REVISION OF MULTIPLE SCLEROSIS CASES ACCORDING TO NEW 2017 MCDONALD CRITERIA AMONG DIAGNOSED PATIENTS IN SULAIMANI CITY

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ABSTRACT

Background

Multiple sclerosis (MS) is a chronic, immune-mediated inflammatory disorder of the central nervous system. The diagnosis of Multiple sclerosis is challenging, owing to having a comprehensive list of differentials and mimickers.

Objectives

To determine the frequency of misdiagnosed Multiple Sclerosis cases diagnosed among those patients in Sulaimani city.

Patients and and Methods

This retrospective observational study was conducted within a period between December 24th. 2019 and June 10th, 2020, on 106 already diagnosed patients. The study included patients diagnosed with the relapse-remitting form of multiple sclerosis. We excluded those patients with progressive forms of multiple sclerosis. We re-evaluated each patient in-depth and stratified the cases according to the diagnosis certainty based on the fulfillment of the 2017 McDonald Criteria. Finally, we returned those suspicious cases to the multiple sclerosis committee of Shar hospital to verify their final diagnosis.

Results

Sixteen (16.9%) out of 106 patients, there was diagnostic uncertainty in which 6 (5.7%) of them received the confirmatory diagnosis of relapse-remitting multiple sclerosis by the committee, and 1(0.9%) patient considered secondary progressive multiple sclerosis. In the remaining 9 (8.4%) patients, we found the clinically isolated syndrome in 5 (4.7%) patients, solitary sclerosis in 1 (0.9%) patient, stroke with polycythemia rubra vera (PRV) in 1 (0.9%) patient, possible cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy in 1 (0.9%) patient, and 1 (0.9 %) patient was undiagnosed.

Conclusion

To sum up, the frequency of multiple sclerosis misdiagnosis was 8.4% in Sulaimani city, slightly lower than the other reporting centers.

Keywords: *Multiple sclerosis, 2017 McDonald criteria, Misdiagnosis, Clinically isolated syndrome, Relapse-remitting MS.*

