Research Article

MR Imaging differences between multiple sclerosis and neuromyelitis optica spectrum disorders: A single institutional study in a tertiary referral center in Sri Lanka

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Abstract

Background and objectives- Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorders (NMOSD) are the commonest demyelinating diseases of the central nervous system with overlapping clinical and radiological features, leading to frequent misinterpretation. This study aimed to describe neuroimaging features for differentiating MS and NMOSD and also comparing NMOSD subcategories.

Methods- A cross sectional study was conducted at a single tertiary referral center in Sri Lanka. The magnetic resonance imaging (MRI) characteristics of 82 MS and 36 NMOSD patients were prospectively evaluated by a fourth-year resident under the supervision of consultant radiologists and were analyzed using standard descriptive statistical tests.

Results- Statistical analyses indicated significance ($p<0.05$) in distinguishing both entities (MS and 36 NMOSD) across lesions in periventricular, subcortical, intracortical, inferior temporal, corpus callosum, and infratentorial locations by MRI. Dawson finger lesions, U fibers, calloso-septal interface involvement and T1 black holes indicated MS, whereas linear ependymal lesions suggested NMOSD. In the spinal cord, peripherally located short-segment lesions were significant for MS ($p=0.000$) and longitudinally extensive lesions involving central grey matter ($p=0.000$) pointed towards NMOSD. There was only a slight variation in lesion distribution between cervical and thoracic cord. MS showed more brain parenchymal volume loss while spinal cord atrophy was higher in NMOSD. Symmetry and location of the optic pathway lesions reinforced the differentiation.

Conclusion- Comprehensive analyses support the use of neuroimaging in distinguishing between NMOSD and MS. However, further multicentric longitudinal studies are required to differentiate NMOSD phenotypes.

Keywords: Multiple sclerosis; Neuromyelitis Optica spectrum disorders, AQP4 positive, MÓG positive; Imaging markers

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Introduction

Multiple sclerosis (MS) and Neuromyelitis Optica Spectrum Disorders (NMOSD) are inflammatory demyelinating diseases of the central nervous system (CNS) and important causes of disability in the young population worldwide. Despite the increasing knowledge and available diagnostic tools, the diagnosis of the CNS inflammatory disorders remains complex.[1]

In the past, both MS and NMOSD were believed to be within the same disease spectrum. However, the discovery of aquaporin 4 antibody (anti-AQP4) and antibodies against the myelin oligodendrocyte glycoprotein (anti-MOG), has revealed that NMOSD has distinct clinical, radiological, laboratory and immunopathological changes that are different from MS.[2] With the revision of diagnostic criteria in recent years, neuroimaging has been included as an important criterion, playing a crucial role in the initial diagnosis and follow up of patients with MS and NMOSD.

Studies conducted in different Asian populations have shown that the clinical profile and radiological patterns of MS slightly differ from those observed in western countries.[3] However, the nature of MS and NMOSD in Sri Lanka remains mostly understudied. Nonetheless, imaging plays a significant role in determining therapy options while waiting for laboratory results.

The objective of this study is to describe the MRI differences between MS and NMOSD in a tertiary referral center in Sri Lanka. By comparing the conventional MRI features of diagnosed MS and NMOSD, this study aims to identify distinct imaging markers in brain, spinal cord, and optic pathway to differentiate MS from NMOSD, particularly in the early stages of the disease. This differentiation is crucial, especially for patients whose antibody status is not available or negative (for anti-AQP4 and anti-MOG), as it can greatly impact early management decisions.

Materials and methods

This cross sectional study was conducted prospectively at the two main units in the radiology department in the National Hospital of Sri Lanka (NHSL) from 1st July 2021 to 30th June 2022. Ethical approval was obtained from the ethics review committees of NHSL and Post Graduate Institute Medicine (PGIM), University of Colombo.

Participants: The study included patients who underwent MRI scans at NHSL with a diagnosis of MS or NMOSD. All the patients with MS fulfilled the 2017 Revised McDonald criteria[4] and the NMOSD diagnosed according to the 2015 IPND Neuromyelitis Optica Spectrum Disorder diagnostic criteria.[5] The MS subcategories included were relapsing remitting MS (RRMS), primary progressive MS (PPMS) and secondary progressive MS (SPMS) depend on the clinical phenotypes.[6] The subtypes of NMOSD considered were AQP4 positive, MOG positive and double negative depend on the status of the antibody.[7] The age of disease onset was determined based on the identification of specific clinical symptom/s.

Image and data acquisition: MRIs were acquired according to local departmental protocols based on the recommendation of MAGNIMS panel in 2019. [8,9]The imaging was performed primarily using 3T and 1.5T

Siemens (Skyra) scanners. The brain protocol included T1W axial (repetition time [TR] 27-400ms, Echo time [TE] 8.7-20ms), T2W sagittal and axial (TR 4500-5200ms, TE 98-102ms), volumetric FLAIR (TR 9000ms, TE 80-111ms), diffusion weighted (DWI/ADC) and volumetric T1W post Gadolinium acquisitions. For spinal cord assessment, sagittal T2W (TR 3200-3500ms, TE 93-100ms), T1W and STIR, and axial T2W (TR 600ms, TE 14ms) and post Gadolinium sequences were obtained. The Axial T2W (fat sat), coronal STIR and post contrast images were acquired for the evaluation of anterior visual pathway. All the acquisitions were performed with standard MR parameters using head and spine matrix coils.

The MR images were retrieved from the workstations, and necessary clinical data was collected from patients' bed head tickets, discharge registers and clinic books. The patients who had multiple MRI examinations within the study period, only the new demyelinating lesions in the subsequent scans were included. The MRI scans with image degradation and vascular lesions involving the cortex were excluded.

Data quality scoring and statistical analysis: All MRIs were interpreted by the fourth-year resident (senior registrar) under the supervision of consultant radiologists. Neuroimaging features were evaluated for brain, spinal cord, and optic pathway lesions. [10,11,12,13]

All the collected data were entered into the Microsoft Excel spreadsheets and analyzed using SPSS (version 27). Parametric and non-parametric techniques were used depending on the data distribution in the analysis. Machine learning algorithms such as naïve bayes (NB), random forest (RFC), support vector classification (SVC) and logistic regression were also used for analysis. The dependent variable was the clinical diagnosis: MS or NMOSD.

Results

A total of 82 patients with MS and 36 patients with NMOSD were enrolled for the analysis of neuroimaging of the brain, spinal cord, and optic pathway.

