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Clinical Profile of CNS Non-MS Inflammatory Demyelinating Diseases: A Cross-Sectional Observational Study from a Tertiary Care Hospital at Srinagar

Murtaza Noor[1*], Ravouf Asimi[2], Feroze A Mir[3], Mohammad Maqbool Wani[4], Injeela Masoom[5]

[1,2,3,4,5]Department of Neurology, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Jammu & Kashmir, India

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***Corresponding author**:
Dr. Murtaza Noor
Email: murtaza.noor7@gmail.com

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ABSTRACT

Background: Inflammatory non-MS CNS demyelinating diseases includes a heterogeneous group of diseases with varying clinical presentation, extent of neural axis involvement and phenotype severity. This study was done to describe the demographic profile and clinical phenotype of these groups of diseases in order to provide data on the local patterns of disease presentation.

Methods: A cross-sectional observational study comprising 65 patients was performed at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar between October 2022 to June 2024 and data was collected on detailed demographic and clinical profile. Appropriate statistical methods were then applied and data analysis was done.

Results: Neuromyelitis Optica Spectrum Disorder (NMOSD, 40%), Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD, 21.5%), and Acute Disseminated Encephalomyelitis (ADEM, 13.8%) were most common, followed by idiopathic primary central nervous system (CNS) demyelination, optic neuritis (ON), and longitudinally extensive transverse myelitis (LETM). Mean age was 40.2 years; 41.5% were aged 21-40. Among 15 pediatric cases, MOGAD, ADEM, and idiopathic ON predominated. NMOSD and MOGAD showed recurrent disabling patterns affecting spinal cord and optic nerves, while ADEM and CNS demyelination involved supratentorial regions; idiopathic LETM and ON affected spine and optic nerves exclusively.

Conclusion: The study reflects the clinical heterogeneity amongst various groups of non-MS CNS inflammatory demyelinating diseases and also provides data on local demographic patterns.

Key Words: Non-MS Demyelination, NMOSD, MOGAD, Clinical phenotypes, Recurrence

INTRODUCTION

Beyond multiple sclerosis, there is a large spectrum of similar inflammatory demyelinating diseases which have distinct clinical presentations and patterns of involvement of the neural axis. These diseases include NMOSD (Neuromyelitis Optica Spectrum Disorder), MOGAD (Myelin Oligodendrocyte Glycoprotein Antibody Disease), ADEM (Acute Disseminated Encephalomyelitis), Idiopathic cases of LETM (Longitudinally Extensive Trans-

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verse Myelitis) and ON (Optic Neuritis), and some rare cases of idiopathic primary CNS demyelination [1,2], and they share a common pathogenesis of immune mediated demyelination. NMOSD [3] and MOGAD are antibody mediated demyelination and have a characteristic involvement of the optic pathways and the spinal cord with a relapsing course and some differences, whereas ADEM [4] and other cases of primary CNS demyelination are monophasic illnesses with predominant demyelination of the supratentorial white matter. Other idiopathic cases have isolated demyelination of the spinal cord and optic nerves respectively. These idiopathic cases have been noted to be as seronegative disease. There are various demographic and other epidemiological differences amongst these groups of diseases. Nearly all of them have a significant impact on the neurological function at onset being quite severe and disabling, with variable involvement of various parts of the neural axis, however they differ from each other in their natural course and prognosis especially once treatment is instituted. Therefore, it is must to classify these disorders into particular groups and to understand their clinic-etiological spectrum. With this aim, this study was conducted at a tertiary care hospital in Srinagar, J & K UT.

MATERIALS AND METHODS

The current study was a hospital based cross sectional observational study that was conducted in the Department of Neurology at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, from October 2022 to June 2024, following approval from the Institute's Ethics Committee (Approval No. RP 249/2022). Recruitment included all male and female patients aged below (>2 years) as well as above or equal to 18 years who met the diagnostic criteria for inflammatory demyelinating diseases of the central nervous system (CNS) other than multiple sclerosis (MS). These included:

Neuromyelitis optica spectrum disorder (NMOSD): Diagnosed as seropositive when serum aquaporin-4 antibody was positive, and as seronegative when antibody was absent but the patient had at least two core clinical characteristics (such as longitudinally extensive transverse myelitis, bilateral optic neuritis, acute diencephalic syndrome, area postrema syndrome, or acute cerebral syndrome) along with MRI-documented features of these syndromes [1].

