



Original article



Current and future trends in multiple sclerosis management: Near East perspective

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ARTICLE INFO

Keywords:

Multiple sclerosis treatment
Near East countries
Disease-modifying therapies
Relapsing remitting multiple sclerosis
Highly active multiple sclerosis
Multiple sclerosis guidelines

ABSTRACT

Background: Multiple sclerosis (MS) prevalence is rising in the Middle East. Most MS medications are available in the region, but not all, possibly affecting neurologists' prescribing habits.

Objectives: To provide an overview of the current practices of Near East (NE) healthcare practitioners by probing their prescribing decisions, to report the COVID-19 impacts on neurologists' prescribing habits, and to explore the future relevance of current medication used in MS management among other newcomers.

Methods: A cross-sectional study was carried out using an online survey from April 27, 2022, to July 5, 2022. The questionnaire was designed with the input of five neurologists representing five NE countries (Iran, Iraq, Lebanon, Jordan & Palestine). They identified several factors that play a crucial role in the optimal care of MS patients. The link was shared among neurologists using snowball sampling.

Results: The survey included 98 neurologists. Effectiveness and safety balance was the most important factor considered when selecting the MS treatment. Among patients with MS, the most challenging factor for the patients was thought to be related to family planning, followed by affordability and tolerability of side effects. In the treatment of mild to moderate relapsing remitting multiple sclerosis (RRMS) in men, Interferon beta 1a SC, Fingolimod, and Glatiramer acetate were the most commonly recommended treatments. Dimethyl fumarate substituted fingolimod in female patients. Interferon beta 1a SC was the safest treatment for mild to moderate RRMS. Interferon beta 1a SC was preferred over other treatments for patients with mild to moderate MS and planning for pregnancy (56.6%) or breastfeeding (60.2%). Fingolimod was not a choice for these patients. Neurologists seemed to discuss the top three treatments of Natalizumab, Ocrelizumab, and Cladribine with patients with highly active MS. When asked to position future disease-modifying therapies five years from today, more than 45% of physicians expressed a lack of information on Bruton's tyrosine kinase (BTK) inhibitors.

Conclusions: Most neurologists in the NE region followed Middle East North Africa Committee for Treatment and Research in Multiple Sclerosis (MENACTRIMS) recommendations for prescribing treatment. The treatment choice also depended on the availability of disease-modifying therapies (DMTs) in the region. Regarding the use of upcoming DMTs, there is a clear need for real-world data, long-term extension studies, and comparative studies to support their efficacy and safety profiles in treating patients with MS.

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<https://doi.org/10.1016/j.msard.2023.104800>

Received 19 December 2022; Received in revised form 10 May 2023; Accepted 4 June 2023

Available online 5 June 2023

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1. Introduction

The global landscape of multiple sclerosis (MS) is changing. On top of its increasing prevalence (Wallin et al., 2019), its phenotypes, clinical presentations, and treatment have all changed. After the dominance of injectables, the treatment landscape has rapidly evolved in the last 13 years with the development of high-efficacy disease-modifying therapies (DMTs) (Moradi et al., 2021).

Previous studies have reported on the epidemiology, risk factors, and clinical aspects of MS in the Middle East (Abbasi et al., 2017; Heydarpour et al., 2014, 2015; Yamout et al., 2008, 2010). However, less attention has been given to the treatment landscape. Nevertheless, it has been confirmed that there has been a persistent shift away from injectable medications toward more efficient oral therapies and monoclonal antibodies (mAbs) (Moradi et al., 2021). The introduction of these more effective therapies increases the chance of lives free from disability for longer.

Current management approaches focus on resolving acute attacks, alleviating symptoms, and decreasing biological activities via DMTs (Hauser and Cree, 2020).

In the Near East (NE) region, prevalence and incidence are also on the rise (Abuawad et al., 2022; Amini et al., 2021; Hassoun et al., 2022) and are expected to keep rising (Amini et al., 2021).