Demographic details: The common age group was 21-40 years for both MS (n=52, 63.4%) and NMOSD (n=17, 47.2%). The mean age in the MS group was 34.5 years (SD=10.8), while in NMOSD, the mean age was 40.8 years (SD=14.6). Both MS and NMOSD were more prevalent in females (n=51, 62.2% in MS and n=27, 75.0% in NMOSD).

Clinical data: The mean age at the disease onset was 28 years (range 8-58 years) among patients with MS, while it was 37 years for NMOSD (range 18-74 years).

Among the MS patients, majority 72% (n=59) were subclassified into RRMS. PPMS accounted for 7% (n=6) of MS, SPMS for 2% (n=2), and 15 patients were not classified into any category. Among the NMOSD patients, 53% (n=19) were positive for AQP4 antibody, 25% (n=09) were positive for MOG antibody and the remaining 22% (n=08) were negative for both antibodies.

Imaging analysis:

Brain: A total of 1250 lesions in 82 MS patients and 296 lesions in 36 patients with NMOSD were evaluated (Table 1).

Patients with MS tended to have a greater number (>5) of brain lesions (n=70). The location of lesions was significantly

different between MS and NMOSD (Figure 1 & 2). Periventricular (n=74, 90%), juxtacortical (n=54, 67%) and sub U subcortical white matter lesions (n=55, 67%) were more frequent in MS, whereas deep white matter lesions showed less variation in distribution between MS and NMOSD.

Intracortical (p = 0.003) and cerebellar lesions (p = 0.000) were solely seen in MS patients in this study, except for one AQP4 positive NMOSD patient with multifocal lesions involving cortex and underlying subcortical white matter. Apart from these locations, the inferior temporal, corpus callosum and deep grey matter were found most often in MS and showed statistical significance ($p<0.05$). Some specific posterior fossa locations were found in MS patients as shown in figure 3.

Table 1: Number and location of the brain lesions in the MS and NMOSD patients

Characteristics	MS (n=82)	NMOSD			p value
		AQP4 (+) (n=19)	MOG (+) (n=09)	Double negative (n=08)	
Number of lesions					
2	1 (1%)	1 (5%)	0	2 (25%)	
3	0	0	0	0	
4	2 (2%)	1 (5%)	1 (11%)	1 (13%)	
5	4 (5%)	1 (5%)	1 (11%)	1 (13%)	
>5	70 (85%)	6 (32%)	3 (33%)	1 (13%)	
Location of the lesions					
Periventricular	74 (90%)	4 (21%)	1 (11%)	0 (0%)	0.000
Deep white matter	46 (56%)	6 (31%)	4 (44%)	4 (50%)	0.275
Sub U subcortical	55 (67%)	6 (31%)	3 (33%)	1 (13%)	0.000
Juxtacortical	54 (68%)	1 (5%)	1 (11%)	0 (0%)	0.000
Intracortical	25 (30%)	1 (5%)	0 (0%)	0 (0%)	0.003
Inferior temporal lobe	63 (77%)	2 (11%)	0 (0%)	0 (0%)	0.000
Corpus callosum	59 (72%)	2 (11%)	1 (11%)	0 (0%)	0.000
Deep grey matter	28 (34%)	3 (16%)	0 (0%)	2 (25%)	0.090
Hypothalamus	9 (11%)	2 (11%)	0 (0%)	1 (13%)	0.770
Brainstem	59 (72%)	6 (32%)	2 (22%)	2 (25%)	0.000
Periaqueductal grey matter	17 (21%)	0 (0%)	1 (11%)	1 (13%)	0.158
Cerebellum	29 (35%)	0 (0%)	0 (0%)	0 (0%)	0.000
Unilateral	4 (5%)	2 (11%)	1 (11%)	1 (13%)	0.665
Bilateral	76 (93%)	7 (37%)	3 (33%)	3 (38%)	

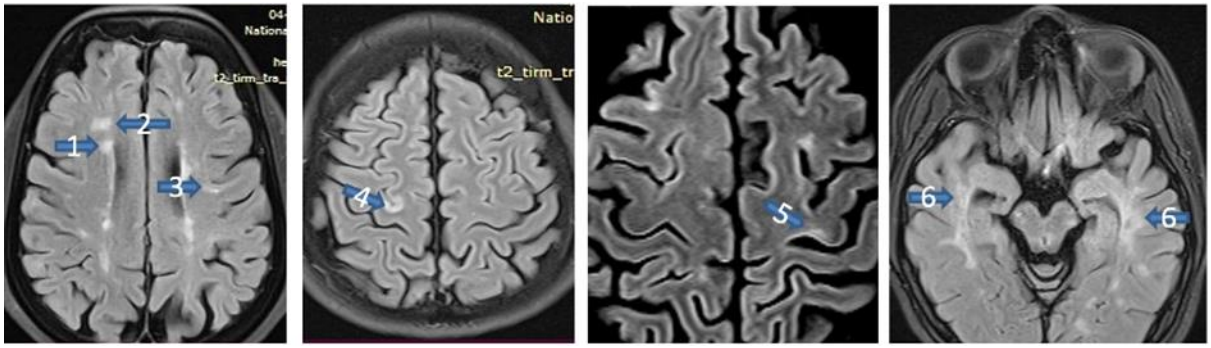

Figure 1: Location of the lesions. Axial, coronal and sagittal FLAIR and T2W images show lesions in the [1] periventricular, [2] deep, [3] sub-U subcortical, [4] juxtacortical, [5] intracortical, and [6] inferior temporal lobe. [10,11,12,13]

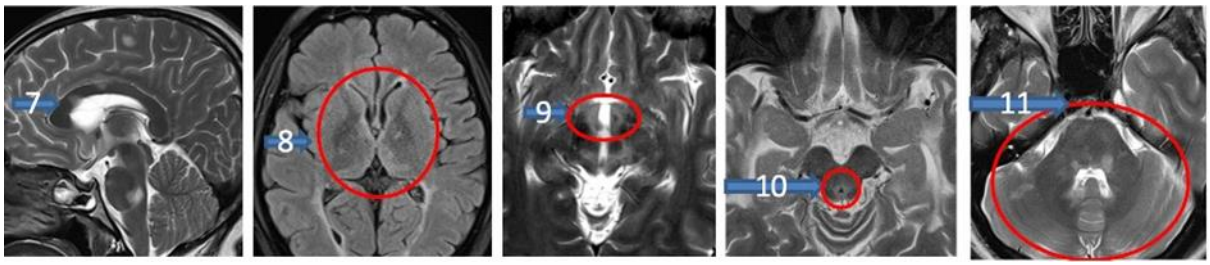

Figure 2: Other locations [7] corpus callosum, [8] deep grey matter, [9] hypothalamus, [11] periaqueductal grey matter, [11] brainstem and cerebellum. [10,11,12,13]