Myelin oligodendrocyte glycoprotein antibody-associated disorder (MOGAD): Diagnosed on the basis of any characteristic demyelinating syndrome (including bilateral optic neuritis, myelitis, or brainstem syndrome based on clinical and MRI findings) with serum MOG antibody positivity [5].

Acute disseminated encephalomyelitis (ADEM): Defined as encephalopathy with headache, with or without seizures or focal neurological deficits, occurring in a post-infectious or post-vaccination setting and with MRI showing large multifocal T2/FLAIR hyperintense lesions involving supratentorial white matter, with or without deep grey nuclei involvement [6,7].

Idiopathic transverse myelitis: Cases of longitudinally extensive transverse myelitis, defined on MRI as T2/FLAIR hyperintensity spanning three or more spinal cord segments, with a negative antibody profile for NMOSD and MOGAD [8].

Optic neuritis: Acute onset unilateral or bilateral painful visual loss with MRI-documented T2/FLAIR hyperintensity involving the optic nerves and with no other apparent cause [9].

Primary CNS demyelination: Any atypical non-MS demyelinating CNS disease with MRI showing T2/FLAIR hyperintense lesions in supratentorial white matter, without fulfilling the diagnostic criteria for the other above-mentioned disorders.

Patients were excluded if they had MS; CNS infections causing demyelination (such as progressive multifocal leukoencephalopathy or HIV); demyelination due to metabolic causes (including alcohol abuse, thiamine deficiency, or osmotic demyelination syndrome); ischemic demyelination; or demyelination related to radiation therapy or chemotherapy.

A total of 65 patients who met the inclusion criteria were enrolled in the study after obtaining written informed consent in their vernacular language. Each patient underwent a detailed clinical evaluation (history and examination) to characterize the neurological involvement. Demographic parameters and clinical profile were recorded appropriately. Lifestyle was graded on a subjective scale for sedentary, moderate and heavy [subjective scale used here was taken from ICMR proforma from the Indian MS and allied demyelinating diseases registry] [10]. Educational status was determined as per the standard educational system while as socioeconomic status was assessed as per the modified Kuppuswamy scale [11]. Exposure to sunlight was classified as <3 hours as low and > 3 hours as adequate because evidence suggests that cumulative >3 hours of weekly sun exposure is generally sufficient to maintain optimal vitamin D levels, while <3 hours per week is often inadequate, particularly in individuals with darker skin, limited outdoor activity, or in higher latitudes. Thus, the cut-off of <3 hours as low and >3 hours as adequate exposure is physiologically justified [12]. These patients also underwent routine baseline investigations along with CSF examination for cytology and oligoclonal bands. The serum was tested for Aquaporin 4 antibodies, MOG antibodies and Anti-nuclear antibodies along with anti-Ro and anti La antibodies in cases who were not diagnosed already and were presenting for the first time, a neurovirus panel, triple serologies and serum ACE was also done to rule out and exclude other possibilities for new cases. For cases who had already been diagnosed in the past and had presented either with a relapse or for a follow up, all these above investigations were not repeated. Data was also recorded on the evoked potentials (visual and brainstem auditory) and the radiological (MRI) find-

ings both of which were vital for the diagnosis and categorization of these disease groups. The motor disability score was based on the EDSS score [13]. All this data was systematically recorded using a structured proforma and patients were classified into specific groups as per the individual diagnosis, following which a data analysis was done using appropriate statistical methods, thereby giving a comprehensive assessment of the detailed disease profiles and patterns.

Statistical Analysis: Statistical analysis was performed using SPSS software. Continuous variables were summarized as means and standard deviations, while categorical variables were presented as frequencies and percentages. The student's t-test was employed to compare the means between two groups, while one-way ANOVA was applied for comparisons involving more than two groups. Fisher's exact test was used when the expected value of any cell was less than 5. A p-value of less than 0.05 was considered statistically significant. This methodological approach ensured a comprehensive assessment of the clinical and demographic profiles of patients with non-MS CNS inflammatory demyelinating diseases, allowing for meaningful comparisons and correlations between different disease subtypes.

RESULTS

Neuromyelitis Optica spectrum disorder (NMOSD) was found to be the most common non-MS CNS inflammatory demyelinating disease comprising 40% of the total cohort of patients (combined seropositive and seronegative cases as shown), followed by MOGAD cases of 21.5% and ADEM cases at 13.8%. Majority of the patients overall fell in the age group of 21-40 years followed by younger and middle age groups. There was stronger female preponderance (6:1) in the NMOSD group, as compared to MOGAD and ADEM that showed a more balanced distribution slightly titled towards male sex, and a notable preponderance of males in cases of primary CNS demyelination (Table 1).

