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Epidemiological, clinical, and therapeutic profile of patients with multiple sclerosis and neuromyelitis optica spectrum in reference centers of Belo Horizonte

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RESUMO

Introdução: Esclerose Múltipla (EM) e Espectro da Neuromielite Óptica (ENMO) são doenças autoimunes e inflamatórias do Sistema Nervoso Central. A EM é mais prevalente que a ENMO, e em ambas se sugere que haja fatores genéticos e ambientais envolvidos. **Objetivo**: Avaliar aspectos epidemiológicos, clínicos e terapêuticos de pacientes diagnosticados com EM e ENMO em centros de referência de Belo Horizonte. **Método**: Estudo observacional, descritivo, longitudinal retrospectivo, realizado com pacientes de dois centros de referência em Belo Horizonte. Foram incluídos maiores de 18 anos, diagnosticados com ENMO ou EM com os critérios atuais. Foram analisadas variáveis epidemiológicas, clínicas e terapêuticas extraídas dos prontuários. Utilizou-se frequência simples e percentual para as variáveis qualitativas e a mediana e o intervalo interquartílico para as quantitativas. **Resultados:** 61 pacientes foram incluídos (57 com EM e 4 com ENMO). 82,0% eram mulheres, a maioria com EM era branca (58,0%) e com ENMO não branca (100,0%). A idade média ao diagnóstico foi de 34 anos na EM e 47 no ENMO. Os transtornos de saúde mental foram os mais prevalentes na EM (31,0%) e no ENMO (50,0%). Sintomas sensitivos foram os mais frequentes na EM (58,0%) e no ENMO (50,0%). 88,0% dos pacientes com EM e 75,0% dos com ENMO estavam em uso de medicamentos. **Conclusão:** O perfil dos pacientes avaliados é semelhante ao retratado na literatura. As principais limitações do estudo incluem método retrospectivo, amostra reduzida e ausência de registro de algumas variáveis em prontuários. Encorajamos a realização de mais trabalhos em outras regiões do Brasil.

Palavras-chave: Neuromielite óptica; Esclerose múltipla; Epidemiologia; Sinais e Sintomas.

ABSTRACT

Introduction: Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorder (NMOSD) are autoimmune and inflammatory diseases of the Central Nervous System. MS is more prevalent than NMOSD, and for both, it is thought that genetic and environmental factors may be involved. **Objectives**: To evaluate epidemiological, clinical, and therapeutic features of patients diagnosed with MS and NMOSD in two medical services in Belo Horizonte

Methods: Observational, descriptive, longitudinal retrospective study performed with patients from two medical services in Belo Horizonte. Individuals older than 18 years, diagnosed with NMOSD and MS with the current criteria were included. Epidemiological, clinical, and therapeutic data extracted from medical records were analyzed. Simple frequency and percentage were used for qualitative variables, and median and interquartile range were used for quantitative variables. **Results**: 61 patients were included (57 with MS and 4 with NMOSD). 82.0% were women, the majority with MS were white (58.0%), and with NMOSD, non-white (100.0%). The mean age at diagnosis was 34 years in MS and 47 in NMOSD. Mental health disorders were the most prevalent comorbidity in MS (31.0%) and NMOSD (50.0%). Sensory symptoms were the most frequently reported (MS: 58.0% x NMOSD: 50.0%). 88.0% of MS patients and 75.0% of NMOSD patients were on medication. **Conclusion**: The profile of the patients evaluated is similar to that portrayed in the literature. The main limitations of this study include the retrospective method, the limited sample size, and the absence of records of some features in medical records. We encourage more studies to be executed in other regions of Brazil.

Keywords: Neuromyelitis Optica; Multiple Sclerosis; Epidemiology.