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INTRODUCTION

Multiple sclerosis is the most prevalent chronic, dysimmune, and inflammatory disorder of the central nervous system (CNS)[1]. The global median prevalence of MS has increased from 30/100,000 in 2008 to 33/100,000 in 2013, according to a report by the MS International Federation [2]. According to the most recent data, MS sufferers worldwide are about 2.5 million persons, and among them, 500,000 are located in the United States [3]. MS affects a wide range of age groups from early childhood to the elderly population, in which its peak is between 20 and 40 years of age [3]. MS is 1.5 to 3 times more prevalent in women than men among all age groups [3]. MS is multifactorial, in which both environmental factors (like low serum vitamin D level, hormonal factors, and obesity) and immunogenetics (like The major histocompatibility complex (MHC)) are played a significant role in the etiology of the disease [2]. The infiltration of perivascular space characterizes the pathological hallmark of MS by autoreactive lymphocytes and activated macrophages resulting in the breakdown of the myelin sheaths that wrap around neurons and the development of demyelinating plaques in the brain and spinal cord, which can be coexisting with neuro-axonal damage [4–6]. Neurological manifestations reflecting these demyelinating plaques are varied [7]. They mostly include vision symptoms, dizziness, focal weakness and clumsiness, sensory impairment such as numbness and tingling, sphincter problem, incoordination, imbalance, gait impairment, fatigue, and cognitive dysfunction [8–10]. Patients may suffer from other paroxysmal symptoms such as intermittent dysarthria, ataxia, itching, transient akinesia, and radicular thoracic sensations of pain or tightness (so-called MS hug), Pulfrich phenomenon, Uhthoff phenomenon, and the useless hand of Oppenheim [11]. Importantly, the lesions' location predicts most of the MS presentations' clinical manifestation, though some symptoms (e.g., fatigue, cognitive dysfunction) are poorly localized within the brain[4]. The MS presentation should meet both dissemination of various neurological symptoms over time and space caused by multiple demyelinating lesions in the CNS [12]. Generally, MS has been classified into three phases, the high-risk phase, the relapsing-remitting phase, and the progressive phase, in which each one of them is characterized by clear phenotypes [13]. These phases are not necessarily discrete and often overlap for some time [12]. MS first shows a relapsing-remitting course, transitioning to a secondary progressive course about 10–20 years after onset [12]. Most MS cases can be diagnosed by clinical or clinical and imaging parameters alone [14]. These should be applied appropriately, and other causes of CNS inflammatory white matter disease (so-called MS mimickers) are ruled out, usually by history, appropriate blood tests, and occasionally by CSF analysis [15]. Visual evoked potential (VEP) recordings or optical coherence tomography (OCT) are usually unnecessary [16]. Still, in a particular situation, they might be of major benefit, especially in the setting of retrobulbar optic neuritis [17]. The McDonald Criteria for diagnosis of MS has been revised many times; the last time was revised in 2017 [18]. The McDonald criteria best validated for those presenting with typical MS syndromes; otherwise, in atypical MS syndromes, the criteria cannot be applied [19]. The typical MS syndromes include unilateral optic neuritis, a partial brainstem syndrome, which may include isolated cranial nerve deficits (including trigeminal neuralgia) but more typically internuclear ophthalmoplegia (unilateral or bilateral); partial cerebellar syndromes, and sensory impairment or motor weakness localizing to the spinal cord, with partial or full recovery [20]. This last revised 2017 McDonald criterion has been validated to reach the diagnosis of MS earlier to initiate disease-modifying therapy as soon as possible and preventing the patient from possible future disabling relapses [21]. The recent 2017 McDonald Criteria for Diagnosis relapse remitting MS is shown (Table 1) [21]. Magnetic resonance imaging (MRI) is the best choice to support MS clinical diagnosis[12]. MS lesions have a propensity to affect specific white matter areas, such as the periventricular and juxtacortical regions, corpus callosum, infratentorial regions (notably the pons and cerebellum), and the spinal cord (preferentially the cervical segment) [22]. The characteristic MS lesions are ovoid, hyperintense on proton density and T2-weighted studies, hypointense on T1-weighted images (so-called black holes). They may enhance either ring-enhancing (closed or open ring) or nodular enhancement in an active lesion[22]. The differential diagnosis of MS is comprehensive, which largely depends on the clinical scenario, including many inflammatory, vascular, infectious, genetic, granulomatous, and other demyelinating disorders [12]. There are different ways in addressing that exhausting list of differentials, and there are also lists of clinical, imaging, laboratory, and CSF red flags and pitfalls that offer a better explanation than MS that can aid in narrowing and better addressing the differentials [12]. Treatment for multiple sclerosis over

the last two decades has undergone a massive change [13]. Several drugs are now present, all of them targeting the disease's inflammatory process [13]. The treatment of MS divides into acute relapse treatment, long term treatment, and symptomatic treatment of MS-related complications [13].

Table 1. The 2017 McDonald Criteria for Diagnosis of Multiple Sclerosis in Patients With an Attack at Onset [a,b].

Number of Clinical Attacks	Number of Lesions With Objective Clinical Evidence	Additional Data Needed for a Diagnosis of Multiple Sclerosis
≥2	≥2	None [c]
≥2	1 (as well as clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomic location d)	None [c]
≥2	1	Dissemination in space demonstrated by an additional clinical attack implicating a different central nervous system site or by MRI
1	≥2	Dissemination in time demonstrated by an additional clinical attack or by MRI or demonstration of CSF-specific oligoclonal bands [e]
1	1	Dissemination in space demonstrated by an additional clinical attack implicating a different central nervous system site or by MRI And Dissemination in time demonstrated by an additional clinical attack or by MRI or demonstration of CSF-specific oligoclonal bands [e]

CSF = cerebrospinal fluid; MRI = magnetic resonance imaging.

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b If the 2017 McDonald criteria are fulfilled, and no better explanation exists for the clinical presentation, the diagnosis is multiple sclerosis. If multiple sclerosis is suspected by a clinically isolated syndrome, but the 2017 McDonald criteria are not completely met, the diagnosis is possible multiple sclerosis. If another diagnosis arises during the evaluation that better explains the clinical presentation, the diagnosis is not multiple sclerosis.

c No additional tests are required to demonstrate dissemination in space and time. However, unless MRI is not possible, brain MRI should be obtained in all patients in whom the diagnosis of multiple sclerosis is being considered. In addition, spinal cord MRI or CSF examination should be considered in patients with insufficient clinical and MRI evidence supporting multiple sclerosis, with a presentation other than a typical clinically isolated syndrome, or with atypical features. If imaging or another test (e.g., CSF) is undertaken and is negative, caution needs to be taken before making a diagnosis of multiple sclerosis, and alternative diagnoses should be considered.

