings. 2 (0.2%) patients tried to commit suicide. 2 (0.2%) patients accepted the diagnosis easily because of the experience with the disease with other family members. The family members for MS patients also experienced feelings of fear, bother, worries, sadness but also supportiveness. 766 (88%) of the patients didn't know their MS type. 105 (12%) knew their MS type.

645 (72%) of the patients could do their home duties without help. 746 (86%) were satisfied and coped with their illness. 723 (83%) could walk. 99 (12%) using either a wheelchair or any type of walk assistant. 572 (66%) could do their functional work easily. 600 (69%) didn't need any help in their daily life. 224 (26%) left their work or marriage or were delayed due to the illness. 339 (39%) were hesitant to tell their surroundings (work, friends and relatives).

About 601 (64.55%) of the patients were using Fingolimod (S1P modulators); 175 (20.95%) were using interferon beta-1a; 135 (14.5%) were using interferon beta-1b (Figure 3).

Overall drug satisfaction was in the patients who are on Fingolimod was (371, 62%), followed by interferon beta-1a (104; 56%) and interferon beta -1b (60; 44%). 668 (77%) of the patients expressed confidence in the treatment provided by their physician.

Patients were requested to mention the number of attacks they had before and after their treatment regime. The incidents of attacks decreased and shifted to a lower degree. Number of patients who reported experiencing attacks one to three times a month decreased and shifted to "Never" experiencing attacks after the therapy (Figure 4).

DISCUSSION

MS prevalence in Jordan

There are a total of 2626 MS patients registered in the Health Insurance Agency Ministry of Health until December 20201. Around 1300 patients are still visiting one of the public referral centers across Jordan to take their MS medications [1]. We only included the patients who visited the MOH institutions. Jordan's population has increased since 2011 due to the political instability in the region and has almost one million refugees [2]. The population Estimates of Jordan based on the latest data from the Department of Statistics is 10,820,644 [3]. Thus, the prevalence of MS in Jordan is 24 per 100000 as it was mentioned in a previous studies [4].
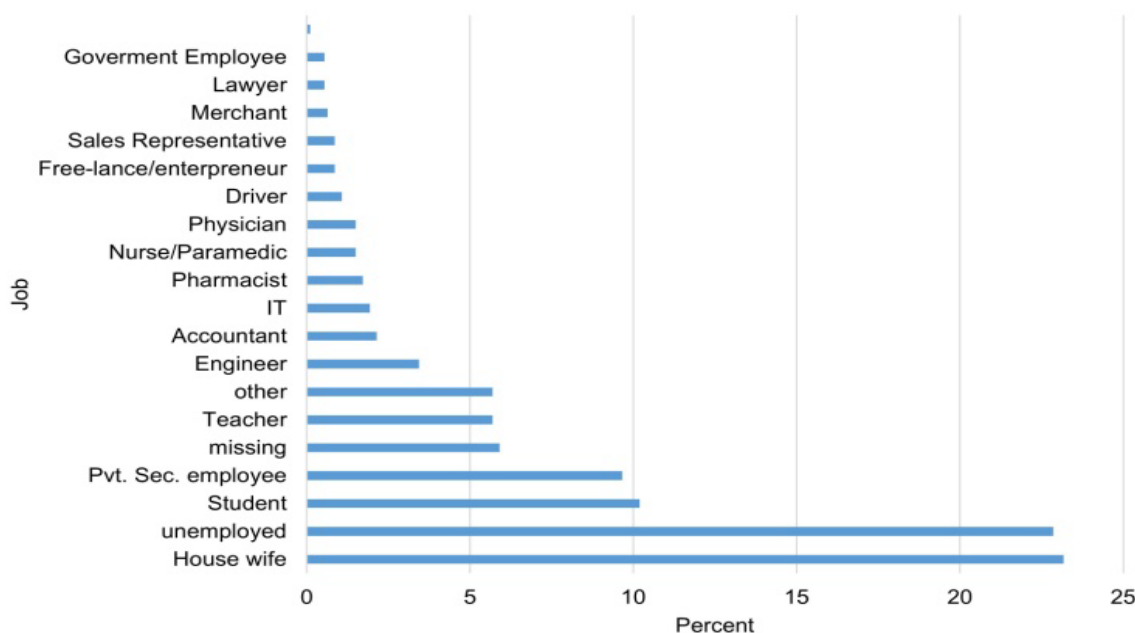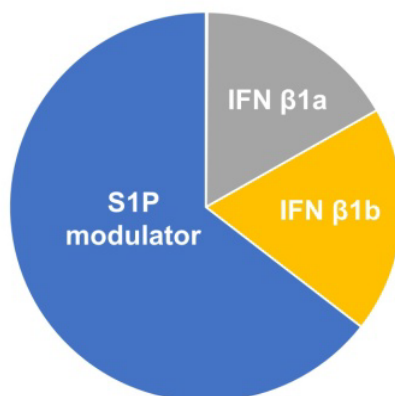