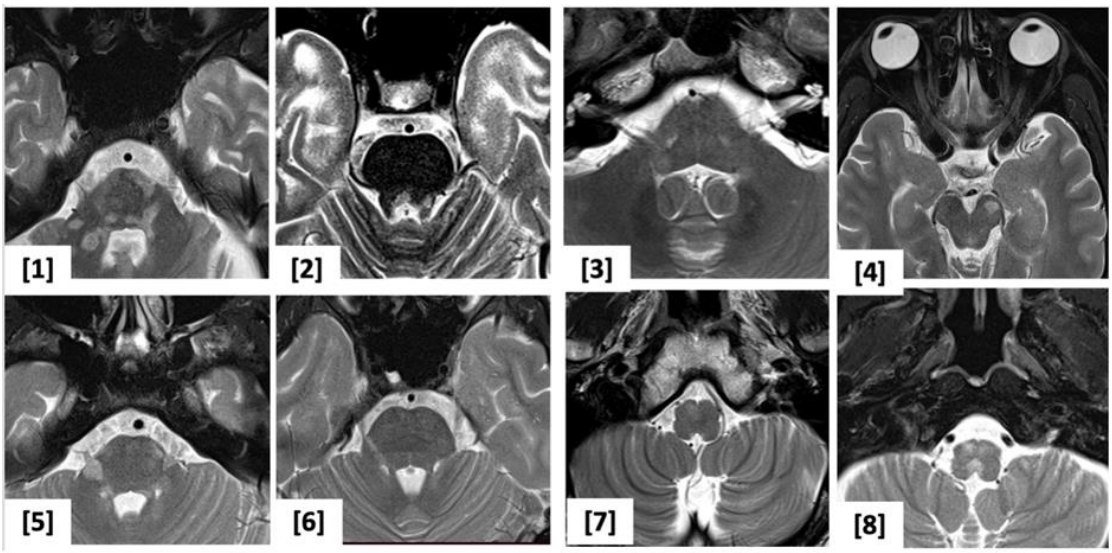

Figure 3: Axial T2W images show typical locations of Infratentorial MS lesions; [1] peripheral brainstem and middle cerebellar peduncles, [2] superior cerebellar peduncle (left), [3] inferior cerebellar peduncle (right), [4] cerebral peduncle (left), [5] pontine trigeminal root entry zone and [6] trigeminal tract (right), [7] ventral paramedian and [8] dorsal median medulla oblongata.

The infratentorial locations of NMOSD lesions were different, with more dorsal involvement along the ependymal margins in AQP4 positive and double negative subtypes. The characteristic involvement of area postrema was seen in two of the AQP4 positive cases, but the significance cannot be proven in this study. Large fluffy lesions were seen in MOG positive NMOSD (Figure 4). Though the location itself was not significant, the morphological features of the hypothalamic and periaqueductal lesions revealed some guidance to differentiate between the two (Figure 5).

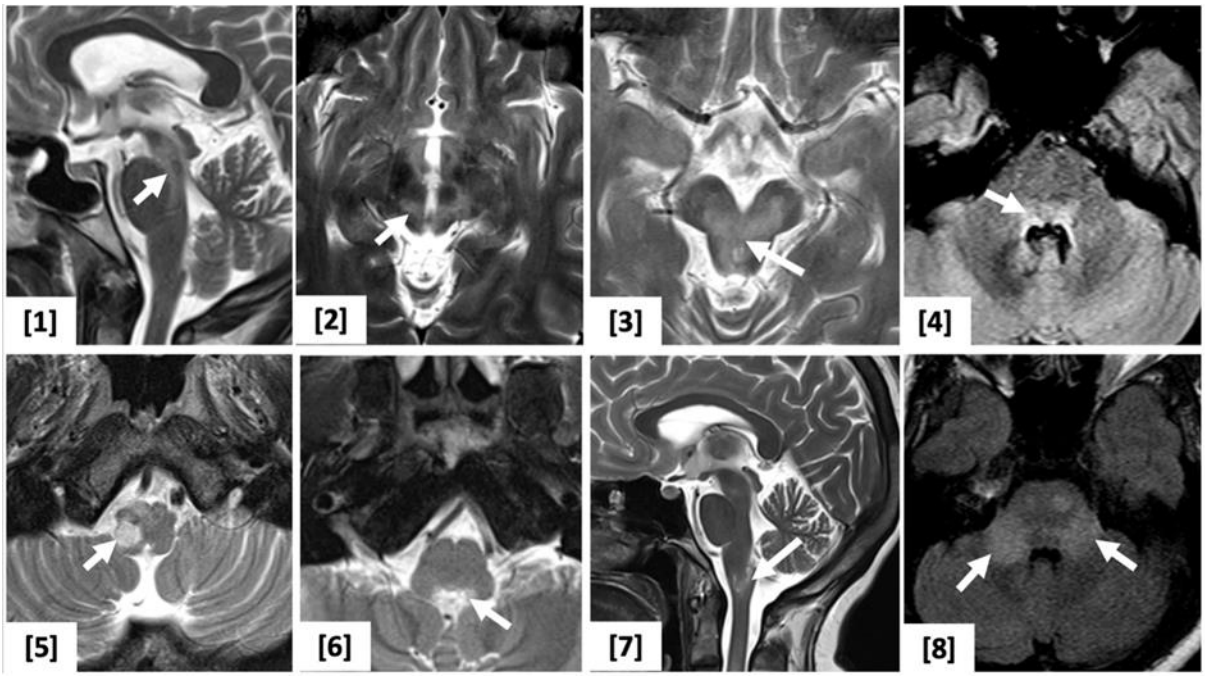

Figure 4: Sagittal and axial T2W and FLAIR images show infratentorial lesions of AQP4 (+) NMOSD [1] to [7] and MOG (+) NMOSD [8]. Confluent brainstem lesions involving periaqueductal grey matter [1], [2], [3], along the floor of the 4th ventricle [4], dorsolateral medulla oblongata [5], area postrema [6], [7] and fluffy lesions of MOGAD [8].