INTRODUCTION

Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorder (NMOSD) are long-term neurological diseases characterized by demyelination of the Central Nervous System (CNS). MS affects multiple regions of the CNS, including the white matter and gray matter of the brain, cerebellum, brainstem, spinal cord, and optic nerve, presenting with a variety of neurological deficits[1]. NMOSD encompasses a group of diseases that primarily affect the optic nerve and spinal cord but can also involve the brain, diencephalon, and the area postrema, the latter being a highly characteristic structure compromised by the disease. The anti-aquaporin 4 antibody is present in approximately 75.0% of patients, being responsible for attacking the water channel found abundantly in the podocytes of astrocytes, cells of the CNS. Some patients may test negative for anti-aquaporin 4 but can still receive an NMOSD diagnosis if they meet the diagnostic criteria of Wingerchuk 2015[2,3]. In both diseases, incomplete recovery after relapses can lead to permanent neurological damage with accumulating morbidity.

The conditions are considered rare. According to the latest updates from the International Federation of Multiple Sclerosis Societies, approximately 2.8 million people worldwide were living with MS in 2020, and 2.9 million in 2023[4,5]. For NMOSD, the global prevalence is around 100,000 cases[6]. The incidence and prevalence of MS and NMOSD vary significantly across different regions, mainly due to geographical location and ethnicity[3,4]. In Brazil, the average prevalence of MS is estimated at 12.5 per 100,000 inhabitants, with 30,000 individuals affected[4], and 18.1 per 100,000 in Belo Horizonte Horizonte[7]. For NMOSD, the rates range from 0.5 to 10 cases per 100,000 inhabitants in various countries[2], with a rate of 4.52 cases per 100,000 in Belo Horizonte[7].

These variations support the hypothesis that environmental, genetic, and epigenetic factors contribute to the pathogenesis of MS and NMOSD, although the etiology of the diseases remains not fully understood. The most implicated environmental risks for MS include living in countries far from the equator, vitamin D deficiency, smoking, obesity, and Epstein-Barr virus infection. For NMOSD, individuals of African and Asian descent are at higher risk. Other factors under discussion include low exposure to infections in childhood, poor diet, smoking, and vitamin D deficiency. Both diseases predominantly affect women; MS typically af-

fects adults between 20 and 40 years of age, while the average age of onset for NMOSD is 39 years[1,2,3,8].

Clinically, MS presents in three phenotypes: relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS). RRMS is characterized by relapse episodes, marked by acute neurological deficits lasting more than 24 hours and the absence of fever, infection, or other causes that could explain the symptoms. Examples of signs and symptoms include motor deficits (monoparesis, paraparesis, hemiparesis), sensory deficits (reduction or loss of one or more sensations), cerebellar deficits (imbalance, incoordination, dysdiadochokinesia), visual deficits (reduced visual function with pain on eye movement), among others. Each relapse may result in complete or partial recovery with accumulated disability. Most of these patients progress to SPMS in the absence of treatment, characterized by a predominance of disability progression independent of relapses. PPMS does not exhibit the initial relapsing phase of RRMS; patients typically experience a gradual increase in disability independent of relapses. Additionally, two other classifications are not considered phenotypes: isolated radiological syndrome (IRS) and isolated clinical syndrome (ICS). IRS is described as having radiological findings suggestive of demyelination on MRI with typical MS characteristics but without clinical manifestations. ICS refers to a single clinical episode suggestive of demyelination without dissemination in time (events separated by more than a month) that meets MS diagnostic criteria[8].

NMOSD is primarily characterized by optic neuritis, usually with severe visual impairment, and transverse myelitis, which is often longitudinally extensive (LTME) and tends to cause severe neurological deficits. Optic neuritis affects the optic nerve, with characteristics including ocular pain, especially with movement, and associated vision reduction or loss. Motor and sensory symptoms primarily occur when there is demyelination of the spinal cord. Other syndromes include area postrema syndrome, diencephalic syndrome, and cerebral syndrome. The area postrema syndrome is associated with the involvement of a specific area in the brainstem, manifesting as intractable nausea and vomiting. The diencephalic syndrome is characterized by narcolepsy and neuroendocrine disorders. The cerebral syndrome presents with hemiparesis, sensory losses, and encephalopathies[9].