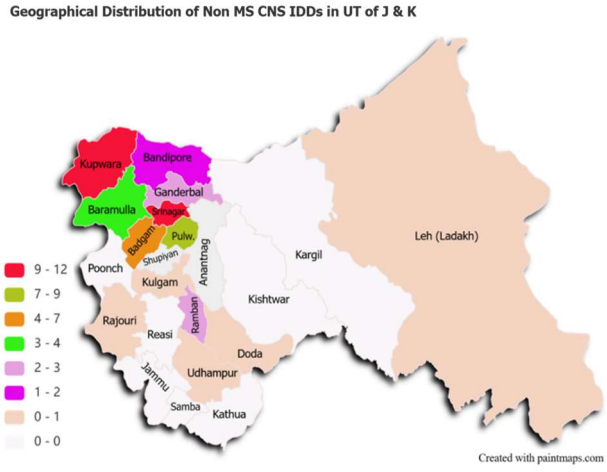

Figure 1: Distribution of patients with non-MS CNS inflammatory demyelinating diseases as per region

Table 1: Distribution of patients with type Non-MS Inflammatory Demyelinating Diseases stratified by sex

Disease Type	Male (%)	Female (%)	Total (%)
Seropositive NMOSD	3 (14.28)	18 (85.71)	21 (32.3)
Seronegative NMOSD	1 (20.00)	4 (80.00)	5 (7.7)
MOGAD	8 (57.14)	6 (42.86)	14 (21.5)
ADEM	5 (55.55)	4 (44.45)	9 (13.8)
CNS Demyelination	4 (80.00)	1 (20.00)	5 (7.7)
Isolated ON/LETM	5 (45.45)	6 (54.55)	11 (16.9)

Table 2: Demographic and Socioeconomic Characteristics of Non-MS Inflammatory Demyelinating Disease Patients

Variable	Cases (%)
Age Distribution	
<20 years	16 (24.6)
21-40 years	27 (41.5)
41-60 years	16 (24.6)
> 61 years	6 (9.2)
Geographical Distribution	
South Zone*	20 (30.76)
North Zone**	13 (20)
Central Zone***	20 (30.76)
Others****	12 (18.46)
Occupation Distribution	
Students	24 (36.9)
Housewives	22 (33.8)
Farmers	7 (10.8)
Labourers	5 (7.6)
Businessman	3 (4.5)
Govt. Employee	4 (6.2)
Educational Status	
Illiterate	18 (27.7)
Primary School	21 (32.3)
Secondary School	9 (13.8)
Graduate and Higher	17 (26.15)
Socioeconomic Status	
Lower Class@	25 (38.5)
Middle Class@@	39 (60)
Upper Class	1 (1.5)
Physical Activity	
Sedentary Lifestyle	18 (27.6)
Moderate Physical Activity	40 (61.5)
Heavy Physical Activity	7 (10.8)

*(Anantnag + Pulwama +Kulgam +Shopian) 9+9+1+1
**(Baramullah + Bandipora+ Kupwara) 3+2+8
***(Srinagar + Ganderbal+ Budgam) 10+3+7
****(Udhampur, Ladakh, Rajouri, Uri, Doda, Ramban, Handwara) 1+1+1+1+1+3+4
@(lower and upper lower) 19 + 6; @@(lower and upper) 21 +18

An equal number of patients were found to belong to the south and central zone districts, followed by the north zone and other districts as shown in table above. A major group in the studied cohort comprised of young people who were college students followed by homemaker females and other occupations. Educational status of the studied group was that most of the patients were uneducated and had only acquired primary school education followed by graduates and secondary school education. Majority of the cases belonged to the lower class on the socioeconomic status scale (Table 2).