Figure 2: the Job of people with MS.

Figure 3: Prescribed drugs.

Risk Factors

Age Group: Initial symptoms typically occur between 23 and 43 years of age (Figure 5). Newly diagnosed cases within the time of the study were 125 (14.3%). The majority of them occurred within the age group from 20 to 31 although there were 6 (19%) patients over fifty years old who were newly diagnosed and it is not a rare case as it used to be thought, some studies suggested that the percentage might be between 4% and 10% [5].

Gender: Women have about twice increased likelihood of developing MS compared with men (Figure 6). This might be due to hormonal factors. What supports this conclusion is the low incidence of MS among children before puberty and between males and females after the menopause. Also, pregnancy affects MS relapses and remissions.

Some scientists also suggest that body fat and the fat load in the body might play a role since there is higher fat load in females in compare with males [6].

Genetics and family history

We noticed in our findings that MS is more frequently seen in patients whose parents were from the same city (increased chance to be relatives). This might be due to genetic factors [7]. What support this conclusion are the other findings regarding family history of MS and closed societies (Parents are either relatives, or from the same families or religion). We found that 154 (95% Cl 130.64 to 180.33) of the cases had one or more MS cases in their family; which means out of 6 MS patients, one had at least an MS patient in their family. Only 5 (95% Cl 1.62 to 11.67) patients had a parent with MS, which means children
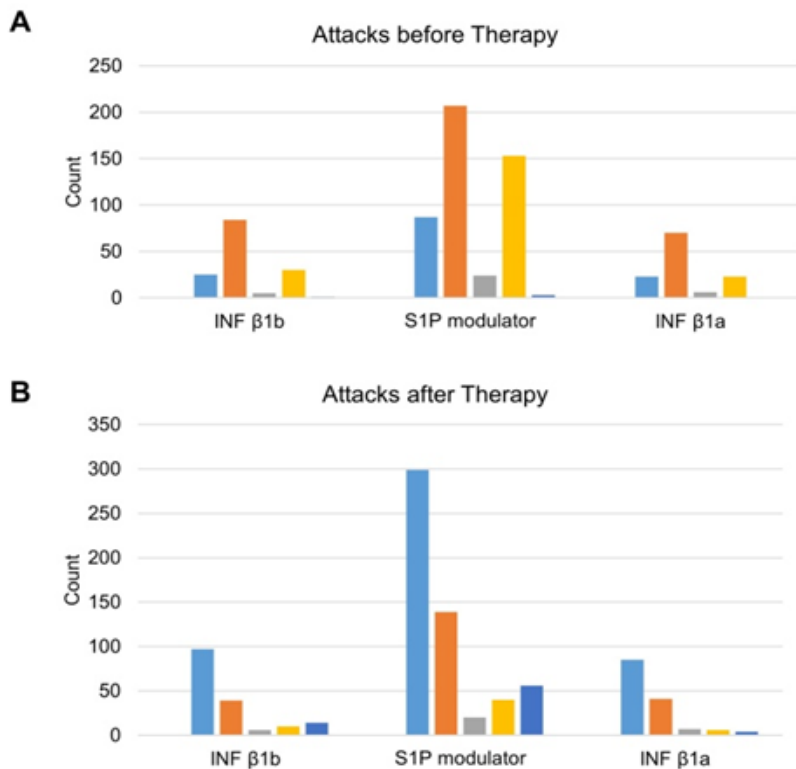

Figure 4: Number of attacks before and after starting therapy regardless of the type of medication.