d Clinical diagnosis based on objective clinical findings for two attacks is most secure. Reasonable historical evidence for one past attack, in the absence of documented objective neurologic findings, can include historical events with symptoms and evolution characteristics for a previous inflammatory demyelinating attack; at least one attack, however, must be supported by objective findings. In the absence of residual objective evidence, caution is needed.

e The presence of CSF-specific oligoclonal bands does not demonstrate dissemination in time per se but can substitute for the requirement for demonstration of this measure.

PATIENTS AND METHODS

This prospective observational study was conducted within a period between December 24th. 2019 and June 10th, 2020. This study was conducted after granting permission from the scientific committee of the faculty of medical sciences. The inclusion criteria included those patients that have been diagnosed as a relapse-remitting MS regardless of time course from diagnosis. The exclusion criteria comprised patients diagnosed with clinically isolated syndrome, radiologically isolated syndrome, primary progressive MS, and those who transitioned to secondary progressive MS. All records of diagnosed MS cases are available in the data registry of the MS department of Shar hospital. Based on those available data, we dismissed the unwanted population for our research. Simple random sampling was followed to select our sample size. We had randomly contacted 152 patients, but 126 of them were agreed to participate, and 106 patients finally attended the study. The patients first provided informed consent through a phone call about their participation in our study, and every detail about our research was clarified. The patients were evaluated through a direct questionnaire-based interview in the MS clinic of Shar hospital on patients' preference dates. The questionnaire provided a detailed patient history, thorough general and neurological examination, laboratory results, CSF findings, and comprehensive imaging findings. The questionnaire was written on three-sheet pages during the interview, then transferred into Microsoft excel. The patient's recoded file and their relatives or caregivers were involved when taking the history of previous relapses. A comprehensive neurological examination was done for every patient, including cranial nerves, motor, sensory, cerebellar, gait, and signs of meningeal irritation except mental state examination, detailed olfactory assessment, and calculation of The Expanded Disability Status Scale (EDSS score). The laboratory results were thoroughly analyzed, and the investigations were ordered depending on our time window. The imaging findings were extensively interpreted. The numbers of the suggestive MS lesions were calculated in each of five areas mentioned in the McDonald criteria (Periventricular, cortical, juxtacortical, infratentorial, and spinal cord) as well as atypical areas. The patients were divided into two groups. The first group was those patients in which their clinical and imaging findings fulfill the 2017 McDonald criteria. The second group was those cases where the minimum 2017 McDonald criteria were not met or had diagnostic pitfalls and red flags that point to better explanations than MS. The suspicious cases were thoroughly evaluated, and the necessary workup was sent according to the study's time frame. The MS committee of Shar hospital re-evaluated all doubtful cases and decided about each case's final diagnosis. The "IBM SPSS Statistics version 25" was used to analyze the data, and both descriptive and inferential statistics were used. Furthermore, P-values of ($\leq$0.05 and <0.001) were considered as statistically significant and highly significant associations, respectively. Also, Pearson Chi-Square was used to determine the significance of the association between independent and dependent categorical variable pairs.

RESULTS

Demographic information relevant to the disease

One hundred and six patients participated in our study, which they were diagnosed with MS between 1999 to 2019. the female cases were 81 (76.4%) patients whereas male cases were 25 (23.6%) with Female: Male ratio = 3.24. The mean age was 36.17 ± 9.59 (SD), in which the minimum age was 13, and the maximum was 62 (Figure 1). Eight (7.5%) patients were smokers compared to 98(92.5%) non-smokers, and only 1 (0.9%) case reported regular alcohol ingestion. The family history for MS was positive in 2 (1.9%) cases.