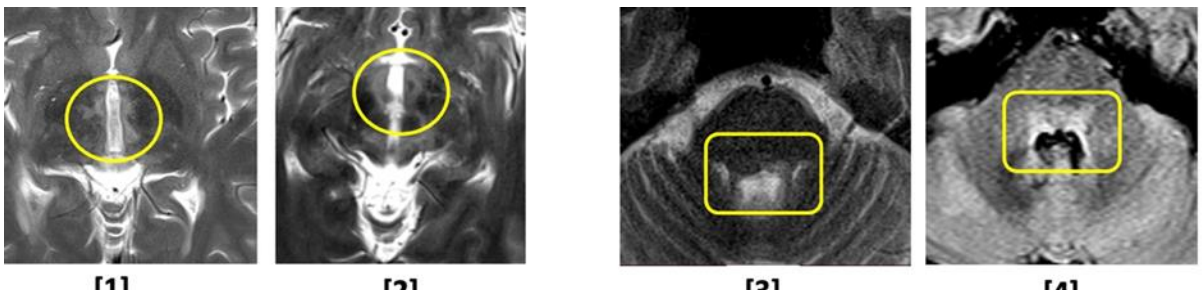

Figure 5: The axial T2W MR images of four different MS and NMOSD patients show periependymal lesions which show asymmetrical ependymal dot type lesions in MS [1,3] and symmetrical and continuous lesions in NMOSD [2,4].

The involvement of the corticospinal tract was observed in both MS and NMOSD and was not a statistically significant differentiating feature. However, in all three (4 %) of the MS patients, lesions were asymmetrical, short segment and discontinuous, whereas in AQP4 positive (15%) and double negative (13%) NMOSD patients the lesions were confluent and longitudinally extensive. There was no involvement of corticospinal tracts in any of the MOG positive NMOSD patients in our study (Figure 6).

The morphological features of the lesions as presented in Table 2 analysed using Chi-squared test, and p values were subsequently calculated (Table 2) (Figure 7). The frequencies of ovoid (Dawson finger and Dawson finger like) lesions, lesions along the subcortical U fibres and calloso-septal interface and T1 black holes were significantly higher in MS than in NMOSD ($p<0.05$).

The punctate type lesions were seen in all groups, the distribution was even and not statistically significant. These were the most common type but not unique in NMOSD and its subcategories.

Table 2: Morphological patterns of the brain lesions in MS and NMOSD patients

Morphological patterns	**MS (n=82)**	**NMOSD**			
		AQP4 (+) (n=19)	**MOG (+) (n=09)**	**Double negative (n=08)**	**p value**
Ovoid					
Dawson fingers	61 (74%)	0 (0%)	0 (0%)	0 (0%)	0.000
Dawson-finger like	17 (21%)	1 (5%)	0 (0%)	0 (0%)	0.092
Punctate	36 (44%)	6 (31%)	2 (22%)	4 (50%)	0.463
U fiber	53 (65%)	2 (11%)	1 (11%)	1 (13%)	0.000
Calloso-septal	58 (71%)	0 (0%)	0 (0%)	0 (0%)	0.000
Bridging callosal	0 (0%)	2 (11%)	0 (0%)0	0 (0%)	0.014
Tumefactive lesion	9 (11%)	4 (21%)	1 (11%)	1 (13%)	0.697
Ependymal linear	0 (0%)	3 (15%)	1 (11%)	1 (13%)	0.006
Ependymal dot	59 (72%)	0 (0%)	0 (0%)	0 (0%)	0.000
T1 black holes	35 (43%)	0 (0%)	0 (0%)	0 (0%)	0.000

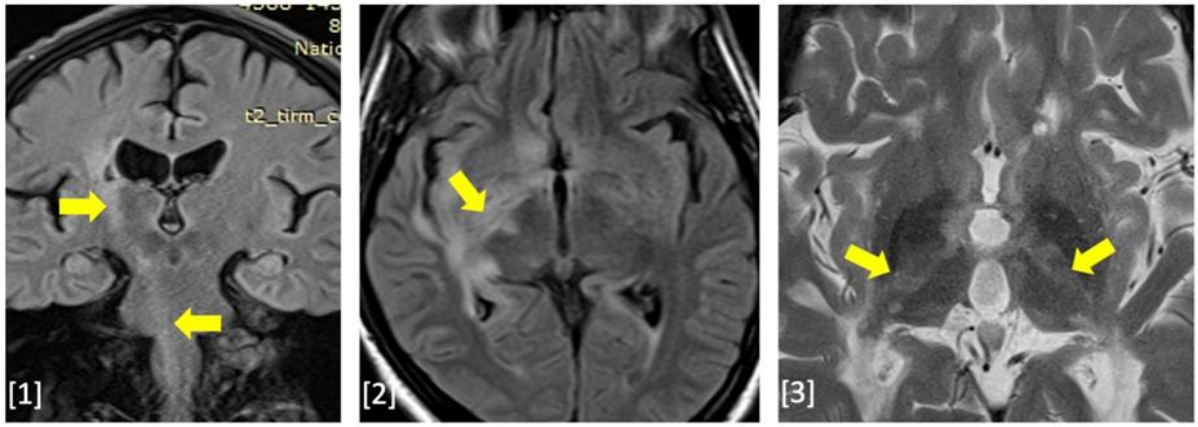

Figure 6: [1] & [2] Coronal and axial FLAIR images of 2 different NMOSD patients show unilateral (right side) corticospinal tracts (CST) involvement which is longitudinally extensive. [3] Axial T2W image of a 23-year-old female diagnosed with RRMS for 9 years show short segment lesions involving bilateral CST (at the level of posterior limbs of the internal capsules).