Disability in NMOSD patients results from the accumulation of damage from each relapse. Therefore, preventing recurrent attacks is essential and is achieved through early diagnosis and preventive treatment[10]. Previous analyses have found that a significant number of NMOSD patients were initially misdiagnosed with MS by their first physicians, and many MS treatments can exacerbate NMOSD. Fortunately, diagnostic delays have significantly decreased in recent years due to factors such as high-sensitivity and specificity anti-aquaporin-4 antibody tests[11].

Both diseases are incurable, with treatment focused on providing the best possible prognosis for the patient. Treatment is divided into relapse management, preventive therapy, and symptomatic therapy. Acute event treatment typically involves high doses of intravenous corticosteroids and, in severe cases, plasmapheresis. Preventive treatment is managed with immunomodulatory or immunosuppressive medications. Despite both being demyelinating diseases, the preventive treatments may differ. Symptomatic treatments aim to mitigate the effects of the disease, such as tremor, spasticity, and fatigue[1,12,13].

Belo Horizonte, the capital of the state of Minas Gerais, is located in the Southeast region of Brazil at a latitude of 19° 48’ 57” South and a longitude of 43° 57’ 15” West. Known for its hills and mountains, it is situated 852 meters above sea level. According to

the Köppen-Geiger climate classification, it has a Cwa climate or subtropical with a dry winter and hot summer. Throughout the year, temperatures are mild and pleasant, generally ranging from 13°C to 29°C, with an annual average of 20.8°C and an average annual humidity of 68.0%. According to the latest census by the Brazilian Institute of Geography and Statistics (IBGE), the city covers an area of approximately 331 km² with a population of 2,315,560. In 2010, women accounted for 53.1% of the population, while men accounted for 46.8%. Regarding ethnicity, 46.3% self-identified as white, 42.1% as mixed-race, 10.2% as black, 1.0% as yellow, and 0.1% as indigenous[14].

This study aims to describe the epidemiological, clinical, and therapeutic aspects of patients diagnosed with MS and NMOSD at referral centers in Belo Horizonte.

METHOD

Study Design

This is an observational, descriptive, longitudinal retrospective study conducted at two reference centers for the care of patients with demyelinating diseases located in Belo Horizonte, Minas Gerais, Brazil. The study was carried out between October 2022 and October 2023.

Sample

The sample size calculation for patients with MS and NMOSD at the studied centers was performed using the following formula:

Figure 1 - Sample Size Calculation Formula

$$n = \frac{z^2_{(1-\gamma)/2} N p(1-p)}{d^2(N-1) + z^2_{(1-\gamma)/2} p(1-p)}$$

Where:
n = sample size
z(1−α) = tabulated value
N = population
p = prevalence
(1−p) = complementary value
d = maximum error

Considering a finite population with N=130 patients affected by the diseases as the estimated population in the reference centers, the calculation was performed to estimate a finite sample size. With a significance level of 5.0%, an error of 10.0%, and a conservative estimate for *p*^ (considered 50.0%), the sample size was determined as 56 participants.

The target population of the study included individuals with Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorder (NMOSD) who receive medical follow-up at the referenced health service. Eligible participants were individuals over 18 years of age, diagnosed with NMOSD according to the Wingerchuk 2015 criteria, and diagnosed with MS according to the McDonald 2017 criteria. Exclusion criteria included individuals under 18 years of age and those who did not meet the established criteria, as well as cases with diagnostic uncertainty.

Instruments

Epidemiological, clinical, radiological, and therapeutic variables were analyzed from medical records.

The epidemiological variables examined included: sex, skin color, age, alcohol use, and smoking. Clinical and radiological variables analyzed included: age at disease onset, number of relapses before disease diagnosis, disease duration, level of disability, number of relapses during follow-up, presence of comorbidities, presence of other autoimmune diseases, presence of lesions on cervical, thoracic, and lumbar spinal MRI, and brain MRI, lesion topography on brain MRI, and initial symptoms at disease onset. Clinical phenotype and oligoclonal bands (OCB) testing were analyzed only for participants with MS, and anti-aquaporin 4 (anti-AQP4) antibody testing was conducted solely for participants with NMOSD. Finally, the therapeutic variables analyzed included: current medication therapy and previously used medications.