MS therapy and management strategies are rapidly evolving (Fernández et al., 2017), becoming more and more complex as many drugs with diverse routes of administration, mechanisms of action, effectiveness, and safety profiles are now available.

The decision-making process for selecting the appropriate medication is a challenging task that necessitates a careful review of the results of clinical and post-marketing research and the capacity to adapt data from clinical studies to patients in clinical practice (Ghezzi, 2018). In addition, different guidelines now exist to help neurologists in decision-making (Montalban et al., 2018; Rae-Grant et al., 2018).

Most of the first- and second-line DMTs approved by the Food and Drug Administration (FDA) and European Medicine Agency (EMA) for treating MS are available in the Middle East. However, some still need to be made available in certain countries, and some are increasingly difficult to access, especially in countries with limited coverage and reimbursement for MS medications (Zeineddine and Yamout, 2020). This could also have an impact on treating physicians' prescribing habits.

This study reports the current practices and future trends of neurologists treating MS across five countries of the NE region (Iran, Iraq, Jordan, Lebanon, and Palestine).

The overall objectives of this study were threefold:

- (1) to provide an overview of the current practices of NE healthcare professionals (HCP) by probing their prescribing decisions. Where discrepancies with guidelines exist, we attempt to explain the reasons behind them
- (2) to report the COVID-19 impacts on neurologists' prescribing habits
- (3) to explore the future relevance of current medication used in MS management among other newcomers

2. Methods

2.1. Study design and protocol

A panel of expert neurologists from Iraq, Iran, Jordan, Lebanon, and Palestine convened for two advisory board meetings to discuss the current and future prescribing habits of NE HCPs in managing MS patients. To better understand the current state of MS management in the region, a cross-sectional observational study was conducted using an online survey. A preliminary questionnaire was created with the support of expert neurologists who evaluated the intelligibility of the questions,

and modifications were made accordingly. The final questionnaire was formatted in SurveyMonkey and Microsoft Forms, and the link was made available for neurologists from the five NE countries through email and the WhatsApp application.

2.2. Questionnaire

The thematic focus of the questions was on the practices of MS medication prescribers.

The Questionnaire included a combination of Likert-type, ranking, multiple-choice, and open-ended questions. It aimed at covering four sections:

- Section 1: demographics and practice-related (sex, age, country, years of experience, nature of work, number of MS patients/month).
- Section 2: nine questions about medication selection for MS patients. This section captured the current practice trends in managing MS patients and provided an overview of the pharmacotherapy available in treating mild to moderate relapsing-remitting multiple sclerosis (RRMS) and highly active MS patients. It also explored multiple factors considered when prescribing an MS treatment depending on the stage of disease and sex.
- Section 3: four questions about current treatment with COVID-19 vaccination. This section examined neurologists' approach to vaccination depending on MS treatment.
- Section 4: five questions about future trends in the treatment algorithm. This section explored trends in positioning multiple DMTs in future clinical practice based on their efficacy and safety and the activity of the disease to help understand the trend of various DMTs in the near future (five years) for managing an MS patient.

2.3. Participants and data collection

Participants included had to be neurologists treating MS patients, practicing in one of the five NE countries of the study. The link was shared among neurologists using snowball sampling from April 27, 2022, to July 5, 2022. A single reminder was sent.

A sample size of 108 respondents was targeted, based on each country representative's recommended number, divided as follows: Jordan: 20 participants; Iran: 40 participants; Lebanon: 15 participants; Palestine: 8 participants; Iraq: 25 participants.

Once the results were compared to guidelines, further meetings with country representatives were planned to try to elaborate and explain any discrepancies or local particularities. As a result, we have split some parts of the analysis by country.