Clinical phenotypes and objective clinical evidence

Visual complaints were the most common initial presentation, while cerebellar and sensory deficits were the least clinically presenting feature (Figure 2). Historywise, with the utilization of recorded data and clinical examination, we revealed that 11 (10.3%) patients presented with atypical MS syndromes in which 4 (3.7%) of them were diagnosed as other than MS, 95 (89.7%) patients with typical symptoms and 4 (3.7%) patients with a combination of both. The number of misdiagnosed patients presented with atypical syndromes had at least one clinical or imaging red flag pointing to an alternative diagnosis. On clinical examination, 62 (58.5%), 18 (17%), 15 (19.8%) patients had abnormal motor, sensory, and cerebellar findings, respectively. Our cranial nerve examination findings depicted that all cases had a normal olfactory, hearing, glossopharyngeal, vagus, Spinal accessory, and Hypoglossal nerve function. Furthermore, seven patients (6.6%) had residual trigeminal neuropathy, and eight (7.6%) patients had an abnormal facial examination. Visual acuity was impaired in 32 (30.2%)

cases, field defect observed in 9 (8.5%) cases, a color problem in 33 (31.5%), an enlarged blind spot in 2 (1.8 %), and optic atrophy in 54 (50.8%) cases.

Final diagnosis after revision

In 90 (84.9%) cases, the definite relapse-remitting MS (RRMS) was established by the 2017 McDonald criteria. In 16 (15.1%) patients, there was uncertainty regarding the fulfillment of the 2017 McDonald criteria, and they were returned to the MS committee to be reviewed. Among the reviewed cases, 5 (4.7%) cases were again diagnosed as RRMS, and one patient was diagnosed as a secondary progressive MS; the rest of the patients were diagnosed as shown in (Table 2).

Imaging findings

All of the participants had at least one initial brain MRI at the time of diagnosis. During our observation, the maximum number of lesions counted in the periventricular area is contrary to the minimum number of lesions observed in infra-tentorial regions (Figure 3). Spinal cord MRI was done only for 32 (30.1%) patients in which 15 (14.1%) subjects were normal, and 17 (16.03%) participants showed spinal cord lesions. All of the cord lesions localized to the cervico-dorsal region, and all of them were peripherally located. There was short segment involvement (not more than two spinal segments) in 10 (9.4%) patients, and 7 (6.6%) participants depicted long segment involvement (3 or more spinal segments). Finally, there was no significant association between spinal cord lesions and the final diagnosis. The association between MS-specific involvement regions and the final diagnosis is shown (Table 3, Table 4, Table 5, and Table 6)

CSF Markers

Twelve (11.3%) patients were required to send for CSF aquaporin-4 immunoglobulin G (AQP4-IgG) testing, and all of them were normal. The CSF anti-MOG antibody was done for 7 (6.6%) subjects; again, all were normal. Finally, among 16 (15.1%) patients sent for oligoclonal band detection in the CSF, only 6 (5.7%) were positive without identifying its pattern, and none of the misdiagnosed patients was undergone CSF oligoclonal band testing.

Disease-modifying therapy exposure

All misdiagnosed patients have been exposed to ≥ 1 disease-modifying therapy. The shortest drug exposure was one year, and the longest was nine years, with a mean duration of 4±2.7 (SD) years. None of the CIS patients experienced a clinical relapse while they were put on disease-modifying therapies..

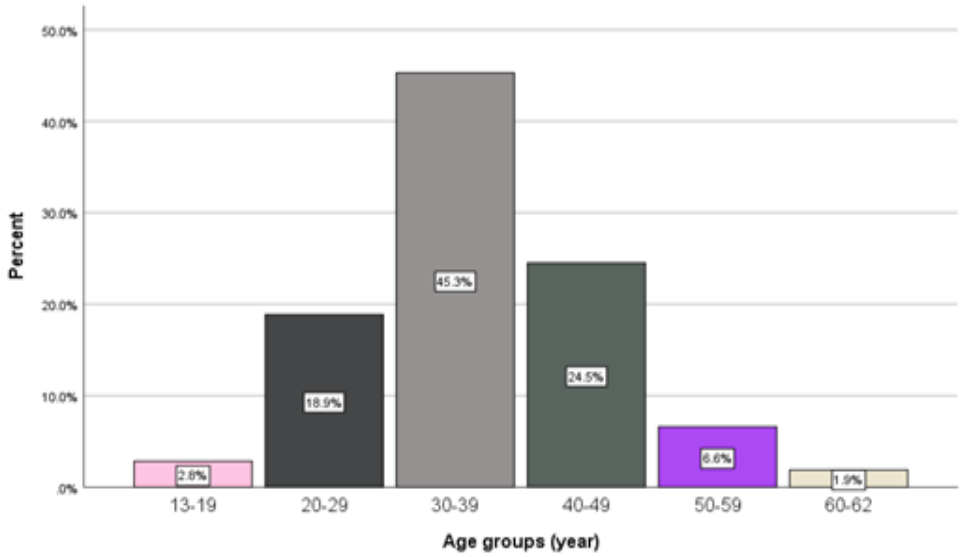

Figure 1. Age distribution.