Neurological disability level was assessed using the Expanded Disability Status Scale (EDSS), originally developed for MS but also the most used for NMOSD.

Procedures

The sample was obtained by approaching patients with MS and NMOSD who attended their respective hospitals for medical care between April and July 2023. After an initial explanation, the consent form was provided for review. Only those who met the inclusion criteria, voluntarily agreed to participate, and signed the consent form were included.

Variables were collected by a review of participants' medical records and recorded in a specially developed electronic spreadsheet in Excel. Personal data were not collected, and participants were identified by numerical codes.

This study was reviewed by the Research Ethics Committee (CEP) of the Faculdade de Ciências Médicas de Minas Gerais (FCM-MG) under protocol 64779922.0.0000.5134 and was approved with Opinion No. 5.840.251. Additional approval was granted by the CEPs of the participating institutions where data collection took place. The research was conducted following the ethical principles of Resolution 466/12 of the National Health Council.

Statistical Analysis

Simple frequency and percentage were used to characterize qualitative variables, while median and interquartile range were used for quantitative variables. The software used for analysis was R version 4.3.1.

RESULTS

A total of 61 patients were included, comprising 57 with MS and 4 with NMOSD. Female patients were more prevalent in both groups (75.0% in MS vs. 100.0% in NMOSD), with a gender ratio of 3:1 in the MS group. In the MS group, most patients were white (58.0%), whereas the sole NMOSD patient evaluated was non-white. Diagnoses in both groups occurred in relatively young patients; however, NMOSD patients were diagnosed more than a decade later than those with MS. The average time to diagnosis was significantly longer for NMOSD compared to MS (10.2 years vs. 4 years), which may have contributed to the later age at diagnosis. Most MS patients were non-smokers (85.0%). Epidemiological data are detailed in Table 1.

Table 1 – Epidemiological data of patients with MS and NMOSD from two reference centers in Belo Horizonte

	Disease	
Epidemiological data	**Multiple Sclerosis**, n = 57	**Neuromyelitis Optica Spectrum**, n = 4
Sex		
Female	43 (75.0%)	4 (100.0%)
Male	14 (25.0%)	0 (0.0%)
Age	41 (33, 4%)	56 (52, 5%)
<20 years	1 (1.8%)	0 (0.0%)
21-30 years	10 (18.0%)	0 (0.0%)
31-40 years	17 (30.0%)	0 (0.0%)
41-50 years	17 (30.0%)	1 (25.0%)
51-60 years	5 (8.8%)	2 (50.0%)
>60 years	7 (12.0%)	1 (25.0%)
Skin color		
White	11 (58.0%)	0 (0.0%)
Non-white	8 (42.0%)	1 (100.0%)
Alcohol use		
No	19 (59.0%)	3 (75.0%)
Yes	13 (41.0%)	1 (25.0%)
Smoking		
No	28 (85.0%)	4 (100.0%)
Yes	5 (15.0%)	0 (0.0%)
Smoking history		
No	2 (25.0%)	0 (0.0%)
Yes	6 (75.0%)	1 (100.0%)

Regarding comorbidities, mental health disorders showed significant prevalence in both diseases (31.0% in MS vs. 50.0% in NMOSD). RRMS was the most prevalent clinical phenotype with 52 patients (96.0%), followed by SPMS with 2 patients (4.0%). Concerning the initial symptoms manifested in MS, sensory symptoms were present in 31 patients (58.0%), motor symptoms in 23 patients (43.0%), brainstem symptoms in 10 patients (19.0%), visual symptoms in 9 patients (17.0%), and other symptoms in 4 patients (7.4%). In NMOSD, motor and sensory symptoms were present in 2 patients (50.0%), other symptoms in 2 patients (50.0%), and visual symptoms in 1 patient (25.0%). NMOSD was found to be more aggressive, with half of the patients experiencing more than 3 relapses before diagnosis, whereas only a minority of MS patients exhibited this characteristic (18.0%). Furthermore, after diagnosis, NMOSD patients showed a higher frequency of relapses compared to MS patients. Regarding medication therapies,