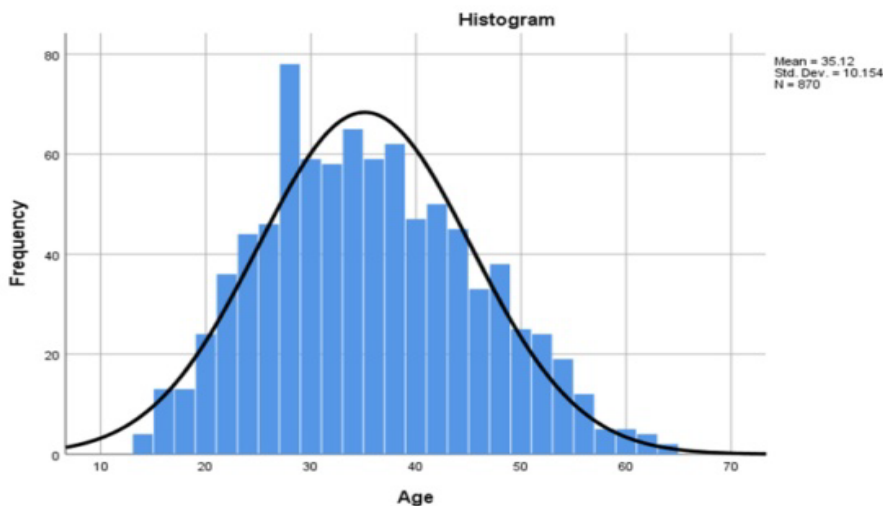**Note:** Never | 01-03 | 04-10 | Frequently | Newly diagnosed

Figure 5: Age frequency of people with MS.

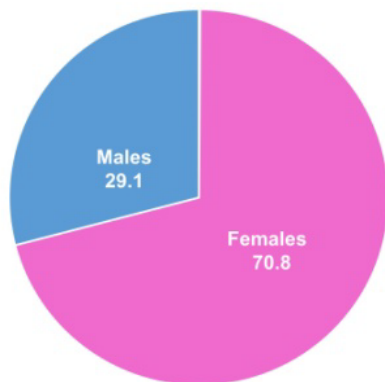Al-Haddadin YB, et al. Int J Pharm 2021; 11(11): 1-6

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Figure 6: Gender percent of people with MS.

of people with MS have a lifetime risk of 1 in 174 to develop MS. On the other hand, we noticed that 46 (95% Cl 33.7 to 61.4) patients had a brother or sister with MS. This means a sibling of a person with MS has a 1 in 19 chance of developing MS. We also noticed that the incidence of developing MS increased in closed societies such as Christians (The rate of illness is higher than their percentage which is estimated by 2.5%). This also gives an indication that genetics and family history might play a role in increasing the risk to develop MS. What supports this conclusion is that parents from the same city might have an incidence rate of 0.62, in other words, out of 2 patients one has parents from the same origin. Being from a closed society means that there is an increased chance that people will get married from their relatives who might share the same genes. However, heredity might play a role in developing MS, but still it is not the major reason to develop the disease.

We noticed that patients with MS that had family history from the mother side had a higher incidence to develop MS than that from the father side. Although the result was insignificant, it might be explained that 374 (95% Cl of 337.05 to 413.89) patients were hesitant to tell their relatives about their illness, thus we don't have sufficient data to come to this conclusion.

Environmental factors and lifestyle

The newly diagnosed cases in the past 5 years increased significantly and this might be due to the modern lifestyle which adds more stress and pressure on people to cope with; technology, environmental pollution and unhealthy food [8]. Some of the patients mentioned that they had the first attack after experiencing problems and different stressful situations.

203 (95% Cl 176.03 to 232.93) patients lived in different countries or cities during their lifetime, this incidence might be due to environmental influence or lifestyle. Environmental factors include pollution* that can be noticed in 89 (95% Cl 71.5 to 109.5) patients of those lived in the Gulf region during the Gulf war II, and patients live in big cities (42% of population live in Amman, North 28.6%, Zarqa 14.3%, Balqa 5.2%, South 8%, Madaba 2%). We can notice the higher risk of developing MS with those who live in Amman (696; 95% Cl 645.25 to 749.69) and incidence rate of 0.8, followed by Central of Jordan (Balqa, Zarqa and Madaba) (131; 95% Cl 109.35 to 155.45), and with incidence rate of with 0.76. However, the higher incidence in big cities and the central of Jordan might be due to the closeness to medical services.