2.4. Data analyses

Data collected through SurveyMonkey were exported to SPSS version 25. Quality control of the survey responses was performed by verifying consistency in answers (no conflicting answers given by the same participant), analyzing the speed of completion for any illogical durations, and checking for straight-lining. Responses were analyzed by each question and summarized. Numbers and percentages were used for categorical variables and the mean and standard deviation for quantitative/Likert-type variables. Open-ended responses were reviewed and reported qualitatively.

3. Results

3.1. Sample characteristics

Ninety-eight neurologists from five NE countries (Iraq, Iran, Lebanon, Jordan, and Palestine) were included in the analysis. The majority had more than 10 years of experience in the field, and 39% received more than 40 MS patients per month (Table 1).

Table 1
Sample characteristics.

| | | n | % |
|--|---------------------|----|------|
| Sex | Female | 30 | 30.6 |
| | Male | 68 | 69.4 |
| Age | Less than 35 | 11 | 11.2 |
| | 36–45 | 39 | 39.8 |
| | 46–55 | 26 | 26.5 |
| | More than 55 | 22 | 22.4 |
| Years of experience | 1–5 | 11 | 11.2 |
| | 6–10 | 26 | 26.5 |
| | 11–15 | 23 | 23.5 |
| | More than 15 | 38 | 38.8 |
| Country | Iran | 48 | 49.0 |
| | Iraq | 15 | 15.3 |
| | Jordan | 14 | 14.3 |
| | Lebanon | 15 | 15.3 |
| | Palestine | 6 | 6.1 |
| Institution type | A community setting | 38 | 38.8 |
| | An academic setting | 60 | 61.2 |
| MS center | No | 48 | 49.0 |
| | Yes | 50 | 51.0 |
| Number of MS patients per month | Less than 10 | 15 | 15.3 |
| | 11–20 | 32 | 32.7 |
| | 21–40 | 13 | 13.3 |
| | More than 41 | 38 | 38.8 |

3.2. Factors and challenges considered while prescribing

Table 2 shows the important ratings of factors considered while prescribing. The balance between efficacy and safety received a mean of 4.58/5, followed by availability at 4.42/5. The table also shows the level of challenge the patients face regarding their treatment. Effects on family planning was found to be the most challenging factor reported by patients regarding their MS treatment (5.2/7), followed by treatment affordability (5.13/7) and tolerability of side effects (4.99/7), according to the neurologists.

3.3. Current trends in MS management

3.3.1. Mild to moderate RRMS

In mild to moderate RRMS, interferon β-1a (IFN β-1a) SC was chosen by most physicians (77% in female patients and 81% in male patients). This was followed by dimethyl fumarate in females (53%) and fingolimod in males (55%). Glatiramer acetate was also among the first three options (48% and 52%, respectively) (Table 3). DMTs chosen the most as first and second options based on their efficacy were IFN β-1a SC and dimethyl fumarate (50% and 24%, respectively). Natalizumab (25%), cladribine tablets (24%), and alemtuzumab (16%) were considered non-options in mild to moderate MS. Choices based on efficacy were further

Table 2
Factors considered when prescribing MS medication.

| | Mean | SD |
|---|------|------|
| Factor importance (1 = Less important, 5 = Very important) | | |
| Efficacy/safety balance | 4.58 | 0.91 |
| Availability | 4.42 | 0.93 |
| Patient compliance | 4.3 | 0.90 |
| Affordability | 4.11 | 0.94 |
| Method of administration | 3.45 | 0.90 |
| Challenge weight (1 = Less challenging, 7 = More challenging) | | |
| Effect on family planning | 5.2 | 1.55 |
| Treatment affordability | 5.13 | 1.51 |
| Tolerability of side effects | 4.99 | 1.31 |
| Self-injection schedules in daily lifestyle | 4.74 | 1.31 |
| Frequency of administration | 4.52 | 1.47 |
| Method of administration (e.g., need for hospitalization) | 4.14 | 1.39 |
| Monitoring burden | 3.92 | 1.36 |

Table 3
Prescribing habits in mild to moderate RRMS.