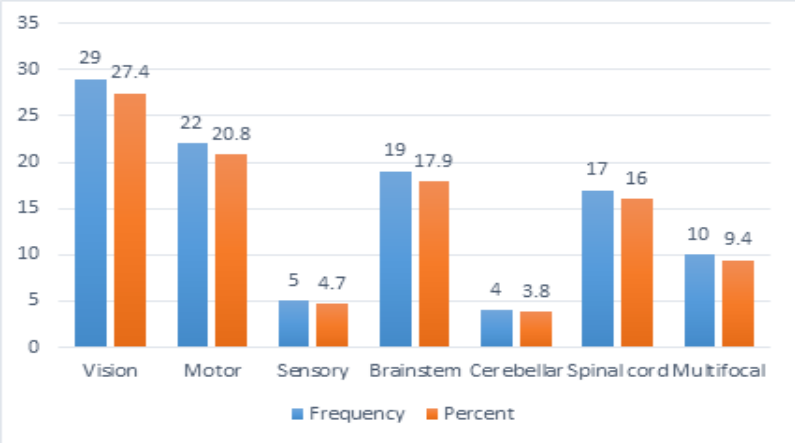

Figure 2. Initial clinical presentations

Table 2. The revised cases and their final diagnosis

Reviewed by committee			Final diagnosis		
			MS (%)	Not MS (%)	Total (%)
Yes	**Final diagnosis if not MS**	**RRMS**	6 (5.7)	0 (0)	6 (5.7)
		CIS	0 (0)	5 (4.7)	5 (4.7)
		Possible CADASIL	0 (0)	1 (0.9)	1 (0.9)
		Secondary progressive MS	1 (0.9)	0 (0)	1 (0.9)
		Solitary sclerosis	0 (0)	1 (0.9)	1 (0.9)
		Stroke with polycythemia vera	0 (0)	1 (0.9)	1 (0.9)
		Undiagnosed	0 (0)	1 (0.9)	1 (0.9)
	Total		7 (6.6)	9 (8.4)	16 (15.1)
No	**Definite RRMS**		90 (84.9)	0 (0)	90 (84.9)
	Total		90 (84.9)	0 (0)	90 (84.9)
Grand total			97 (91.5)	9 (8.4)	106 (100)

RRMS:Relapse-remitting multiple sclerosis, CIS: Clinically isolated syndrome,
CADASIL:Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy.

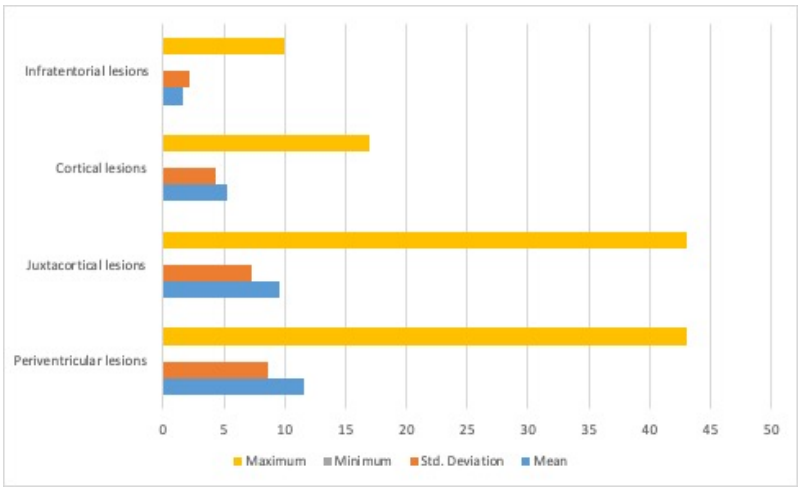

Figure 3. The distribution of lesions in the MS-specific regions.

Table 3. The association between cortical lesions and the final diagnosis.