Table 3: Showing distribution of patients as per Sunlight Exposure in Non-MS CNS Inflammatory Demyelinating Diseases

Parameter	Cases (%)
Sunlight Exposure	
<3 hours	42 (64.5)
≥3 hours	23 (35.3)
Seropositive NMOSD	
<3 hours	14 (66.7)
≥3 hours	7 (33.3)
Seronegative NMOSD	
<3 hours	4 (80)
≥3 hours	1 (20)
MOGAD	
<3 hours	11 (78.6)
≥3 hours	3 (21.4)
Sunlight Exposure by Disease Type	
ADEM	
<3 hours	2 (22.2)
≥3 hours	3 (77.8)
CNS Demyelination	
<3 hours	5 (100)
≥3 hours	0 (0)
Idiopathic ON and LETM	
<3 hours	7 (63.6)
≥3 hours	4 (36.4)

Highest percentage of cases were found to have a moderate physical activity in their routine lifestyle, followed by sedentary lifestyle and only a minority were involved in heavy physical activity. In totality majority of the cases had a low sunlight exposure, as exemplified in the below table (Table 3); data regarding sunlight exposure across individual disease types revealed that primary CNS demyelination cases had the highest proportion with a limited exposure (<3 hours) (100%) whereas ADEM patients had the largest proportion with the most extended sunlight exposure (>3 hours).

As seen in the below table (Table 4), the distribution of BMI varied across the different disease groups, as nearly half of the seropositive cases of NMOSD, MOGAD and ADEM were overweight, whereas seronegative NMOSD cases and the primary CNS demyelination group had a normal BMI in majority; in idiopathic cases of LETM/ON, BMI distribution was comparable in the 3 categories as shown. Data on comorbid conditions revealed that hypertension was the most co-pravelant disease followed by Type 2 diabetes mellitus and one patient had a past history of herpes zoster infection. None of the patients had family history of similar condition; there was a family history of hypertension, diabetes and malignancy and depression in small percentage amongst all groups. One case of MOGAD had a family history of primary CNS demyelination in the father; rest 2/3rd of all cases had a negative family history. The disease severity was classified on the basis on the clinical phenotype at presentation, all patients of NMOSD had a severe presentation, as were the MOGAD and ADEM cases. 2 patients of primary CNS demyelination had a mild to moderate presentation and 3 patients had a severe presentation, in the group of idiopathic ON and LETM majority (83.3% and 80% respectively) had severe phenotype, these numbers reflect the disabling nature of these diseases.

Based on the clinical neurological syndrome and the radiological findings used for the diagnosis, supratentorial involvement was found in all cases of ADEM and primary CNS demyelination, followed in frequency by seronegative cases of NMOSD. Involvement of the optic pathways was seen in most cases of idiopathic seronegative ON, and a significant number of NMOSD and MOGAD cases, with no ON involvement in ADEM, primary idiopathic CNS demyelination and idiopathic LETM. Likewise, brainstem was found to be involved mostly and only in cases of NMOSD and MOGAD, and rarely in ADEM. Cerebellum was reported to be the least involved structure with involvement only seen in NMOSD and MOGAD.

Table 4: BMI distribution of studied patients

Disease Type	BMI			
	Underweight (%)	Normal (%)	Overweight (%)	Obese (%)
Sero positive NMOSD	1 (4.8)	9 (42.9)	10(47.6)	1 (4.8)
Sero negative NMOSD	0 (0.00)	3 (60.0)	2(40)	0 (0.00)
MOGAD	2 (22.2)	5 (35.7)	6 (42.9)	1 (7.1)
ADEM	2 (22.2)	3(33.3)	4(44.4)	0(0.00)
CNS Demyelination	1 (20.0)	3 (60.0)	1 (20.0)	0 (0.00)
Idiopathic ON and LETM	1 (9.1)	3 (27.3)	4(36.4)	3(27.3)

Table 5: Distribution of various neurological involvements across different disease types

Disease Type	Supratentorial Involvement (%)	Optic Pathway Involvement(%)	Brainstem Involvement(%)	Cerebellar Involvement(%)	Spinal Cord Involvement(%)	Diencephalic Syndrome (%)
Seropositive (NMOSD)	2 (9.5)	7 (33.3)	6 (28.6)	1 (4.8)	19 (90.5)	1 (4.8)
Seronegative (NMOSD)	2 (40)	3 (60)	2 (40.0)	0 (0.0)	5 (100)	0 (0.0)
MOGAD	2 (14.3)	6 (42.9)	2 (14.3)	1 (7.1)	6 (42.9)	0 (0.0)
ADEM	9 (100)	0 (0.0)	1 (11.1)	0 (0.0)	1 (11.1)	0 (0.0)
CNS (Demyelination)	5 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
LETM	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (45.5)	0 (0.0)
ON	0 (0.0)	6(45.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 6: Distribution and mean values of the Expanded Disability Status Scale (EDSS) at onset and discharge across various disease types