| Top choices of therapies for mild to moderate RRMS based on sex* | | | |
|--|----|-----------------------|----|
| In female patients | % | In male patients | % |
| Interferon beta-1a SC | 77 | Interferon beta-1a SC | 81 |
| Dimethyl fumarate | 53 | Fingolimod | 55 |
| Glatiramer acetate | 52 | Glatiramer acetate | 48 |
| Interferon beta-1a IM | 45 | Interferon beta-1a IM | 45 |
| Interferon beta-1b | 41 | Interferon beta-1b | 29 |
| Fingolimod | 17 | Dimethyl fumarate | 22 |
| Natalizumab | 14 | Teriflunomide | 18 |
| Cladribine tablets | 13 | Natalizumab | 11 |
| Teriflunomide | 12 | Cladribine tablets | 9 |
| Ocrelizumab | 6 | Ocrelizumab | 8 |
| Alemtuzumab | 6 | Alemtuzumab | 8 |

| Likelihood to prescribe as first choice based on efficacy for mild to moderate RRMS | | | |
|---|----|-----------------------|----|
| 1st choice | % | Not a choice | % |
| Interferon beta-1a SC | 50 | Natalizumab | 25 |
| Dimethyl fumarate | 24 | Cladribine tablets | 24 |
| Ocrelizumab | 6 | Alemtuzumab | 16 |
| Fingolimod | 5 | Fingolimod | 8 |
| Interferon beta-1a IM | 5 | Glatiramer acetate | 8 |
| Interferon beta-1b | 4 | Ocrelizumab | 5 |
| Cladribine tablets | 2 | Interferon beta-1a IM | 4 |
| Teriflunomide | 2 | Interferon beta-1b | 4 |
| Glatiramer acetate | 1 | Teriflunomide | 4 |
| Natalizumab | 1 | Dimethyl fumarate | 1 |
| | | Interferon beta-1a SC | 1 |

| Likelihood to prescribe as first choice based on efficacy for mild to moderate RRMS stratified by country | | | | |
|---|-------------------------------|-------------------------------|-------------------------------|------------------------------|
| Iran | Iraq | Jordan | Lebanon | Palestine |
| Interferon beta-1a SC (39.6%) | Interferon beta-1a SC (63.6%) | Interferon beta-1a SC (72.7%) | Interferon beta-1a SC (45.5%) | Interferon beta-1a SC (100%) |
| Dimethyl fumarate (35.4%) | Interferon beta-1b (18.2%) | Fingolimod (9.1%) | Dimethyl fumarate (27.3%) | |
| Ocrelizumab (10.4%) | Interferon beta-1a IM (9.1%) | Interferon beta-1a IM (9.1%) | Teriflunomide (9.1%) | |
| Fingolimod (6.3%) | Cladribine tablets (9.1%) | Interferon beta-1b (9.1%) | Interferon beta-1a IM (9.1%) | |
| Glatiramer acetate (2.1%) | | | Cladribine tablets (9.1%) | |
| Interferon beta-1a IM (2.1%) | | | | |
| Natalizumab (2.1%) | | | | |
| Teriflunomide (2.1%) | | | | |

*Percentages do not add up to 100% because the questions allowed respondents to select multiple answers.

stratified by country. IFN-beta-1a SC remained the first choice in all countries.

3.3.2. Highly active MS

Table 4 describes prescribing habits in highly active MS. Natalizumab (31%), ocrelizumab (29%), and cladribine tablets (28%) were selected as the top choices. In treatment naïve patients with highly active disease, ocrelizumab (28%) was the most frequently chosen as first choice based on its efficacy, followed by cladribine tablets (23.8%). Rankings of the different DMTs changed amongst countries. Ocrelizumab was the first choice in Iran (41.7%), cladribine tablets in Iraq and Lebanon (54.5% and 63.6%, respectively), and fingolimod in Jordan (54.5%). In Palestine, three DMTs - fingolimod, ocrelizumab, and rituximab had the same frequency.