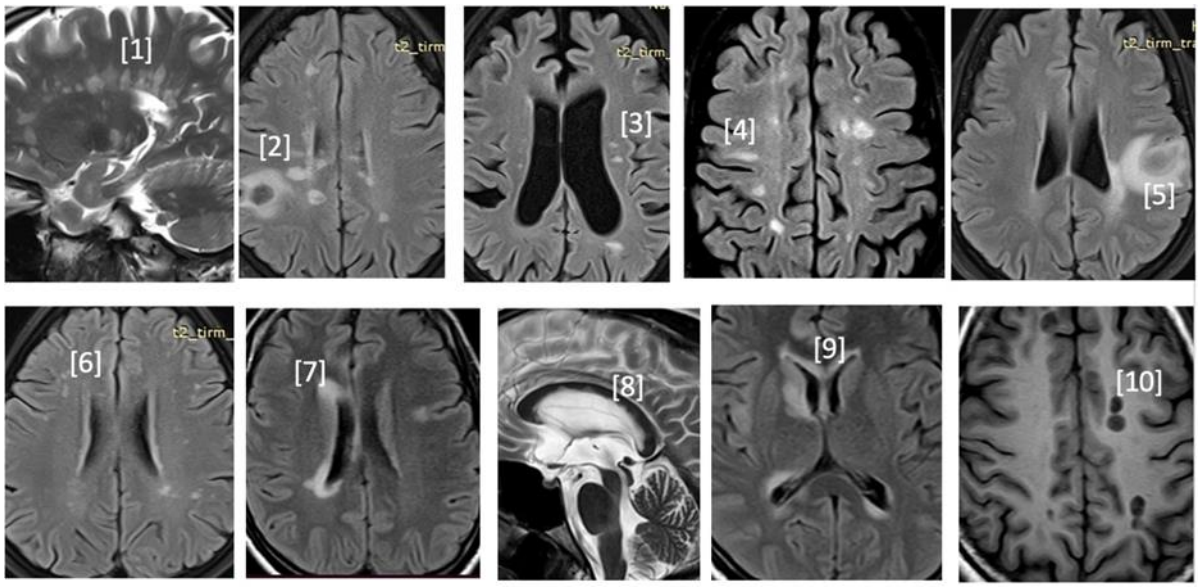

Figure 7: T1W, T2W and FLAIR MRI show morphology of the lesions; [1] Dawson fingers, [2] ovoid, [3] Dawson finger-like lesions (in NMOSD), [4] subcortical-U fiber, [5] tumefactive (>2cm), [6] punctate, [7] peri-ependymal (linear), [8] periependymal-dot, [9] bridging corpus callosal and [10] T1 black holes.

Linear ependymal lesions were present in 13% (5 out of 36) NMOSD patients (15%, 11%, 12% in AQP4 positive, MOG positive and double negative cases, respectively), but absent in MS (Figure 8). Within this type, the typical "bridging callosal lesions" were present in a patient with AQP4 positive NMOSD.

None of the enhancement patterns (nodular, open, closed ring, peripheral, cloud like, and peri ependymal) showed statistical significance ($p>0.05$). However, cloud-like, and patchy enhancement patterns were seen only in AQP4 positive NMOSD patients. (Figure 9). Pencil thin pattern or leptomeningeal enhancement were not detected in our population. The diffusion patterns (central or peripheral diffusion restriction and elevated diffusion) did not show any significance in characterization ($p>0.05$) (Figure 10).

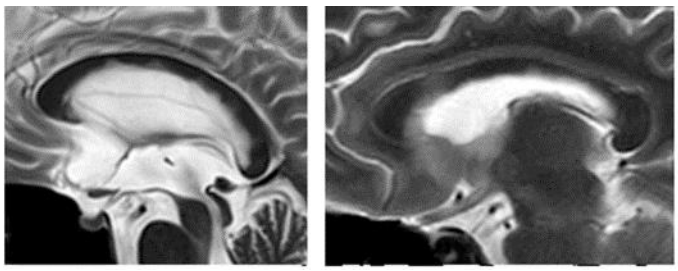

Figure 8: T2 weighted sagittal images show lesions in the corpus callosum in MS (dot-dash sign) and :QP4 positive NMOSD patients respectively. No characteristic callosal lesions were found in MOG positive NMOSD.

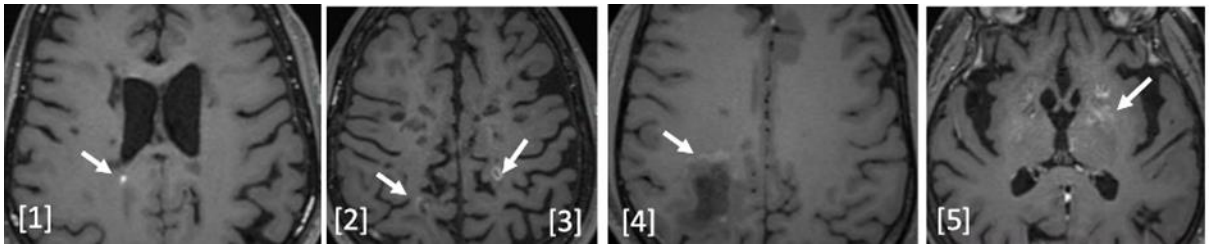

Figure 9: Enhancement patterns of the lesions; Axial T1W post contrast images show [1] nodular, [2] open ring and [3] closed ring, [4] cloud-like and [5] patchy enhancement.

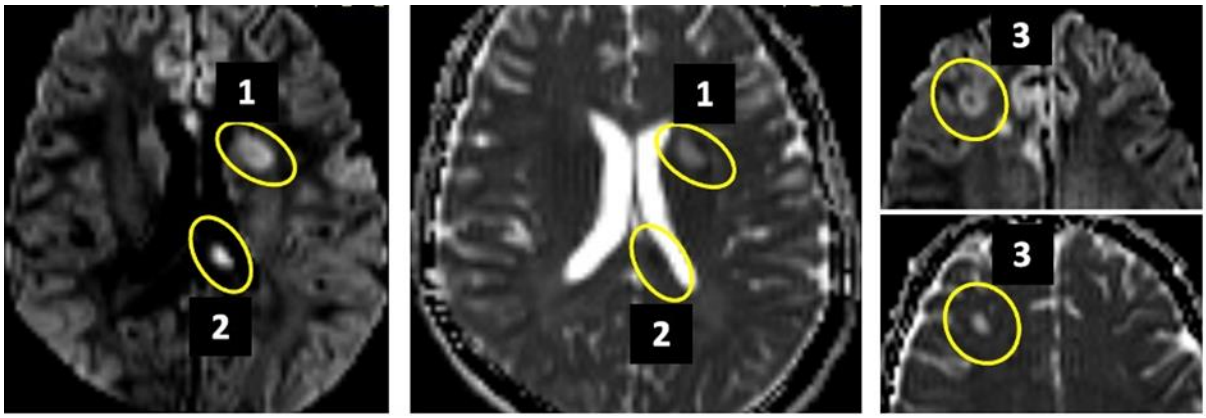

Figure 10: Patterns of diffusion restriction. DWI and corresponding ADC maps show lesions with [1] elevated diffusion, which is the commonest pattern, [2] central diffusion restriction and [3] peripheral diffusion restriction.

Cortical volume loss was most frequently seen in MS. A few patients also showed atrophy of the corpus callosum, mid brain, and cerebellum. Subcortical or white matter volume loss was seen in all the categories.