50 patients (88.0%) with MS and 3 patients (75.0%) with NMOSD were undergoing treatment at the same time of data collection. In both groups, most patients were being treated with high-efficacy therapies. Details on clinical and therapeutic data are listed in Table 2. The frequency of medication use according to the disease can be seen in Figure 2.

Table 2 – Clinical and therapeutic data of patients with MS and NMOSD from two reference centers in Belo Horizonte

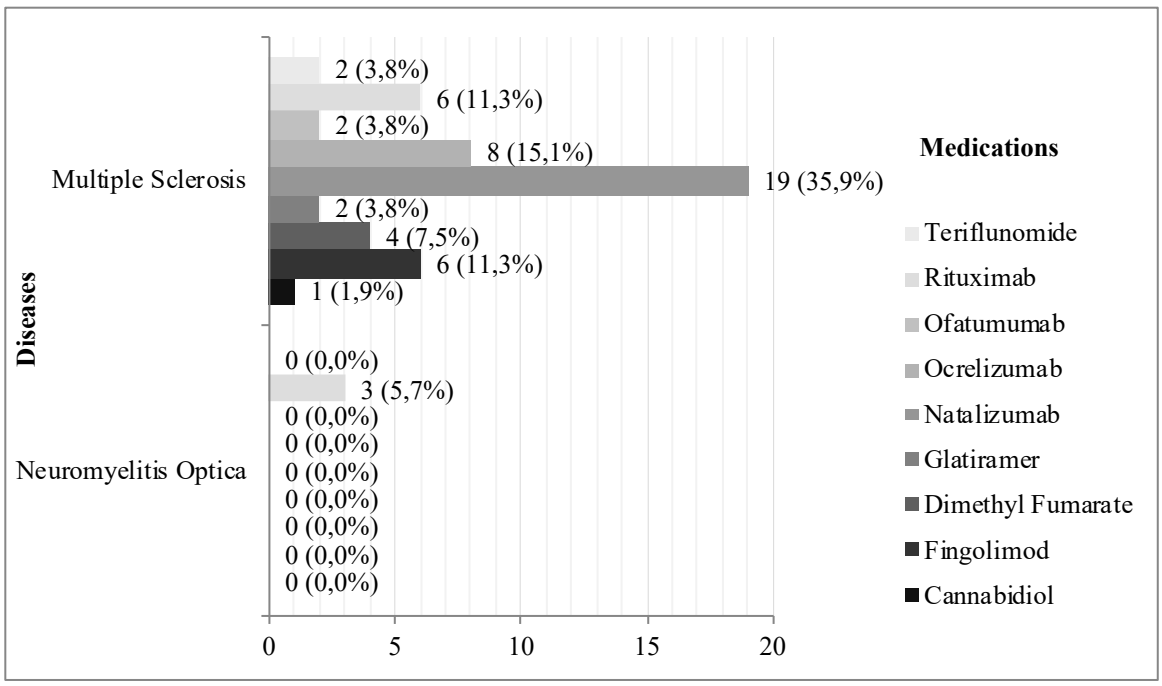
	Disease	
Clinical data	**Multiple Sclerosis**, n = 57	**Neuromyelitis Optica Spectrum**, n = 4
Age at disease onset		
<20 years	2 (3.5%)	0 (0.0%)
21-30 years	22 (39.0%)	0 (0.0%)
31-40 years	18 (32.0%)	1 (25.0%)
41-50 years	8 (14.0%)	2 (50.0%)
51-60 years	5 (8.8%)	1 (25.0%)
>60 years	2 (3.5%)	0 (0.0%)
Relapses before diagnosis		
≥3 relapses	9 (18.0%)	2 (50.0%)
<3 relapses	40 (82.0%)	2 (50.0%)
Disease duration		
<1 year	13 (23.0%)	0 (0.0%)
1-5 years	19 (33.0%)	1 (25.0%)
6-10 years	9 (16.0%)	1 (25.0%)
>10 years	16 (28.0%)	2 (50.0%)
First EDSS		
0-5	33 (80.0%)	1 (33.0%)
5,5-9,5	8 (20.0%)	2 (67.0%)
Last EDSS		
0-5	30 (75.0%)	1 (33.0%)
5,5-9,5	10 (25.0%)	2 (67.0%)
Relapses after diagnosis		
≥3 surtos	7 (14.0%)	2 (50.0%)
<3 surtos	44 (86.0%)	2 (50.0%)
Comorbities		
No	19 (35.0%)	1 (25.0%)
Yes	35 (65.0%)	3 (75.0%)
SAH	9 (16.0%)	1 (25.0%)
T2DM	4 (7.3%)	1 (25.0%)