Table 4
Prescribing habits in highly active MS.

| Top choices of therapies for highly active MS patients | |
|--|----|
| Drug | % |
| Natalizumab | 31 |
| Ocrelizumab | 29 |
| Cladribine tablets | 28 |
| Rituximab (off label) | 27 |
| Fingolimod | 16 |
| Alemtuzumab | 12 |
| Interferon beta-1b | 6 |
| Interferon beta-1a IM | 6 |
| Interferon beta-1a SC | 3 |
| Teriflunomide | 2 |
| Dimethyl fumarate | 1 |
| Glatiramer acetate | 0 |

| Likelihood to prescribe as first choice based on efficacy in treatment naïve patients with highly active disease | |
|--|----|
| Drug | % |
| Ocrelizumab | 29 |
| Cladribine tablets | 24 |
| Natalizumab | 21 |
| Fingolimod | 19 |
| Rituximab | 5 |
| Alemtuzumab | 2 |

| Likelihood to prescribe as first choice based on efficacy in treatment naïve patients with highly active disease stratified by country | | | | |
|--|----------------------------|---------------------------|----------------------------|---------------------|
| Iran | Iraq | Jordan | Lebanon | Palestine |
| Ocrelizumab (41.7%) | Cladribine tablets (54.5%) | Fingolimod (54.5%) | Cladribine tablets (63.6%) | Fingolimod (33.3%) |
| Natalizumab (20.8%) | Natalizumab (36.4%) | Ocrelizumab (18.2%) | Natalizumab (27.3%) | Ocrelizumab (33.3%) |
| Fingolimod (16.7%) | Ocrelizumab (9.1%) | Alemtuzumab (9.1%) | Fingolimod (9.1%) | Rituximab (33.3%) |
| Cladribine tablets (12.5%) | | Cladribine tablets (9.1%) | | |
| Rituximab (6.3%) | | Natalizumab (9.1%) | | |
| Alemtuzumab (2.1%) | | | | |

3.4. Safety

IFN β-1a SC was selected as the safest treatment when treating mild to moderate RRMS, with 80.7% of participants giving it a score of 5/5, 5 being the highest degree of safety. Interferons and GA had median scores of 5, while fingolimod, alemtuzumab and natalizumab had medians of 3 (results not shown).

3.5. DMTs and family planning

In Table 5, participants were asked about their top choices for women planning pregnancies and breastfeeding. IFN β-1a SC was the

Table 5
Choice of DMTs in patients with mild to moderate multiple sclerosis planning for pregnancy and breastfeeding.

| Planning for pregnancy | | Breastfeeding | |
|-------------------------------|------------------------------|-------------------------------|----------------------------|
| 1st choice | Not a choice | 1st choice | Not a choice |
| Interferon beta-1a SC (56.6%) | Fingolimod (56.6%) | Interferon beta-1a SC (60.2%) | Fingolimod (48.2%) |
| Glatiramer acetate (28.9%) | Teriflunomide (12%) | Glatiramer acetate (22.9%) | Cladribine tablets (18.1%) |
| Interferon beta-1a IM (6%) | Dimethyl fumarate (7.2%) | Interferon beta-1a IM (7.2%) | Teriflunomide (14.5%) |
| Teriflunomide (3.6%) | Natalizumab (7.2%) | Cladribine tablets (2.4%) | Alemtuzumab (6%) |
| Interferon beta-1b (2.4%) | Alemtuzumab (6%) | Interferon beta-1b (2.4%) | Natalizumab (6%) |
| Cladribine tablets (1.2%) | Cladribine tablets (4.8%) | Teriflunomide (2.4%) | Ocrelizumab (3.6%) |
| Natalizumab (1.2%) | Ocrelizumab (2.4%) | Alemtuzumab (1.2%) | Glatiramer acetate (2.4%) |
| | Glatiramer acetate (1.2%) | Dimethyl fumarate (1.2%) | Dimethyl fumarate (1.2%) |
| | Interferon beta-1a SC (1.2%) | | |
| | Interferon beta-1b (1.2%) | | |

first choice for treating a patient with mild to moderate multiple sclerosis and planning for pregnancy (56.6%), as well as for a patient who is breastfeeding (60.2%). As per the neurologists, fingolimod was not a choice for these patients (56.5% and 48.2%, respectively).

