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Neuroimmunological Shifts in Disease-Modifying Therapy Use Among Multiple Sclerosis Patients: A Regional Study from Sulaymaniyah, Iraq

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Background: Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system with a growing global prevalence. In Iraq, diagnostic rates are increasing alongside changes in environmental exposures. ***Objective***: To describe the regional epidemiological burden of MS and the patterns of disease-modifying therapy (DMT) prescriptions in Sulaymaniyah, stratified by gender, age, and temporal changes in therapeutic approaches to immune-targeted treatments. ***Methods***: This retrospective, registry-based observational study utilized data from the Shar Hospital MS registry (2007-2025). A total of 697 confirmed MS cases were identified, of which 643 were eligible for therapeutic analysis. Extracted variables included age, sex, residential area, and prescribed DMTs. Temporal changes in DMT prescribing and associations between sex and DMT type were analyzed using chi-square tests, while age differences by sex were assessed using independent-samples t-tests. ***Results***: The cohort was mainly female (72.6%), with a mean age of 42.86±13 years. No significant difference in mean age was seen between sexes (p=0.60). DMT prescribing patterns changed notably over time (p<0.001), with less use of broad immunomodulators such as fingolimod and interferon beta and more use of high-efficacy immune-targeted therapies, especially B-cell-depleting monoclonal antibodies. No statistically significant link was found between sex and DMT type (p=0.066). ***Conclusions***: In this registry-based cohort, MS mainly affected females, and DMT prescribing shifted over time toward higher-efficacy immune-targeted therapies. Prospective studies incorporating clinical outcomes such as relapse activity, disability progression, and MRI measures are needed to assess the effectiveness and long-term impact of these evolving treatment strategies in this setting.

Keywords: Disease-modifying therapy; Corticosteroids; Geographical distribution; Multiple Sclerosis.

التحولات المناعية العصبية في استخدام العلاجات المعدلة للأمراض بين مرضى التصلب المتعدد: دراسة إقليمية من السليمانية، العراق

الخلاصة

الخلفية: التصلب المتعدد (MS) هو مرض مزمن يسبب إزالة المياة في الجهاز العصبي المركزي مع انتشار متزايد عالميا. في العراق تزداد معدلات التشخيص جنبا إلى جنب مع التغيرات في التعرضات البيئية. **الهدف**: وصف العبء الوبائي الإقليمي لمرض التصلب المتعدد وأنماط وصفات العلاجات المعدلة للمرض (DMT) في السليمانية، مع تصنيفها حسب الجنس والعمر والتغيرات الزمنية في الأساليب العلاجية الموجهة للمناعة. **الطرائق**: استخدمت هذه الدراسة الرصدية القائمة على السجلات بأثر رجعي بيانات من سجل التصلب المتعدد في مستشفى شار (2007-2025). تم تحديد ما مجموعه 697 حالة مؤكدة للتصلب المتعدد، منها 643 مؤهلة للتحليل العلاجي. شملت المتغيرات المستخرجة العمر، الجنس، المنطقة السكنية، والأدوية الموصوفة DMT. تم تحليل التغيرات الزمنية في وصف DMT والارتباطات بين الجنس ونوع DMT باستخدام اختبارات كاي-تربيع، بينما تم تقييم الفروق العمرية حسب الجنس باستخدام اختبارات t العينات المستقلة. **النتائج**: كانت المجموعة في الغالب إناث (72.6٪)، بمتوسط عمر 42.86±13 سنة. لم يلاحظ فرق كبير في متوسط العمر بين الجنسين (p=0.60). تغيرت أنماط وصف DMT بشكل ملحوظ مع مرور الوقت (p<0.001)، مع تقليل استخدام معدلات المناعة الواسعة مثل فينغوليمود وإنترفيرون بيتا واستخدام أكثر للعلاجات المناعية عالية الفعالية، خاصة الأجسام المضادة وحيدة النسيلة التي تستنزف خلايا B. لم يتم العثور على علاقة ذات دلالة إحصائية بين الجنس ونوع DMT (p=0.066). **الاستنتاجات**: في هذه المجموعة القائمة على السجل، كان التصلب المتعدد يؤثر بشكل رئيسي على الإناث، وتحول وصف DMT مع مرور الوقت نحو علاجات مناعية أكثر فعالية. هناك حاجة إلى دراسات مستقبلية تتضمن نتائج سريرية مثل الانتكاس، وتطور الإعاقة، ومقاييس الرنين المغناطيسي لتقييم فعالية وتأثير هذه الاستراتيجيات العلاجية المتطورة في هذا السياق.