Migraine	7 (13.0%)	0 (0.0%)
Mental health disorders	17 (31.0%)	2 (50.0%)
Other autoimune diaseases	1 (2.0%)	1 (25.0%)
Cervical spine lesion on MRI		
No	9 (26.0%)	0 (0.0%)
Yes	26 (74.0%)	2 (100.0%)
Thoracic spine lesion on MRI		
No	8 (32.0%)	1 (100.0%)
Yes	17 (68.0%)	0 (0.0%)
Lumbar spine lesion on MRI		
No	3 (75.0%)	1 (100.0%)
Yes	1 (25.0%)	0 (0.0%)
Brain lesion on MRI		
No	3 (7.0%)	1 (50.0%)
Yes	40 (93.0%)	1 (50.0%)
Juxtacortical	27 (67.5%)	0 (0.0%)
Periventricular	35 (87.5%)	0 (0.0%)
Infratentorial	26 (65.0%)	1 (100.0%)
First symptons		
Visual	9 (17.0%)	1 (25.0%)
Brainstem	10 (19.0%)	0 (0.0%)
Sensitive	31 (58.0%)	2 (50.0%)
Motor	23 (43.0%)	2 (50.0%)
Others	4 (7.4%)	2 (50.0%)
Aphasia	2 (50.0%)	0 (0.0%)
Seizure	1 (25.0%)	0 (0.0%)
Urinary incontinence	0 (0.0%)	2 (100.0%)
Neuritis	1 (25.0%)	0 (0.0%)
Clinical phenotype		
RRMS	52 (96.0%)	-
SPMS	2 (4.0%)	-
OCB testing		
Not perfomed	1 (4.3%)	0 (0.0%)
Performed	22 (96.0%)	0 (0.0%)
Negative	4 (18.0%)	0 (0.0%)
Positive	18 (82.0%)	0 (0.0%)

Anti-AQP4 testing		
Not performed	1 (3.7%)	0 (0.0%)
Performed	26 (96.0%)	4 (100.0%)
Negative	25 (96.0%)	1 (25.0%)
Positive	1 (3.8%)	3 (75.0%)
Therapeutic data	**Multiple Sclerosis**, n = 57	**Neuromyelitis Optica Spectrum**, n = 4
Current medication		
No	7 (12.0%)	1 (25.0%)
Yes	50 (88.0%)	3 (75.0%)
Previous medication		
No	18 (33.0%)	0 (0.0%)
Yes	37 (67.0%)	4 (100.0%)

Abbreviations: EDDS = Kurtzke Expanded Disability Status Scale; SAH = Systemic Arterial Hypertension; T2DM = Type 2 Diabetes Mellitus; MRI = Magnetic Resonance Imaging; RRMS = Relapsing-Remitting Multiple Sclerosis; SPMS = Secondary Progressive Multiple Sclerosis; OCB = Oligoclonal Bands; anti-AQP4 = Anti-Aquaporin 4.