3.6. Future trends in MS management

In Figs. 1.a and 1.b, positive values represent higher expectations while negative values show lower expectations. Cladribine tablets and ocrelizumab are expected to be considerably more prescribed in five years in both mild to moderate activity RRMS and high disease activity RRMS. However, glatiramer acetate and interferons are expected to be prescribed less (Figs. 1.a and 1.b). Concerning upcoming DMTs, around a quarter of the participants declared they expected ofatumumab (24.4%), siponimod (29.5%), and ozanimod (26.9%) to be used as first-line treatment five years from now. The highest percentage of physicians expected them to be used as second-line treatment (47.5%, 46.2%, and 39.7%, respectively). As for Bruton’s tyrosine kinase (BTK) inhibitors, most neurologists admitted not knowing where to place these recent compounds in development (46.2%) (Fig. 1.c).

Neurologists were asked to rate their expectations for the use of the upcoming DMTs based on their efficacy/safety profile on a scale of 1 to 5. Out of the four newcomers, ofatumumab received the highest frequency of 5/5 (17.9%), but most neurologists placed the compounds at 3/5 and 4/5. Interestingly, most neurologists declared not having enough clinical information around the drug to answer that question, especially for the BTK inhibitors (46.8%) (Fig. 1.d).

4. Discussion

To our knowledge, this study is the first to evaluate current practices of NE neurologists treating MS patients and to explore their expectations of both currently available and upcoming DMTs. The neurologists appeared to adhere to guidelines, with preferences varying based on drug availability and affordability in their respective countries..