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INTRODUCTION

Multiple sclerosis (MS) is a chronic, immune-mediated disease of the central nervous system (CNS) characterized by inflammatory demyelination and neuroaxonal injury. These pathological processes disrupt neural signal transmission within the brain, spinal cord, and optic nerves, leading to diverse neurological manifestations, including sensory disturbances, motor weakness, gait impairment, and visual dysfunction. MS is driven by dysregulated immune responses mediated by T cells, B cells, and pro-inflammatory cytokine networks directed against the CNS. Over time, many patients develop progressive tissue damage associated with sustained disability and reduced health-related quality of life [1]. Despite significant progress in understanding MS immunopathology, the underlying causes remain uncertain, and there is no cure. However, disease-modifying therapies can minimize inflammatory disease activity, reduce the frequency of relapses, and, in many

patients, delay the progression of disability [2]. The global burden of MS is increasing. In 2020, approximately 2.8 million people were living with MS worldwide, representing a significant rise compared to 2013 [3]. Researchers widely acknowledge the existence of sex differences in MS. The female-to-male ratio is about 2:1 and can reach 4:1 in some regions, suggesting interactions between genetic susceptibility, hormonal factors, and environmental exposures [4,5]. In the United States, nearly 1 million individuals were diagnosed with MS by 2019, emphasizing the growing public health challenge and the need to improve long-term management strategies [6]. In Iraq, prevalence is also increasing. A retrospective study of 4,355 patients (2000-2018) found that 4.07% of cases were diagnosed before age 18, and the female-to-male ratio was approximately 2.18:1. These findings highlight the rising burden and the necessity for region-specific interventions. Additionally, the overall prevalence in Iraq has been estimated at 11.73 per 100,000 population. The rate among children under 12 was 0.26 per 100,000. The age at diagnosis ranged from 8 to 61 years, with a mean of 32.3 ± 9.8 years and a median of 32 [7]. Management of MS includes treating acute relapses, addressing symptoms, and long-term disease modification with disease-modifying therapies (DMTs), which decrease inflammatory activity and may slow disability progression [8,9]. Common DMTs include interferon beta, which mainly modulates cytokine signalling; fingolimod, which restricts lymphocyte egress and T-cell migration; and ocrelizumab, a monoclonal antibody that depletes B cells [8]. The choice of DMTs depends on disease phenotype and activity, as well as factors like drug availability, cost, clinician preference, and patient characteristics [10]. Access to higher-efficacy therapies in Iraq, including Sulaymaniyah city, is often inconsistent, with treatment options governed by public health policy and local prescribing guidelines. Understanding current prescribing habits is crucial for identifying care gaps and improving patient outcomes. This study aims to characterize the local epidemiological burden of MS and analyze prescribing trends of disease-modifying therapies. The study aims to guide clinical decision-making and optimize therapeutic strategies within the regional context.

METHODS

Study design and setting

A retrospective, registry-based observational study was carried out at the Multiple Sclerosis (MS) unit of Shar Hospital in Sulaymaniyah, Iraq. Data from the Shar Hospital MS registry, including MS cases documented between 2007 and 2025, were utilized. Data extraction and cleaning took place from March to May 2025 using the hospital's electronic database. The main objectives were to characterize the local and regional epidemiological profile of MS and to analyze temporal trends in the prescribing of disease-modifying therapy (DMT) (Figure 1).

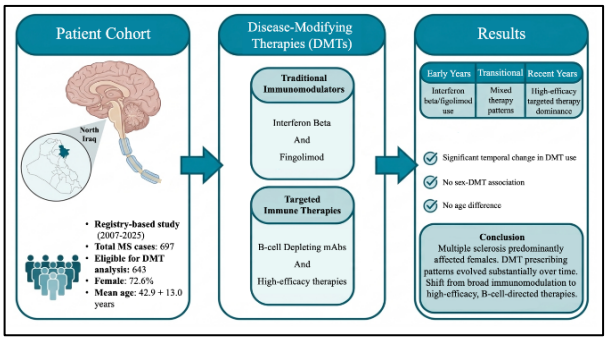


Figure 1: Flow chart diagram.

Participants and sample size

Eligibility criteria included a confirmed MS diagnosis recorded in the Shar Hospital MS registry between 2007 and 2025 and sufficient data for relevant analyses. Records lacking key demographic variables (age, sex, or residential area) were excluded from analyses that required them. For treatment-related analyses, patients who were transferred, misdiagnosed, or deceased prior to treatment initiation were excluded. Additionally, patients with primary progressive MS who had not started treatment and those documented by the treating physician as ineligible for treatment were excluded.