Figure 2 – Current medication used for the disease



DISCUSSION

In our study, we observed a predominance of both diseases in female individuals, matching what is described in the literature[1,3]. We also noted a higher prevalence among white patients with MS, and the only patient with NMOSD evaluated for this variable was non-white, which is consistent with the majority of international and national epidemiological studies[7,16,17,18,19]. Data on ethnicity were available in only a minority of the records, which is an important aspect to collect in future prospective studies, considering the high degree of miscegenation in the Brazilian population and the wealth of information these data could provide.

It is noteworthy that historically, MS is believed to be more common among white individuals. However, recent evidence has reported changes in the disease's demographics worldwide, showing that its frequency in non-white ethnic groups is higher than initially thought, likely due to underestimation[20]. Additionally, multiple studies have identified worse outcomes in black and Latino populations. This suggests that the origins of such differences may not only be genetic but also related to socioeconomic issues impacting access to healthcare for marginalized populations and in low-income countries[21]. In NMOSD, only one case where ethnicity was recorded was non-white, consistent with descriptive studies in the Caribbean islands, Rio de Janeiro, and Belo Horizonte, which found a predominance of the disease in non-white populations[7].

MS typically affects individuals aged 20-40 years[8]. In reference centers in Belo Horizonte, the average age at diagnosis of MS was 34 years, with the most significant age group being 21-30 years (39.0%). Some studies report an average age of onset for NMOSD as 39 years, while others observed an average of 40 years in patients positive for anti-AQP4[3]. We observed an average age at diagnosis of 47 years, with 50.0% of NMOSD patients within the 41-50 years range. One patient (25.0% of the sample) was within the age range most commonly found in the literature (31-40 years). This small difference in age in our study may be related to the less representative sample of NMOSD patients (4 patients in total), potentially indicating a limitation in the analysis of this data. Additionally, the longer time to diagnose NMOSD may have impacted this result.

Lifestyle habits, such as current and past smoking and alcohol use, were evaluated. Tobacco use is associated with an increased risk of developing and worsening MS. Tobacco use, including passive exposure, is possibly associated with HLA (human leukocyte antigen) genes involved in the risk of developing MS. It has also been observed that there is a dose-response effect, meaning cumulative doses of tobacco are related to an increased risk, with previous smoking being associated with a worse disease prognosis[22]. A similar association has been documented for NMOSD, with evidence suggesting that toxic components of cigarettes may involve epigenetic changes. One study observed an increased likelihood of IgG-seropositivity for NMOSD in smokers[23]. In our study, among the 33 MS patients with information on current smoking, 15.0% were smokers, and among the 8 evaluated for past smoking, 75.0% had a positive history. For NMOSD, all 4 patients were not using tobacco at the time, and only 1 patient was evaluated for past smoking, with a positive result.

Regarding comorbidities, we found that mental health disorders, notably anxiety and depression, were the most prevalent - 31.0% of MS patients had other diseases, and 50.0% of NMOSD patients did. Systemic Arterial Hypertension (SAH) was the second most common condition in MS (16.0%) and NMOSD (25.0%). These trends are consistent with the literature on the subject. Previous diseases are relevant as they are associated with higher relapse rates, greater

physical and cognitive impairment, and increased mortality[24,25]. The higher lifetime prevalence of depression in this population compared to those without these diseases has been widely reported, reaching 50.0% in MS patients and 46.0% in NMOSD patients. In these patients, depression appears to be more severe, with etiological factors including genetic, immunological, and psychosocial components, as well as structural brain changes and neuroinflammation. Comorbid depression is associated with suicidal ideation, poorer treatment adherence, and lower quality of life. Additionally, a meta-analysis identified that anxious symptoms are present in over 60% of patients, which also correlates with lower quality of life in MS/NMOSD patients. Therefore, it is crucial for attending physicians to be attentive to symptoms of these disorders to act preventively and offer early treatment[26].