None of the statistically significant imaging differences were found between the NMOSD sub-categories when analysed with Chi-squared test ($p>0.05$) (Table 3).

Spinal cord: 208 lesions in 82 MS patients and 58 lesions in 36 NMOSD patients were analysed (Table 4).

Table 3: Association between location of the brain lesions in NMOSD categories

Location	p- values		
	AQP4 vs MOG	AQP4 vs Double negative	MOG vs Double negative
Sub U subcortical	0.926	0.159	0.331
Deep grey matter	0.207	0.573	0.110
Linear ependymal	0.741	0.826	0.929
Corticospinal tract	0.207	0.826	0.274
Area postrema	0.338	0.056	0.296

Table 4: MRI features of the spinal cord and analysis

MR Characteristics	MS (n=82)	NMOSD (n=36)			P value
		AQP4 (+) (n=19)	MOG (+) (n=09)	Double negative (n=08)	
Number of lesions					
1	9 (11%)	11 (58%)	5 (56%)	3 (38%)	0.000
2	4 (5%)	4 (21%)	1 (11%)	0	
3	4 (5%)	1 (5%)	0	0	
4	12 (15%)	0	0	0	
5	3 (4%)	0	0	0	
>5	43 (52%)	1 (5%)	0	1 (12.5%)	
Lesion location					
Central					
Grey Matter	3 (4%)	16 (84%)	5 (56%)	4 (50%)	0.000
Grey & white matter	70 (85%)	14 (74%)	5 (56%)	2 (25%)	0.000
Peripheral					
Dorsal	67 (82%)	2 (11%)	0	1 (13%)	0
Lateral	68 (83%)	3 (16%)	1 (11%)	1 (13%)	0
Anterior	22 (27%)	7 (37%)	2 (22%)	1 (13%)	0.595
Longitudinal extension					
Short segment	69 (84%)	1 (5%)	1 (11%)	0	0.000
Long segment	7 (9%)	17 (89%)	5 (56%)	4 (50%)	0.000
Enhancement patterns					
Ring	9 (11%)	0	0	0	0.233
Nodular	3 (4%)	1 (5%)	0	0	0.845
Cloud-like	1 (1%)	1 (5%)	0	0	0.602
Shaggy	1 (1%)	3 (16%)	0	0	0.013

Involvement of the spinal cord was high in patients with MS (n=74, 90%). However, lesions in spinal cord were seen in 89% of AQP4 positive, 67% of MOG positive and 50% of double negative NMSOD patients.

The craniocaudal length of the cord lesions was significantly longer in NMOSD (median length: 6 vertebral segments) compared to MS (median length: less than one vertebral segment). However, this was not a differentiating feature among NMOSD subgroups. The longitudinally extensive signal abnormalities present in the 5% of MS patients were particularly due to coalescing nature of the lesions.

A predilection for the cervical and upper thoracic spine was noted in both MS and NMOSD, compared to lower thoracic and conus medullaris involvement.

The involvement of conus medullaris was demonstrated in 11% of MOG positive NMOSD but not in the AQP4 positive or double negative subtypes. Short segment conus lesions were seen in 5% (n= 4) of MS patients.

The intramedullary location showed significant variation between MS and NMOSD subtypes ($p < 0.05$); central grey matter lesions were more frequent in NMOSD (84%, 55.5% and 50% in AQP4 positive, MOG positive and double negative respectively) than in MS (4%). The involvement of the dorsal and lateral compartments in peripheral locations was common in MS (Figure 11).

Extensive involvement in the transverse section, more than 2/3rd of cord's circumference was predominantly seen in NMOSD (39%) compared to only 5% of MS cases. The characteristic "T2 bright spotty" lesions were identified in 22% of NMOSD patients, including 5 out of 19 AQP4 positive, 1 out of 9 MOG positive and 2 out of 8 double negative cases.

The commonest enhancement patterns were ring and nodular in MS patients and shaggy and cloud-like enhancement in NMOSD (Figure 12,13). This did not show any statistical significance.

The frequency of spinal cord atrophy was significantly higher in AQP4 positive and double negative NMOSD categories ($p = 0.004$), whereas the focal spinal cord swelling was slightly higher in MS but did not show statistical significance.

None of these features were helpful in differentiating NMOSD subtypes from each other (Table 5).

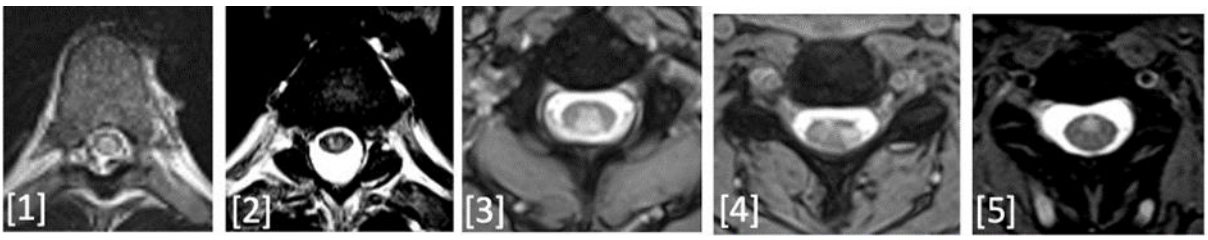

Figure 11: Location of the spinal cord lesions in the transverse section of the cord; [1] central lesions involving >2/3rd of the cord circumference, [2] central grey matter, peripheral lesions in the [3] dorsal, [4] lateral and [5] anterior compartments of the spinal cord.