Disease Type	Frequency	Minimum	Mean	Maximum	SD	P Value
EDDS at onset						
Seropositive (NMOSD)	21.00	3.50	6.67	8.50	1.21	<0.001
Seronegative (NMOSD)	5.00	6.50	7.10	8.00	0.82	
MOGAD	14.00	0.00	4.35	8.00	3.00	
ADEM	9.00	4.50	7.61	9.50	1.43	
CNS (Demyelination)	5.00	1.00	3.20	6.00	2.08	
ON/LETM	11.00	0.00	3.63	9.50	3.77	
EDDS at Discharge						
Seropositive (NMOSD)	21.00	1.50	3.78	6.50	1.10	0.02
Seronegative (NMOSD)	5.00	2.50	3.40	4.50	0.65	
MOGAD	14.00	0.00	2.53	5.50	1.56	
ADEM	9.00	1.00	4.44	9.50	2.98	
CNS (Demyelination)	5.00	1.00	3.00	5.50	2.03	
ON/LETM	11.00	0.00	1.81	7.50	2.01	

Spinal cord was found to be severely affected in majority of the cases of NMOSD, idiopathic LETM and MOGAD and in a rare case of ADEM and not at all idiopathic primary CNS demyelination and idiopathic ON cases. Diencephalic involvement was reported only in a rare case of NMOSD.

For seropositive NMOSD, 21 patients had a mean EDSS of 6.67 at onset, which improved to 3.78 at discharge. In contrast, seronegative NMOSD had a mean EDSS of 7.10 at onset and 3.40 at discharge. MOGAD patients showed a mean EDSS of 4.35 at onset and 2.53 at discharge, while ADEM patients had a mean of 7.61 at onset, decreasing to 4.44 at discharge. CNS demyelination showed a mean EDSS of 3.20 at onset and 3.00 at discharge, while idiopathic ON and LETM patients had a mean EDSS of 3.63 at onset, which improved to 1.81 at discharge. The data revealed a significant difference in the mean of EDD levels at onset and at discharge across different disease types with a $p<0.001$, meaning thereby that this scale truly quantifies the extent of motor disability exhibited by these patients (as this was found statistically significant) and therefore reflects the severity of the clinical phenotype and the disabling nature of these disease groups at nadir (worst EDSS at onset).

DISCUSSION

We studied a local cohort of 65 patients with different groups of allied non-MS inflammatory CNS demyelinating diseases and presented their clinical and sociodemographic profile. The relative frequencies of various groups of diseases in our mixed cohort showed a higher percentage of NMOSD, MOGAD, followed by ADEM, and the least frequent cases belonged to idiopathic cases of seronegative LETM, ON and primary CNS demyelination respectively. Sivaroja Y et al [14] and Manisha M et al. [15] have similarly reported NMOSD as a predominant group in similar mixed cohorts and Cobo Calvo A et al [16] has reported a similar relative frequency of MOGAD. Wallner-Blazek M et al [17] has reported cases of idiopathic primary CNS demyelination who were double seronegative (minority in our population). A similar relative frequency of ADEM has been reported by Alvaro Cobo Calvo M et al [16], Zhang W et al [18] and Jain RS et al [19]. Our 23.8% of ON cases is also consistent with the data from Fragaso DC et al (25%) [20]. Among paediatric cohorts, Flanagan EP et al [21] has reported NMOSD to be a less frequent diagnosis; and Cobo Cobo Calvo A et al [16] has shown ADEM to be a frequent cause for CNS demyelination which are both consistent with our study.

The overall age in our study ranged from 21-40 years in majority (mean age 40.2 years), and minority of patients over 60 years. Gajula RK et al [22] has reported a similar age range between 20 to 40 years. Jarius S et al [23] and Cobo-Calvo A et al [16] also have shown a similar age range (16.7-41.7 years) for adult MOGAD, and a median of 37 years for seropositive NMOSD. ADEM was primarily seen in children (20%) in our study, with a mean age of 11.4 years, as seen in literature [6]. Primary CNS demyelination and idiopathic ON affected younger adults, as also shown by Fragoso DC et al [20] (mean age of 28.2 years) and Ambika S et al. (mean age 32.37 years) respectively. [24]