Unlike world data which reported that north areas have higher risk to develop MS, this is related to the fact that we performed this survey in Albashir Hospital in Amman which considered a referral to the south and central of Jordan and Amman. The same note regarding the place of birth; it was the highest in Amman, followed by the Gulf region, followed by Zarqa. We can't prove that there is a relation between the place of birth and the increased risk of developing MS, but we can

notice that the place of birth in highly polluted places might increase the possibility of developing MS.

Stressful lifestyle might play a role in increasing risk to develop MS [9]. Some of the patients mentioned that the first attack came after experiencing stressful situations as the death of their father, failing in Tawjihi (the national high school exams). We found signs of the effect of occupation on the risk of developing MS, and the high frequency found within the housewives who had the highest chance to develop MS (214; 25%). One of the explanations might be that the rates of female labour force participation in Jordan are quite low (15%) based on data from the worldbank [10]. Also, MS incidence within females is higher than males. However, when we compare housewives (214; 35.02%) with other females (employees, students and retired) (297; 48.61%), we can notice that worker females have more chances to develop MS. Some studies suggest that female employees have a more stressful life than housewives. Students also have higher incidence to develop MS, studies show that students suffer a stressful life [11].

Vitamin D deficiency: There is increasing evidence linking vitamin D deficiency to MS [12]. This was seen in our findings that (393; 95% Cl 355.1 to 433.84) of the patients had vitamin D deficiency when diagnosed with incidence rate of 0.45.

Burden of the disease: There are more than 2000 registered MS patients in the MOH centers only until the end of 2020. Around 1300 of them are on different medications. 658 patients are on Fingolimod, 101 are on Dimethyl fumarate, 182 are on Interferon beta 1a (INF β 1a 44), 48 are on Interferon beta 1a (INF β 1a 30), 176 are on Interferon beta 1b (INF β 1b), 65 are on Ocrelizumab and 45 are on Natalizumab, with a total cost of 17,916,666 US dollars.

The disease burden is not only economically, but it also affects mental health, lifestyle and daily activities to the patients and their family members. MS is most common in the young adults group and the disease is not fatal, that means patients might live long, yet suffer from increasing disabilities over time. So, it is important to increase awareness of the disease among medical staff and ordinary people to diagnose or to refer patients to neurologists as early as possible, so that they can be on drug modifying treatments as soon as possible, also it is important to have access to newer DMT and technologies, and have a precise decision and right timing when switching between DMT to decrease the frequency and severity of attacks and thus decrease the chances of worsening the old symptoms or having new ones and accordingly slow the progression of disabilities. However, the immediate diagnosis increased in the last ten years from 37% to 63% in comparison with those who were diagnosed before 10 years or more (49% to 51%). This might be due to the increase in the awareness between medical staff, but still there is more to do to increase the awareness since the symptoms of MS are similar to other diseases such as otitis media, disc, facial nerve, strokes, and other diseases.

First presentation for MS

Although the first presentation varies among patients, still there are common symptoms that might speed up the diagnosis and the referral to a neurologist. The most distinguished symptom was optic neuritis; when a patient first visited the clinic for numbness, the physician usually suspects vitamin B12 deficiency and starts treatment accordingly until other vision problems occur, then the ophthalmologist refers the patient to a neurologist for further assessment. Many patients had more than one symptom before the diagnosis.

Acceptance of the diagnosis: Faith plays an important role in the acceptance of the diagnosis. 60% of the patients who showed acceptance expressed their faith perspective. Those who experienced any negative feelings were due to the lack of knowledge of the disease.

As we notice that most of the patients who have not had any background to the disease sought information from the internet which made them fear the illness the most.