Data collection and handling

Data were collected from the MS unit of the Neurology Department at Shar Hospital, following approval from the hospital administration and the Ministry of Health in Sulaymaniyah. Extracted variables included demographic information (age, sex), residential area, and prescribed disease-modifying therapies (DMTs). Documented therapies comprised fingolimod, teriflunomide, rituximab, ocrelizumab, natalizumab, mitoxantrone, and interferon beta-1a and beta-1b. Geographic distribution was assessed based on recorded residential areas. Data management was carried out in Microsoft Excel for sorting, grouping, and preparing for analysis. Documentation completeness varied by calendar year, notably in early registry entries, resulting in some cases being ineligible for specific analyses.

Ethical approval and data protection

This study adhered to established ethical principles concerning patient privacy and data protection. No personally identifiable information, such as names or contact details, was accessed. The Ministry of Health in Sulaymaniyah officially authorized access to the necessary clinical data for research purposes, with permission granted by both the administration of Shar Hospital and the MS unit within the Neurology Department (Approval number 4310, date 09.03.2025). All data were handled with strict confidentiality and used solely for this study.

Statistical analysis

Categorical variables were summarized as frequencies and proportions. Continuous variables were reported as mean with standard deviation or median with interquartile range, as appropriate. Temporal variation in DMT prescribing and associations between sex and DMT type were evaluated using chi-square tests. Differences in age by sex were assessed using independent-samples t-tests.

RESULTS

A total of 697 patients with multiple sclerosis were initially identified in the Shar Hospital MS registry. Thirty-four cases were excluded due to incomplete records or missing key demographic information such as age, sex, or residential data, leaving 663 patients eligible for the primary analyses. A subsequent data review resulted in the exclusion of six patients due to death, 26 because of transfer to other hospitals, and two due to ineligibility for treatment. Two patients were reclassified as misdiagnosed, 15 patients with primary progressive multiple sclerosis had not commenced treatment, and three patients either declined or discontinued treatment. After these exclusions, 609 patients remained eligible for demographic analyses and assessments of treatment eligibility. Of these, 609 patients had complete demographic data for age and sex analyses, while 476 had complete medication data for treatment-related analyses. Among the 609 patients included, 442 (72.6%) were female, and 167 (27.4%) were male. The mean age of the study population was 42.86 ± 13 years. The most common age group was 40-49 years (29.2%), followed by 50–59 years (23.6%). No statistically significant difference in age was observed between female and male patients (Table 1).

Table 1: Demographic features of the study population (n=609)

Variables	Groups	Result n(%)
Gender	Male	167(27.4)
	Female	442(72.6)
Geographical distribution	Sulaymaniyah	415(68.2)
	Kirkuk	71(11.7)
	Chamchamal	16(2.6)
	Xanaqeen	14(2.3)
	Darbandixan	9(1.5)
	Kalar	9(1.5)
	Halabja	9(1.5)
	Others	66(10.8)
Age	10 – 19	14(2.3)
	20 – 29	66(10.8)
	30 – 39	132(21.7)
	40 – 49	178(29.2)
	50 – 59	144(23.6)
	60 – 69	64(10.5)
	≥ 70	11(1.8)

For treatment-related analyses, disease-modifying therapy (DMT) prescribing patterns were assessed among patients with available medication data (n= 476) (Tables 2 and 3).

Table 2: Observed frequencies between time interval and medications used

Medications	Number of patients throughout the years				Total
	2008-2012	2013-2016	2017-2020	2021-2024	
Gilenya	26	32	25	19	102
BF	34	48	42	39	163
Rituximab	16	24	29	37	106
Ocrevus	0	14	23	35	72
Aubagio	0	3	9	21	33
Total	76	121	128	151	476

Table 3: Expected frequencies between time intervals and medications used

Medications	Number of patients throughout the years				*p*-value
	2008-2012	2013-2016	2017-2020	2021-2024	
Gilenya	16.3	25.9	27.4	32.3	
BF	26	41.4	43.8	51	
Rituximab	16.9	26.9	28.5	33.7	<0.001
Ocrevus	11.5	18.3	19.4	22.9	
Aubagio	5.3	8.4	8.9	10.5	

The relationship between DMT type and sex was also examined within this group. The findings show a notable temporal change in the use of disease-modifying therapy (DMT). The Chi-square test (χ^2 = 58.83, df = 12, p< 0.001) confirms that the use of older medications, such as interferon beta (BF) and Gilenya, has decreased, while newer agents, including Ocrevus and Aubagio, have become more prominent. The expected frequency table provides statistical support, and the line chart illustrates trends across four-time intervals (Figure 2).