A female preponderance was observed in NMOSD, idiopathic LETM, and idiopathic optic neuritis (ON), with an overall female-to-male ratio of 3:2. Wingerchuk DM et al [1] has reported a female to male ratio of 9:1 in NMOSD, and Maillart E et al [25] and Ambika S et al. [24] have reported female predominance in idiopathic LETM and idiopathic ON respectively. MOGAD comparatively demonstrated a male predominance (3:4 in our study), consistent with Cobo-Calvo-Calvo Á et al [26]. Also, ADEM in our cohort showed a male predominance (4:5), similar to Pavone P et al [27]. Primary CNS demyelination in our study exhibited a strong male predominance (1.8:1). Recent studies by Papp V et al. and Tobin WO et al. suggest a contrasting female preponderance in such cases [28, 29] However, older study of Seewan A et al. (7:5), reported a balanced gender distribution [30]. This stronger male predisposition may represent a potential novel finding, or may suggest a need for a careful longitudinal follow-up which may later explain their distinct gender bias.

Majority of the cohort belonged to the central districts of the Kashmir region of the J and K UT, there have been no current local epidemiological studies to make a comparison of this, however we have constructed a map to show the relative frequency of patients with different diagnoses from different parts of the region, though this data cannot be generalizable and be representative of our population. Also, majority of the patients over all belonged to lower middle and lower class, which highlights the potential disparities in healthcare access and disease detection. While the association between lower socioeconomic status (SES) and greater disease severity is well-documented in multiple sclerosis (as reported by Katz Sand I et al. [31] and Gray-Roncal K et al. [32]), similar correlations in NMOSD and MOGAD and other idiopathic conditions remains understudied and requires further research. In terms of physical activity, no strong association was found between a sedentary lifestyle and increased disease severity. However, studies like Li Q et al. [33] and Motl RW et al [34] have shown that increased physical exercise can improve outcomes in NMOSD. Further research is needed to confirm this.

In our study, NMOSD patients showed a wide range of BMI, with majority in overweight. (25-29.9) and obese (≥30) categories especially in NMOSD and idiopathic LETM patients, however there was no strong statistical correlation found between higher BMI and disease severity. Previous studies, such as Marrie RA et al. [35], have linked higher BMI in MS to increased disability risk, however there is a lack of studies in the literature exploring these associations in non-MS demyelinating diseases, and this might again represent a novel finding and requires further study.

In our study, disease severity was assessed using the Expanded Disability Status Scale (EDSS). All patients with seropositive NMOSD, MOGAD, and ADEM exhibited severe phenotypes at presentation. NMOSD is known for its high disability [26]. ADEM, especially in pediatric cases, presents severely as reported by Cobo-Calvo A et al [26] and Pavone P et al [27] aligning with our initial high EDSS in ADEM. Similarly, Maillart E et al [25] described severe presentations in seronegative LETM, with an EDSS onset of 6.0, and Ambika S et al. [24] reported significant vision loss in seronegative ON, aligning with the severity patterns observed in our study. Also, Tobin WO et al [29] reported a mean EDSS of 3.5 in idiopathic CNS demyelination similar to 3.20 of mean EDSS at onset in such cases suggesting moderate disability.

In our study, we assessed neural axis involvement using clinical data and MRI.In NMOSD, we observed, a significant spinal cord involvement predominantly followed by bilateral optic nerve and brainstem involvement and rarely supratentorial, cerebellar and diencephalic involvement. Wingerchuk DM et al. [1] has highlighted LETM as a defining characteristic of NMOSD. Also, Sellner J et al. [36] and Wingerchuk DM et al [1] both have shown that bilateral optic neuritis as a hallmark feature of NMOSD. Comparatively, Fragoso DC et al [20] reported higher supratentorial (72%) and brainstem (55%) involvement. Further clarification and larger longitudinal studies are warranted to confirm these observations and explore this variability.

In our study, majority of the MOGAD patients exhibited a predominant spinal cord and bilateral optic nerve involvement followed by a lesser degree of brainstem, supratentorial and cerebellar involvement in decreasing order. These findings align closely with the review by Xu Y et al., which reported cerebral cortical encephalitis in 12.77%, brainstem involvement in 17.03%, myelitis in 34.04%, and optic neuritis in 38.3% of MOGAD cases, reflecting comparable neural axis involvement patterns [37]. These patients were found to have a similar frequency of optic nerve involvement as seen by Ambika S et al. (43% cases), (42.9% seen in our study) [24]. Hana Larassati H et al [38] also identified reported similar bilateral optic neuritis in one-third of MOG-EM cases, further corroborating our findings. While Fragoso DC et al [20] again has reported higher rates of supratentorial (39.25%) and brainstem (72.7%) involvement, the lower rates in our study could be attributed to the smaller sample size, limiting statistical power and variability in detection.