Brain MRI		Final diagnosis		Total	p-value
		MS	Not MS		
Number of Cortical lesions	0-5	57	8	65	**0.016**
		53.8%	7.5%	61.3%	
	6-10	24	0	24	
		22.6%	0.0%	22.6%	
	11-15	10	0	10	
		9.4%	0.0%	9.4%	
	16-20	3	0	3	
		2.8%	0.0%	2.8%	
	>40	2	2	4	
		1.9%	1.9%	3.8%	
Total		96	10	106	
		90.6%	9.4%	100.0%	

Table 4. The association between periventricular lesions and the final diagnosis.

Brain MRI		Final diagnosis		Total	p-value
		MS	Not MS		
Number of Periventricular lesions	0-5	18	8	26	**<0.001**
		17.0%	7.5%	24.5%	
	6-10	30	0	30	
		28.3%	0.0%	28.3%	
	11-15	21	0	21	
		19.8%	0.0%	19.8%	
	16-20	15	0	15	
		14.2%	0.0%	14.2%	
	21-25	5	0	5	
		4.7%	0.0%	4.7%	
	26-30	3	0	3	
		2.8%	0.0%	2.8%	
	31-35	1	0	1	
		0.9%	0.0%	0.9%	
	>40	3	2	5	
		2.8%	1.9%	4.7%	
Total		96	10	106	
		90.6%	9.4%	100.0%	

Table 5. The association between infra-tentorial lesions and the final diagnosis.

Brain MRI		Final diagnosis		Total	p-value
		MS	Not MS		
Number of Infratentorial	0-5	89	8	97	0.002
		84.0%	7.5%	91.5%	
	6-10	6	0	6	
		5.7%	0.0%	5.7%	
	>40	1	2	3	
		0.9%	1.9%	2.8%	
Total		96	10	106	
		90.6%	9.4%	100.0%	

Table 6. The association between juxtacortical lesions and the final diagnosis.

Brain MRI		Final diagnosis		Total	p-value
		MS	Not MS		
Number of Juxtacortical	0-5	28	7	35	0.008
		26.4%	6.6%	33.0%	
	6-10	30	1	31	
		28.3%	0.9%	29.2%	
	11-15	22	0	22	
		20.8%	0.0%	20.8%	
	16-20	10	0	10	
		9.4%	0.0%	9.4%	
	21-25	2	0	2	
		1.9%	0.0%	1.9%	
	26-30	2	0	2	
		1.9%	0.0%	1.9%	
	>40	2	2	4	
		1.9%	1.9%	3.8%	
Total		96	10	106	
		90.6%	9.4%	100.0%	

DISCUSSION

The new 2017 revised McDonald criteria came with significant changes that helped the patients receive early diagnosis and initiation of appropriate therapy. It also provides recommendations to avoid misdiagnosis, which allows being explicitly applied for those patients presenting with typical MS syndromes [23,24]. Our study was conducted on 106 MS patients in which the diagnosis of 16 (16.9%) of them was questionable.

After the revision by the Shar hospital committee, 6 (5.7%) of them received the confirmatory diagnosis of relapse-remitting MS, and 1(0.9%) patient considered secondary progressive MS. In the remaining 9 (8.4%) patients, we found the clinically isolated syndrome in 5 (4.7%) patients, solitary sclerosis in 1 (0.9%) patient, stroke with polycythemia rubra vera (PRV) in 1 (0.9%) patient, and 2 (1.8%) patients were undiagnosed. In one of the two undiagnosed patients, we found typical clinical and radiological features of CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy). However, the patient refused to do further workup. Further analysis of the demographic data showed that most misdiagnosed patients were female with the female: male ratio of 8:1. Although the exact prevalence of MS misdiagnosis is still unknown and varied, it is a common problem in clinical practice.