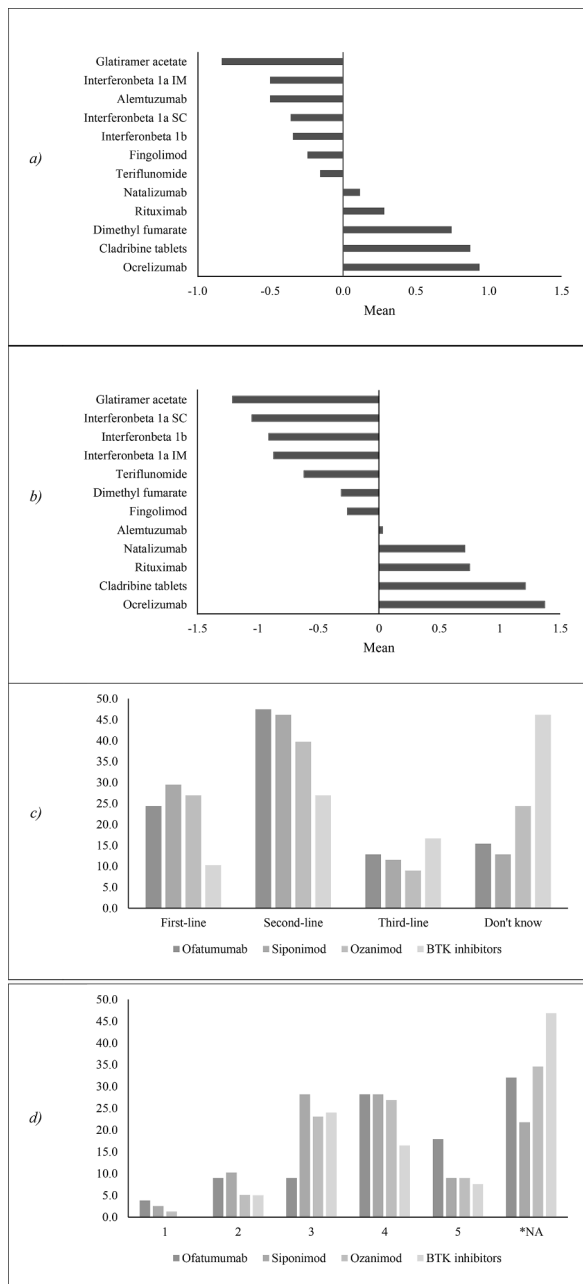


Fig. 1. a) Where do you see the following DMTs five years from today in your clinical practice for mild to moderate activity RRMS?; b) Where do you see the following DMTs five years from today in your clinical practice for managing high disease activity RRMS?; c) Where will you position the following DMTs five years from today in your clinical practice treatment algorithm for RRMS?; d) Based on currently available clinical data, please rate your expectation for the use of the following DMTs based on their efficacy/safety profile on a scale of 1 to 5. (1= less recommended, 5=more recommended, NA= Not applicable for those options in which you have no clinical information).

Moreover, they require more clinical data on new therapies.

When asked about their treatment choices, IFN β -1a SC, fingolimod, and GA were the most cited treatments physicians would discuss with their male patients with mild to moderate RRMS. Fingolimod was substituted with dimethyl fumarate in female patients. The growing availability and dissemination of safety data pertaining to dimethyl fumarate use during pregnancy has resulted in an increased prevalence of DMF use among women. Notably, previous studies have not found any elevated risk of adverse pregnancy outcomes or fetal abnormalities

associated with gestational exposure to DMF (Gold et al., 2015; Hellwig et al., 2022). The neurologists seemed to be cautious in their prescription of DMTs to women with mild to moderate RRMS, particularly with fingolimod (which is contraindicated during pregnancy) and teriflunomide (not recommended) (Varytè et al., 2021). In contrast, MENACTRIMS guidelines recommend using IFN β , Glatiramer acetate, teriflunomide, and dimethyl fumarate as first-line for mild to moderate disease, and fingolimod or siponimod for patients with contraindications or adverse effects. In case of suboptimal response, MENACTRIMS suggests therapy escalation with fingolimod, siponimod, natalizumab, cladribine tablets or ocrelizumab (Yamout et al., 2020).

Cladribine tablets, natalizumab, and ocrelizumab were reported as the top three treatments physicians would discuss with their patients with highly active MS. MENACTRIMS recommendations for the highly active disease are to use fingolimod, siponimod, natalizumab, cladribine tablets or ocrelizumab as first-line. Therapy escalation with natalizumab, alemtuzumab, cladribine tablets or ocrelizumab will follow if a patient with the highly active disease does not respond to first-line treatments (Yamout et al., 2020).

For treatment naïve patients with highly active disease, cladribine tablets, ocrelizumab, and natalizumab were the top treatment choices. Treatment choices are often determined by factors such as cost-effectiveness and availability, resulting in varying results across different countries. The stratification of the data showed that cladribine tablets were the first choice in countries where it was available. Further, IFN β -1a SC was preferred for treating mild to moderate RRMS across all NE countries due to its widespread availability, despite the unique challenges each it faces. The study findings revealed that ocrelizumab was more commonly used than rituximab. This trend could be attributed to the fact that rituximab lacks regulatory approval from entities such as the EMA and FDA, rendering it ineligible for insurance coverage. In contrast, ocrelizumab is extensively covered by insurance, which could explain its higher usage rate.