In our study, all ADEM patients (100%) exhibited extensive supratentorial involvement. Brainstem involvement was observed in only 1 case, and there was no cerebellar or optic nerve involvement, and cervical spinal cord involvement was also seen in only 1 case (11.1%). Mukhtiar K et al. [39] noted supratentorial involvement in all of their ADEM cases, with brainstem involvement in 23.3% and spinal cord involvement in 10%, consistent with our observations. Flanagan EP et al [21] has however reported spinal cord involvement in 20-54% of ADEM cases, often alongside supratentorial cortical lesions. Contrasting findings may be due small sample size and mixed nature of the cohort.

In our study, 80% of idiopathic optic neuritis (ON) cases presented with bilateral simultaneous optic neuritis. This observation is largely consistent with findings from Ambika S et al. [24], and Fragoso DC et al [20] who have both reported double seronegative cases exhibiting bilateral optic involvement in comparable frequencies. While our study showed a higher proportion of such involvement, this may be attributed to the smaller cohort of idiopathic optic neuritis cases in our study, suggesting the need for larger, more homogeneous patient samples to validate these trends.

Regarding longitudinally extensive transverse myelitis (LETM), all such cases in our study had long-segment spinal cord involvement affecting the cervical and dorsal regions as consistent with Pandit L et al [40] and Fragoso DC et al [20]. Maillart E et al. [25] and Jain RS et al [19] have noted that double seronegative LETM cases had dorsal cord involvement more than cervical. Our cases hence had a higher percentage of combined cervical and dorsal cord involvement, as compared to these studies.

LIMITATIONS

This was a hospital-based study of patients who presented from different parts of the UT; hence the results cannot be generalised; also, the small and unequal sample size does not allow a more precise statistical analysis.

CONCLUSION

The study highlights the various demographic, social and clinical profiles of non-MS demyelinating diseases. NMOSD, MOGAD and idiopathic groups were more common in adults, whereas ADEM and MOGAD were more frequent in the paediatric groups. These conditions predominantly affected younger age groups and while seropositive NMOSD exhibited a distinct female predominance and severe disease course, other conditions like MOGAD and ADEM showed more balanced gender distributions and variable severity profiles. The patterns of neurological involvement, along with motor impairments, show the differing impacts of these diseases on patient disability. These findings contribute valuable insights into their clinical spectrum of non-MS inflammatory demyelinating diseases, such as disease subtype, severity, and individual patient characteristics and also give an insight into the local demographic profile.

Abbreviation

Acronym	Full Form
CNS	Central Nervous System
MS	Multiple Sclerosis
NMOSD	Neuromyelitis Optica Spectrum Disorder
MOGAD	Myelin Oligodendrocyte Glycoprotein Antibody Disease
ADEM	Acute Disseminated Encephalomyelitis
LETM	Longitudinally Extensive Transverse Myelitis
ON	Optic Neuritis
SKIMS	Sher-i-Kashmir Institute of Medical Sciences
MRI	Magnetic Resonance Imaging
CSF	Cerebrospinal Fluid
EDSS	Expanded Disability Status Scale
SPSS	Statistical Package for the Social Sciences
HIV	Human Immunodeficiency Virus
ACE	Angiotensin Converting Enzyme
ICMR	Indian Council of Medical Research
SES	Socioeconomic Status
UT	Union Territory
BMI	Body Mass Index

Author's Contributions: MN was primarily responsible for the conception and design of the study, played a key role in data analysis and interpretation, and took the lead in drafting and preparing the manuscript. **FAM** contributed significantly to the conception of the study and assisted in the interpretation of the findings. **RA** and **MW** jointly contributed to the overall research design, ensuring methodological soundness, and were actively involved in the verification and validation of the study results. **IM** was responsible for the collection of study materials, and also contributed to the analysis and interpretation of the data, thereby supporting the robustness of the study outcomes.

Availability of Data: The data supporting the findings of this study are available from the corresponding author upon reasonable request at *murtaza.noor7@gmail.com.*

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