Regarding symptoms present at the first disease relapse, we observed that sensory symptoms were more common, affecting 58.0% of MS patients and 50.0% of NMOSD patients. Among other symptoms not classified in the major categories (visual, brainstem, sensory, and motor), aphasia found in two MS patients was particularly interesting. It is known that MS patients can present a range of symptoms related to higher cognitive functions, such as language, although less commonly than other cognitive impairments and sensory deficits. Language disorders may occur due to dysarthria, cognitive issues, or cerebellar problems[27].

In our study, 88.0% of MS and 75.0% of NMOSD patients received current treatment with disease-modifying therapies (DMTs). According to the Clinical Protocol and Therapeutic Guidelines for Multiple Sclerosis from the Brazilian Ministry of Health, first-line treatments include beta-interferons, glatiramer, teriflunomide or dimethyl fumarate or azathioprine for low or moderate activity MS, and natalizumab for high activity disease[15]. For the Brazilian Committee for Multiple Sclerosis (BCTRIMS), the first-line treatment is beta-interferons, dimethyl fumarate, glatiramer, pegylated interferon, and teriflunomide for patients with low or moderate activity RRMS, and alemtuzumab, cladribine, fingolimod, natalizumab, or ocrelizumab for high activity RRMS. For active SPMS, ocrelizumab is recommended. Additionally, BCTRIMS consensus highlights the importance of individualizing prescriptions according to patient preferences and needs, relying on current evidence, and performing continuous re-evaluation and monitoring for medication changes to avoid therapeutic inertia[28].

Among MS patients currently using medication at the two reference centers in Belo Horizonte, the majority were using high-efficacy drugs (66.1%), as were NMOSD cases (100.0% using Rituximab), reflecting a treatment profile aiming for the maximum possible disease control. This fact is potentially associated with the relative stability observed in EDSS scores over time, demonstrating the importance of adequate follow-up of these patients in specialized centers, whether public or private, of high quality. Cannabidiol is considered a symptomatic treatment for both diseases, controlling symptoms such as pain, spasticity, and anxiety, with its use becoming more common recently[29]. In the studied group, its use remained uncommon.

The data showed that delays in diagnosing MS and particularly NMOSD are still common, with a minority of patients in both groups having a diagnosis established within less than 1 year after the first clinical symptom, and a considerable group after 5 years (MS 44.0% vs. NMOSD 75.0%). Among the 49 MS patients with documented pre-diagnosis relapses, 18.0% had 3 or more relapses before diagnosis. Among the four NMOSD patients, 50.0% also had more than 3 relapses before diagnosis. The main hypothesis for this finding is related to the fact that most patients do not promptly initiate diagnostic investigation at

reference centers for demyelinating diseases. Barin et al., 2020, argue that one of the factors associated with prolonged time between symptom evaluation and MS diagnosis is contact with a non-neurologist physician who does not perform additional diagnostic actions. Prolonged diagnosis of NMOSD affects patient risks and morbidity[30]. Being rare diseases, still little known, even by the medical community, may interfere with some professionals' inexperience in recognizing a relapse and referring to a specialist. Thus, the importance of studying MS and NMOSD in the Brazilian population is emphasized.

CONCLUSION

Overall, the profile of patients in the evaluated centers is similar to that reported in other national and international series. However, it is important to highlight the limitations of our study, primarily being a retrospective work with convenience sampling. The small sample size and the study's locations (two specialized services in the state capital) may also reduce the external validity of the findings. Another challenge encountered by the researchers was the absence of certain variables in the patient records, which may diminish the representativeness of the information. That said, we believe the objective of describing the characteristics of patients treated at two reference centers in Belo Horizonte was achieved. We hope to have contributed to the epidemiological study of MS and NMOSD, providing a broader understanding of these diseases in our setting, and encouraging further research in other regions of Brazil.

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THE AUTHORS DECLARE THAT THERE IS NO CONFLICT OF INTERESTS IN RELATION TO THIS ARTICLE.