A multicenter case series consisting of patients who had been erroneously diagnosed with MS depicted that over 50% carried the MS misdiagnosis for at least three years, and 5% were misdiagnosed for over 20 years. In another study on those referral patients to MS subspeciality centers with a question of MS diagnosis, 30%–67% were finally determined not to have MS [19, 23, 25]. We found that the diagnosis error arose in the two forms. The first form is an over-estimation of typical MS syndromes by early MS diagnosis assignment, which happened in 5 CIS patients. The second form is having a low index of suspicion in those patients present with atypical syndromes or having red flags that occurred in 3 patients. The most abundant clinical presentation was visual complaints, specifically optic nerve involvement, which corroborates the previous results [26]. According to a study conducted on 695 patients, 93.9% of the patients presented with typical MS symptoms, 6.1% with atypical MS symptoms, and 13.2% with a combination of both typical and atypical symptoms. The same survey concluded that 13.5% of patients received the alternative diagnosis in which migraine, neuromyelitis spectrum disorders, CIS, and nonspecific white matter abnormalities were among the most frequent alternative diagnoses, respectively [5]. Our results differ to some extent from this study in which typical MS symptoms encountered in a higher number of patients 11 (10.3%) in contrast to a lower number of typical 95 (89.7%) and combined 4 (3.7%) typical and typical symptoms [5].

There was a general agreement regarding the predilection of MS lesion to the aforementioned brain and spinal cord areas (periventricular, juxtacortical, infratentorial, and spinal cord) in which the cortical lesions were recently added to the criteria [27]. Our study provides additional evidence for a significant association between these areas and the final MS diagnosis except for the spinal cord lesions in which the association was insignificant (p-value = 0.711) (data not shown). This might be explained by the fact that a limited number of patients underwent spinal cord imaging [28]. Although CSF oligoclonal band testing is not necessary for every patient, especially those with typical clinical and MRI findings, but can provide supportive paraclinical evidence of multiple sclerosis and substitutes the dissemination of time according to the new criteria [29]. In our study, few numbers of patients, 16 (15.1%), had CSF aspiration for oligoclonal band testing, which showed no significant statistical association with the final diagnosis. None of the misdiagnosed patients had been performed CSF oligoclonal band testing, including CIS patients. Given that our findings regarding CSF oligoclonal band are based on a limited number of patients, the results from such analysis should consequently be treated with the utmost caution [30].

The most remarkable result of the data is that despite hazardous erroneous drug exposure among CIS patients, none of them experienced a clinical relapse. We should sound a note of caution concerning such findings because it could be an effect of disease-modifying therapy or be adventitious findings. We can assume three chief contributors affecting the diagnostic accuracy of the patients based on the recommendations from the McDonald criteria 2017.

Firstly, the criteria warrant regarding those patients presenting with atypical syndromes with corresponding clinical and imaging red flags in which they should receive a prompt evaluation for alternative diagnoses before making a decision. In that regard, the fulfillment of more than the minimum requirements of the

McDonald criteria is necessary to avoid misdiagnoses, which was a problem in four misdiagnosed patients [25].

The second diagnostic pitfall was a rush in assigning MS diagnoses among CIS patients. They were all lacking the dissemination in time criteria that could be reached with finding an oligoclonal band in the CSF. However, none of them underwent CSF aspiration, especially two patients whose diagnosis was made after 2017 [14,31].

Finally, during our observation, we found that 4 out of 5 CIS patients have presented with a varying degree of visual loss, which may have a significant psychological impact on the patients in which all of them stated that they could not tolerate another attack affecting their vision. From our point of view, the patients also might have been involved in early decision-making.

It is plausible that several limitations might have influenced the results obtained. As anticipated, there were some discrepancies between the recorded clinical attacks and what some patients reported, which a recalling bias might contaminate our data. However, the authors of the 2017 revisions to the McDonald criteria have recommended the proper use of para-clinical (i.e., visual evoked potentials, CSF examination) and radiographic data to substitute for a second clinical attack; unfortunately, due to a restricted time window, we depended only on objective clinical findings which is a downside of our data [24]. Another source of error was the non-uniformity among MRI qualities and slice thicknesses. The restricted use of paraclinical testing was disappointing, especially CSF oligoclonal band testing, which could significantly affect the diagnostic decision and reduce misdiagnosis. We assume three satisfactory explanations for this low number of CSF-OCB testing. Firstly, most of the patients willingly refused to do it; secondly, the local laboratories have little experience in CSF-OCB testing and patterns; thirdly, some patients had been diagnosed before CSF-OCB testing gained popularity in our locality.

In conclusion, even though the misdiagnosis of MS is uncommon in our locality, it is slightly lower than the other reporting centers. According to our study, the most commonly encountered alternative diagnosis was clinically isolated syndrome (CIS) followed by solitary sclerosis, stroke with polycythemia vera, possible CADASIL, and undiagnosed.

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