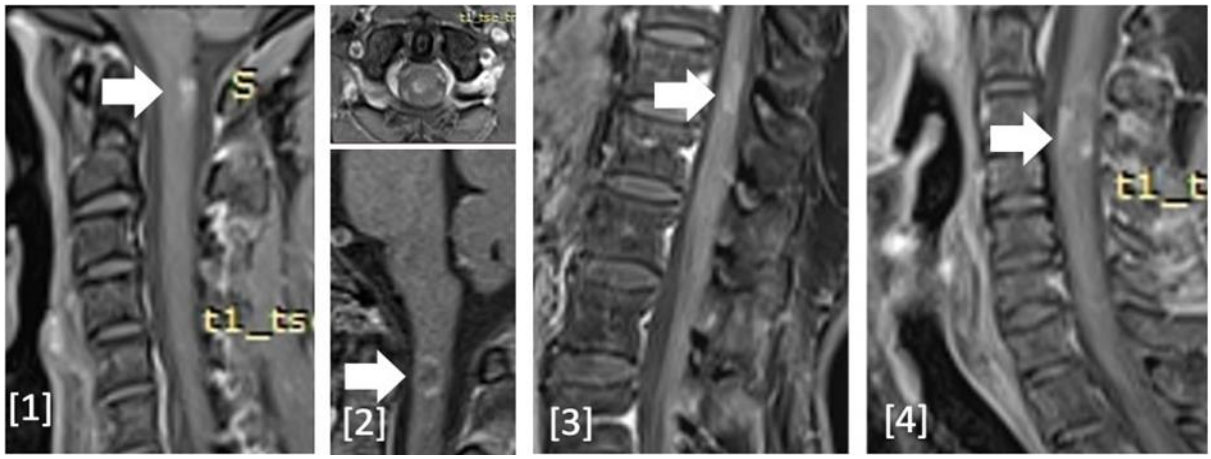

Figure 12: Enhancement patterns of spinal cord lesions; [1] nodular, [2] complete or incomplete ring, [3] cloud-like and [4] patchy.[9]

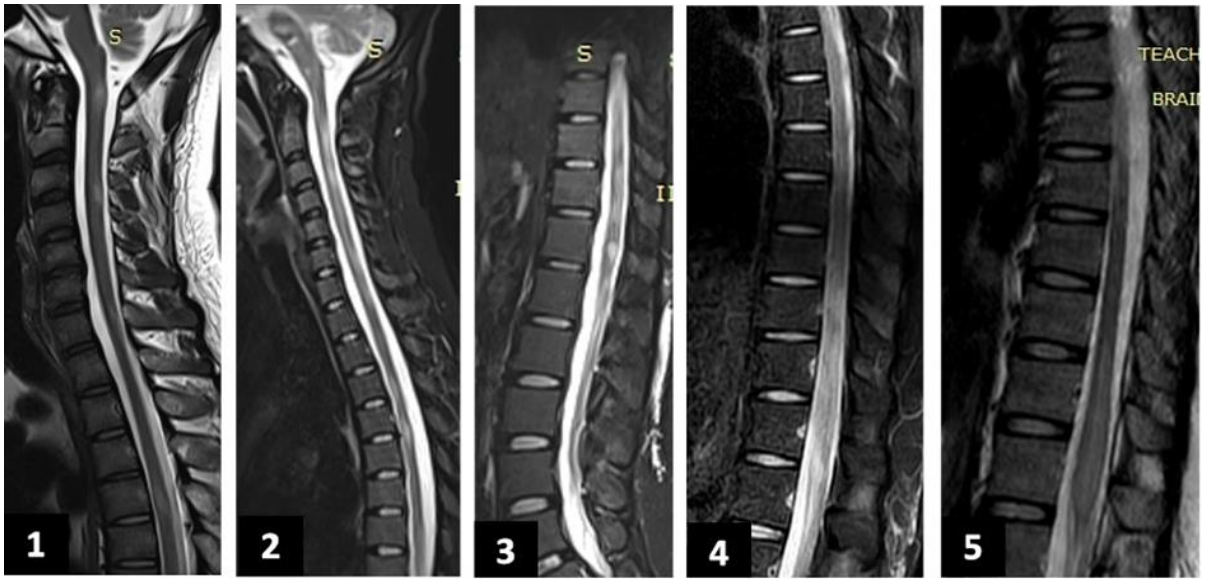

Figure 13: T2-weighted sagittal MR images of typical short segment [1] and atypical coalescing [2] lesions in multiple sclerosis. Though cervicothoracic spinal cord involvement is predominant in MS, 5% cases show involvement of conus medullaris [3]. Images [4] and [5] shows typical long segment lesions of AQP4 positive NMOSD and MOG positive NMOSD respectively.

Table 5: Association between location of the spinal cord lesions in NMOSD categories

Location	**p-values**		
	AQP4 vs MOG	**AQP4 vs Double negative**	**MOG vs Double negative**
Central grey matter	0.102	0.063	0.818
>2/3rd circumference involvement in the transverse section	0.338	0.052	0.312
T2 bright spots	0.359	0.943	0.454

Optic pathway:

There were no statistically significant differences in the laterality of lesions between MS and NMOSD (p=0.500). The symmetry and location of the lesions were significant (p < 0.05) in differentiating MS from NMOSD, but not in distinguishing between the NMOSD subtypes. The retrobulbar, intra-orbital and intracanalicular involvement were more frequently observed in MS and MOG positive NMOSD, while the optic chiasm and optic tract involvement were present more often in AQP4 positive and double negative NMOSD. Short segment lesions (those involve less than half the length of the optic nerve) were more frequent in MS (p <0.05) (Figure 14).

We couldn't demonstrate enhancement characteristics of the optic pathway. Perineural enhancement was found (p <0.05) in only one MOG positive NMOSD patient. Volume loss of the optic pathway was observed in all groups. There were no distinguishing neuroimaging features that are statistically significant in differentiating the subcategories of NMOSD.

Evaluation of brain, spinal cord and optic pathway predictions are described in Table 6. This machine algorithm showed promising results in distinguishing the MS and NMOSD

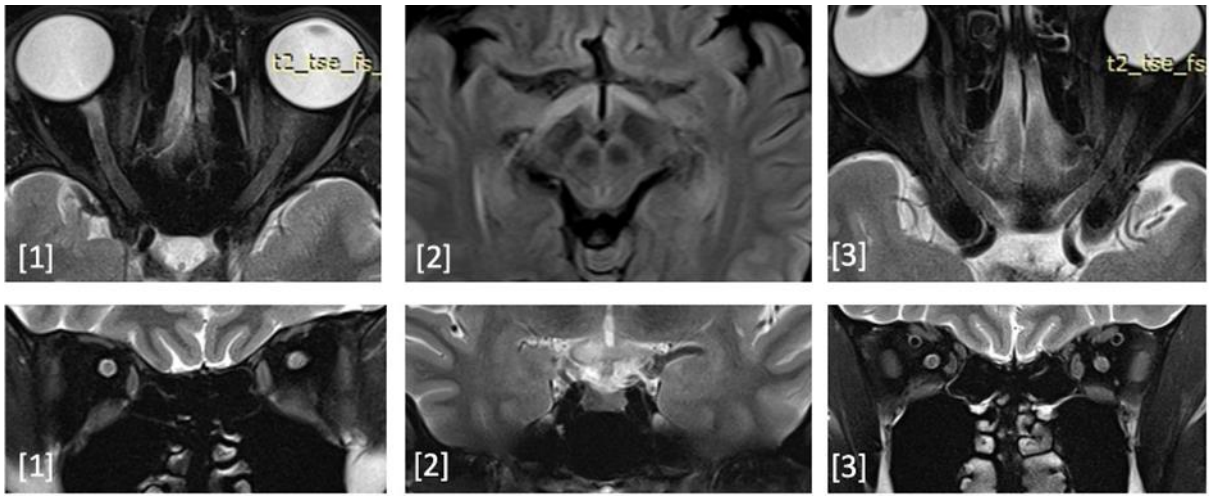

Figure 14: Imaging characteristics of optic nerve lesions; [1] asymmetrical, short segment lesions of MS, [2] symmetrical lesions of AQP4 positive involve optic chiasm and optic tracts, [3] symmetrical, long segmental lesions of MOG positive cases involve anterior most visual pathway.