Life disturbances: MS might cause permanent physical disability, but this is only true for 12% of the patients who lost the ability to walk without any type of walking aid. Still 74% can do their home duty without any help, and 74% are still working. 66% were able to do their jobs easily, and 66% didn't need any help in their daily life. So, MS might interfere with the daily life of the patients, and this might increase the feelings of depression, stress and nervousness, putting in mind that youth is the most affected group. 26% of the patients left their work, marriage, study, or faced some delay in one of those aspects due to illness. This added more stress and frustration to the patients and their families.

Treatment satisfaction

As we mentioned earlier, there are seven modifying disease medications in the Ministry of Health hospitals, but in this study we only interviewed the patients that visit the out-patient pharmacy that dispenses

It is noticed that the percentage of total satisfaction with the tablet form is the highest with 62%, and this might be due the ease of taking the tablet form, also the side effects of using the injections like injection site reaction, flu-like symptoms. We also noticed that among patients on the injectable forms, there were a high satisfaction among the patients who take INF β 1a 30 are more than those on INF β 1a 30 and INF β 1b, and this might be because of the frequency of taking the medication (once weekly).

We noticed that patients trusted the medication that was prescribed for them by their physicians and were satisfied by the results. Some patients mentioned that they are free of attacks for years after starting the treatment, or switching to the tablet form. Those who expressed doubt and dissatisfaction were because they didn't feel any positive change in their condition. This might be the main reason that 73 (8.7) patients either stopped their treatment for a while or are non-adherence to their medications. Another reason might be the feeling that they are better, especially at the beginning of the treatment.

CONCLUSION

Initial MS symptoms typically occur between 23 and 43 years of age, and women have about twice increased likelihood of developing MS compared with men. Risk factors that can induce MS are genetic factors, environmental factors, lifestyle or vitamin D deficiency. There is increased awareness among medical staff in the last ten years. This is very important to speed up the diagnosis and to start the treatment as soon as possible. It is important to have access to the newest generations and classes of the medications to decrease the burden of disease.

The first presentation of the disease varies among patients; some patients experienced more than one attack with different presentations.

Optic neuritis is clearly the indicator that doctors suspect MS. Other symptoms might resemble other diseases and thus delay the diagnosis or the referral to a neurologist.

Those who experienced any negative feelings were due to the lack of knowledge of the disease. There is a lack of awareness of MS not only among patients but also families and people. MS might interfere with patient lifestyle and their family; some lost their jobs and others got divorced after the diagnosis, but overall there is a great support from most of the families and this can help the patient in all aspects.

LIMITATION STATEMENT

The short period of study might not elaborate the overall epidemiological data, thus requires further follow-up studies. Also, although the hospital in which the study was conducted is considered the major referral centre for MS cases in Jordan, yet findings can be differ if more sites were included.

REFERENCES

1. Data was collected directly from the Health Insurance Agency - Ministry of Health.

2. UNHCR continues to support refugees in Jordan throughout 2019 – UNHCR Jordan

3. PopulationEstimates.pdf (dos.gov.jo) Table 2.1 Population of the Kingdom by Sex According to the 1952, 1961, 1979 ,1994,2015 and 2018 Censuses, and Estimated Population for Some Selected Years.

4. El-Salem K, Al-Shimmery E, Horany K, et al. *J. Neurol.* **2006**; 253 (9): 1210-1216.

5. Martinelli V, Rodegher M, Moiola L, *et al. Neurol. Sci.* **2004**; 25: s350-s355.

6. Multiple Sclerosis: Why Are Women More at Risk? | Johns Hopkins Medicine

7. Cree BA. *Handb. Clin. Neurol.* **2014**; 122: 193-209.

8. High Levels of Air Pollution Linked to Increased MS Risk (medscape.com)

9. Djelilovic-Vranic J, Alajbegovic A, Tiric-Campara M, et al. *Materia. Socio-medica.* **2012**; 24 (3): 142-147.

10. Labor force participation rate, female (% of female population ages 15+) (modeled ILO estimate) - Jordan | Data (worldbank.org)

11. A comparative study on stress levels among working women and housewives with reference to the state of Kerala by Harilal A and Santhosh V A (nmims.edu)

12. Sintzel MB, Rametta M, Reder AT. *Neurol. Ther.* **2018**; 7 (1): 59-85.