The results of our study showed that the neurologists surveyed predict that in five years' time, ocrelizumab, cladribine tablets, and dimethyl fumarate will be prescribed more frequently for managing mild to moderate activity RRMS, while GA and IFN β will be prescribed less frequently, according to their opinions. This highlights a future trend for neurologists to adopt the "hit hard early" strategy. Attacking hard early on showed superiority in deleterious disease outcomes after a few years of treatments in several phase II and III studies (Hauser et al., 2017; Kappos et al., 2011; Montalban et al., 2017). This could also be attributed to GA and IFN β 's route of administration and acute adverse events. The primary advantage of IFN β and GA is their safety, as also reported in our study. However, their drawbacks, as mentioned above, have led to poor adherence (Devonshire et al., 2011). In managing high disease activity RRMS, most participants think cladribine tablets and ocrelizumab will be prescribed significantly more in five years. This could be due to the relatively better safety profile of these two drugs, amongst others used for highly active disease.

When asked about upcoming DMTs, no clear differentiation was found in the positioning of the different DMTs, except for BTK inhibitors. Many physicians lack knowledge about BTK inhibitors, the newest of the four. This lack of information was also noticed when neurologists were asked to rate their expectations for using the upcoming DMTs based on their efficacy/safety profile. Ofatumumab and siponimod received the highest percentages, with around 30% of neurologists reporting they would probably use them based on their efficacy/safety profile. Nevertheless, most participants admitted not having clinical information about the upcoming DMTs.

5. Limitations

This study employed a comprehensive methodology to investigate the current and future prescribing habits of neurologists in the NE region for managing patients with MS. One of the strengths of this study is the

involvement of a panel of expert neurologists from the 5 countries involved. Their insights and expertise helped in shaping the questionnaire and ensuring its relevance to the NE region.

Despite these strengths, several limitations should be acknowledged. First, the study's reliance on self-reporting through an online survey introduces the potential for response bias and self-selection bias. Neurologists who chose to participate may differ from those who did not, potentially influencing the generalizability of the findings. Additionally, participants may not fully understand the questions being asked in the online questionnaire; however, they had the option of contacting the investigator if they found themselves in this situation.

Further, the use of a convenience sampling method via snowball sampling may have introduced selection biases, as the sample may not be fully representative of all neurologists in the NE region. Information bias through social desirability may be present; however, the online nature and the anonymity of the data collection procedure minimize this bias.

Lastly, the specific healthcare systems, cultural contexts, and resource availability in the NE countries may influence prescribing decisions and limit the applicability of the study's results in different regions. Moreover, the gender distribution among neurologists is imbalanced in the NE region, with more male neurologists, especially among those with 15 to 20 years of experience. This gender imbalance further restricts the generalizability of the findings to populations with different gender distributions as gender might influence prescribing habits.

6. Conclusion

This study showed that cladribine tablets, ocrelizumab, and natalizumab were reported as the top treatment choices for treatment naïve patients with highly active disease in NE countries, with cladribine tablets being the first choice in countries where it was available. IFN β -1a SC was the first treatment choice when treating mild to moderate RRMS based on its efficacy; this was true in all NE countries. Also, neurologists seemed to follow MENACTRIMS recommendations.

IFN β -1a SC is considered the safest DMT, while alemtuzumab was rated the least safe.

Neurologists see increased cladribine tablets and ocrelizumab prescribing for managing mild to moderate activity RRMS and high disease activity MS in the future. In addition, there is a clear need for real-world data, long-term extension studies, and comparative studies concerning newcomers, especially for BTK inhibitors. Ultimately, neurologists would want to prescribe medication that would simplify the treatment algorithm and control the disease efficiently and safely.

CRedit author statement

All authors listed have significantly contributed to the development and the writing of this article.

Role of funding source

This study was sponsored by Merck Serono Middle East FZ-Ltd., Dubai, UAE, an affiliate of Merck KGaA, Darmstadt, Germany (Cross-Ref Funder ID: 10.13039/100009945). Editing support was provided by Rouba Zeidan of MEDCON and was funded by Merck Serono Middle East FZ-Ltd., Dubai, UAE, an affiliate of Merck KGaA, Darmstadt, Germany (Cross-Ref Funder ID: 10.13039/100009945).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.msard.2023.104800](https://doi.org/10.1016/j.msard.2023.104800).

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