Table 6: Evaluation of brain prediction

Model	Weighted means		
	Precision	F-measure	ROC-area
SVM	0.933	0.874	0.930
Random forest	0.935	0.892	0.930
Naïve Bayes	0.965	0.888	0.936
Logistic regression	0.933	0.874	0.897

Discussion

Evaluation of neuroimaging of CNS demyelinating diseases is always challenging due to overlapping clinical features. While the detection of AQP4 and MOG antibodies provides a consistent measure to diagnose NMOSD, a significant proportion of patients (22% in this study) negative for both antibodies. Furthermore, a significant delay is experienced in obtaining antibody results in Sri Lanka and antibody tests may not be affordable for everyone.

In the current study we compared the neuroimaging features of MS and NMOSD, as well as the subtypes of NMOSD, using a limited sample size. We found imaging differences between MS and NMOSD that are significant. The findings did not reach statistical significance in the subcategorization of NMOSD subtypes, although certain lesion locations were found to be specific for each subtype.

NMOSD shows a wider spectrum of MRI features in the literature, but still evolving[7]. The immunology, pathology and genetics underlying NMOSD subgroups are distinct. Recent papers have analyzed the imaging differences between AQP4 and MOG positive diseases but there are very few studies comparing NMOSD cases that are negative for both AQP4 and MOG antibodies[14.]

The extent of the MS lesions particularly in the periventricular, juxtacortical and inferior temporal lobe, is comparable in most parts of the world but higher than some parts of Asia. [15,16,17,18] A study from China reported periventricular and juxtacortical, and inferior temporal lobe lesions of 56.3% and 37.5%, respectively.[18]

Brain lesions were found in 52% of the AQP4 positive NMOSD patients in our study, slightly higher compared to the recent paper from Sri Lanka.[16] Comparing with other countries in Asia it resembles rates in China (n=129, 50.9%) and India (n=28, 60.9%), but lower than Japan.[18,19,20] A study conducted in Taiwan shows that brain lesions were found in 81% of the patients.[13]

44% of brain involvement was found in MOG positive NMOSD in our study and it is higher than available data from literature describing a more restricted phenotype primarily involving optic nerves and spinal cord.[21]

The double negative subgroup of NMOSD demonstrated 63% of brain involvement in this study, requiring further studies from other parts of the world for better comparison.

Factors such as genetics or environmental influences specific to different regions may contribute to imaging differences, warranting further studies.[21]

Although there were no statistically significant differences in the location and morphology analysis among NMOSD subtypes, we did find a few characteristic lesions as described in the literature. For example, bridging callosal and area postrema lesions and cloud-like enhancement were observed in AQP4 positive NMOSD, confluent corticospinal tract involvement was seen in AQP4 positive and double negative NMOSD and large fluffy lesions were found in MOG positive NMOSD. Further multicentric studies in Sri Lanka are needed to reveal the imaging significance of these findings.

Regarding the spinal cord lesions, our findings mostly align with the literature, except for a higher frequency of involvement of the cervical spine in both MS and NMOSD, with a small variation in the distribution.

Longitudinally extensive spinal cord lesions in NMOSD were a common finding, consistent with similar studies.[23,24] In our study, short segment lesions found in 5% of AQP4 positive and 11% of MOG positive NMOSD patients. This again tallies with a study conducted by Mayo clinic, which demonstrated 14% of initial myelitis episodes in NMOSD presented as short segment lesions with subsequent longitudinally extensive transverse myelitis in 92%. Therefore, further follow up studies are recommended in these population.[24]

In optic pathway as expected from the literature, the anterior most segments; intraorbital, intracanalicular, and intracranial lesions were more frequent in MS (n=68) and MOG positive NMOSD (n=4) in our study. Noticeably our data revealed higher anterior most segmental involvement, along with optic chiasm and optic tract lesions in AQP4 positive (n=6) and double negative NMOSD (n=1). This may be due to chronic changes secondary to involvement of optic chiasm and tracts, and analysis of the initial imaging studies is warranted. Involvement of the optic chiasm and optic tracts is again a specific feature in AQP4 positive NMOSD.[25]

Limitations: There are a number of limitations present in our study. The study suffered from recruitment bias because of small study population and unequal number of MS and NMOSD patients. We recruited consecutive patients in both acute and chronic phases and the follow up and treatment durations were inconsistent between groups.

We were unable to identify any imaging markers that would distinguish the NMOSD subgroups from one another. The lesser number of the patients with MOG positive (n=09) and double negative (n=08) might affect the statistical results.

The initiation of treatment on the clinical grounds before imaging especially with steroid pulses obscures the enhancement characteristics significantly. Our post contrast delay was not adequate in the detection of leptomeningeal enhancement which usually needs 10-minute delay. Although cortical lesions are now increasingly described in the recent literature with MS, our present MRI protocol which was used is not optimal.

Conclusions and recommendations: Visually detailed analyses showed imaging differences between MS and NMOSD in terms of the number, location, and morphology of the lesions. The study validated neuroimaging differences in the brain and spinal cord and optic pathway within the Sri Lankan population. These observations may have significant clinical implications.

We recommend conducting multicentric studies with large sample sizes to validate the imaging characteristics of NMOSD. Additionally, updating the imaging protocols to include the potential diagnostic role of cortical lesions and enhancement patterns in distinguishing between MS and NMOSD is advisable. Incorporating

imaging techniques such as 3D double-inversion recovery (DIR), phase-sensitive inversion recovery (PSIR) or magnetization-prepared rapid acquisition with gradient echo (MPRAGE), as well as delayed post contrast imaging will be valuable in this regard.

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