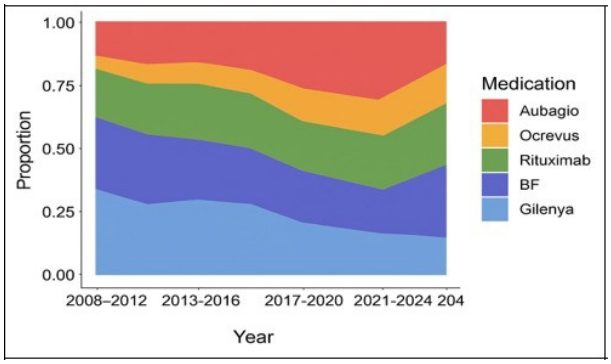


Figure 2: This chart visually captures how medication usage has shifted across the four-time intervals. It reflects the significant trend revealed by the Chi-square test with older medications like BF and Gilenya declining and newer ones like Ocrevus and Aubagio rising over time.

DISCUSSION

This registry-based cohort from Sulaymaniyah shows that multiple sclerosis mainly affects females, with an average age in the early forties and a peak disease burden during middle age. These findings provide region-specific insights into MS epidemiology in Iraq and reflect global trends of rising MS prevalence, likely due to improved diagnostic methods and advances in immune-targeted treatments [1]. The observed female predominance (72.6%) matches the widely recognized global female-to-male ratio of about 2:1, a pattern linked to hormonal influences on immune regulation and differences in T- and B-cell responses [11]. Regional studies from Iran have also noted similar sex

distributions, further supporting the consistency of this pattern across neighboring populations [4]. The average age of the cohort (42.86 years) aligns with findings from other Middle Eastern MS populations, where diagnosis usually occurs between 34 and 38 years. The slightly higher age observed in Sulaymaniyah may reflect regional variations in environmental exposures, healthcare access, or immune-related disease dynamics [12]. In contrast, diaspora cohorts often report a younger age at diagnosis, around 30 years, suggesting possible influences from genetic background, lifestyle, or environmental factors on immune activation and disease onset [13]. No statistically significant age difference was found between male and female patients in this cohort, consistent with large population-based analyses, including previous studies that report nearly identical mean ages between the sexes [14]. Small discrepancies seen in other cohorts might be due to context-specific demographic or methodological factors rather than genuine biological differences [15]. A notable temporal shift towards high-efficacy immune-targeted disease-modifying therapies was observed ($\chi^2 = 58.83$, df = 12, $p < 0.001$). Over time, the use of first-generation immunomodulators such as interferon beta (BF) and fingolimod (Gilenya) declined, while the adoption of newer agents, including ocrelizumab (Ocrevus) and teriflunomide (Aubagio), increased. This transition reflects a broader change in MS treatment strategy that favors early initiation of high-efficacy therapies, especially those targeting B-cell–mediated immune mechanisms through anti-CD20 monoclonal antibodies [16]. Recent evidence supports this approach, demonstrating reduced disability progression and improved long-term outcomes with early aggressive immune intervention [17]. Despite this therapeutic progress, no significant link was found between patient sex and disease-modifying therapy (DMT) choice ($\chi^2 = 8.78$, df = 4, $p= 0.066$), suggesting that prescribing decisions are mainly based on disease course and clinical judgment rather than gender. This aligns with previous findings that MS treatment strategies are largely sex-neutral in routine clinical practice [18]. However, evidence of potential sex-related differences in treatment response hints at the possibility of future outcome-driven, gender-stratified therapeutic approaches [19]. Furthermore, while many low- and middle-income countries still face barriers to accessing high-efficacy therapies, the rising use of these agents in Sulaymaniyah indicates partial alleviation of such challenges and closer adherence to international treatment standards [20]. Several limitations must be recognized. The retrospective design and dependence on registry data pose the risk of missing documentation, especially in earlier years, which can lead to underreporting of clinical variables. Moreover, the lack of longitudinal outcome measures, such as relapse frequency, disability progression, MRI activity, and pharmacoeconomic data, restricts the assessment of the long-term clinical and immunological effects of changing treatment strategies. Future prospective studies that incorporate clinical, radiological, and immunological outcomes are essential to enhance MS management and to further develop immune-targeted therapies in this region.

Conclusion

Analysis of the Shar Hospital multiple sclerosis registry (2007–2024) identified 697 confirmed cases, of which 476 had complete medication data for analyzing disease-modifying therapy. The cohort was predominantly female, with a mean age of 42.86 years. Prescribing patterns changed significantly across the four time points, with decreased use of fingolimod and increased use of higher-efficacy therapies, particularly rituximab and ocrelizumab. Future research should investigate patient outcomes following treatment and utilize larger study samples to obtain more robust data.

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Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

The data that supports the findings of this study are available from the corresponding author upon a reasonable request.

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