Comparison of Clinical and Radiological Features of Aquaporin4 (AQP-4) Antibody Positive Neuromyelitis Optica Spectrum Disorder (NMOSD) and Anti Myelin Oligodendrocyte Glycoprotein (Anti-MOG) Syndrome–Our Experience from Northwest India

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Abstract

Background: More and more cases of myelin oligodendrocyte glycoprotein (MOG) antibody are being diagnosed with the availability of laboratory tests helping us to know the differing patterns from AQP-4 antibody disease and we need to understand the natural course, treatment, and prognosis in a better way. Objectives: Neuromyelitis optica spectrum disorder (NMOSD) and anti-MOG syndromes are immune-mediated inflammatory demyelinating conditions of the central nervous system (CNS) that mainly involve the optic nerves and the spinal cord. We conducted this study to compare demographic, clinical, laboratory, and radiological features of AQP-4 antibody and MOG antibody positive patients. Methods: A single-centre retrospective observational study from a large tertiary care university centre of Northwest India conducted during 2019–2021. We screened all patients presenting with acute CNS demyelinating attacks and recruited total 47 patients of which 25 were positive for AQP4 antibody and 22 were positive for MOG antibody. No patient tested positive for both antibodies. Data were collected using a standardized format including demographic, clinical, laboratory, and neuroimaging data. Results: In our study, total 47 patients were included, amongst which 25 patients were AQP4 antibody and 22 patients were MOG antibody positive. Though there was no gender preponderance, pediatric patients were more frequently affected in MOG antibody positive group. In AQP-4 antibody positive patients, myelitis was most common presenting clinical feature followed by optic neuritis (ON), simultaneous ON with myelitis, and brainstem syndrome. In MOG antibody positive group, myelitis was the commonest phenotype followed by ON, brainstem syndrome, and cerebral syndrome. The neuroimaging revealed involvement of medulla mainly area postrema, cervicodorsal spinal cord and extension of cervical lesion up to brainstem more commonly in AQP4 antibody group, on the other hand involvement of upper brainstem (midbrain and pons), cortex, and conus was more common in MOG antibody group. Conclusion: We have made an attempt to find differentiating features in AQP-4 vs. MOG antibody positive cases but they were of no statistically significance value as the numbers were small. Further larger studies may prove helpful in planning better strategies in two groups.

Keywords: AQP-4, MOG, myelitis, NMOSD, optic neuritis

INTRODUCTION

Neuromyelitis optica spectrum disorder (NMOSD) and anti-myelin oligodendrocyte glycoprotein (anti-MOG) syndromes are immune-mediated demyelinating conditions of the central nervous system (CNS) that mainly involve the optic nerves and the spinal cord. AQP-4 and anti-MOG syndromes usually share a number of clinical manifestations, but they are independent diseases with different pathophysiological mechanisms. NMOSD is associated with antibodies that target aquaporin-4 (AQP-4), particularly present in the astrocytic processes at the blood-brain barrier (BBB). Anti-MOG syndromes result from damage to MOG, a membrane protein present on oligodendrocyte cell surfaces and on the outermost surface of myelin sheaths. Moreover, two-third of NMOSD patients test positive for AQP-4 antibody, while about one third of AQP-4 antibody negative NMOSD patients are detected positive for anti-MOG antibody. MOG antibody was initially thought to be responsible for a benign monophasic illness affecting optic nerves and spinal cord, but further reports suggested

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other presentations such as pediatric acute disseminated encephalomyelitis (ADEM), acute brainstem syndrome, cortical encephalitis, and meningoencephalitis.[15-18] There are limited number of clinical studies which compared clinical and radiological characteristics between AQP-4 positive and MOG positive antibody, so we conducted a study to compare demographic, clinical, laboratory, and radiological features of aquaporin-4 (AQP-4) antibody and MOG antibody positive patients.

AIMS AND OBJECTIVES
To compare demographic, clinical, laboratory, and radiological features of AQP-4 antibody and MOG antibody positive patients.

MATERIAL AND METHODS
Study design
An observational retrospective study was carried out in the neurology department of a large tertiary care university centre of north-west India from January 2019 to January 2021 and data were collected as per the proforma designed for the study. Approval was taken from institutional ethics committee.

Inclusion criteria
Patients admitted at our centre with CNS demyelinating attacks fulfilling following diagnostic criteria[19] and were either AQP-4 or MOG antibody positive.

Diagnostic criteria for NMOSD with AQP4-IgG
1. At least 1 core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses

Core clinical characteristics
1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

Exclusion criteria
1. Other demyelinating diseases like multiple sclerosis.
2. Other causes presenting as optic neuritis and/or myelitis like tuberculosis (TB), autoimmune diseases like SLE and granulomatous lesion like sarcoidosis.

Methodology
We screened all patients who presented to us with acute CNS demyelinating attacks like optic neuritis (ON), transverse myelitis, acute disseminated encephalomyelitis (ADEM) and other focal or multifocal demyelination.[20] We recruited total 47 patients of which 25 tested positive for AQP-4 antibody and 22 tested positive for MOG antibody. An informed consent was taken from all of them for participation in the study. Positivity for AQP-4 and MOG antibodies was determined by AQP-4 cell based assay (CBA) with visualization of binding to human embryonic kidney cells. Data were collected using a standardized proforma including demographic data (age at onset, gender), clinical data (phenotype at onset, associated symptoms), radiological data (3T MRI of the brain, optic nerve, and spinal cord with T1W, T2W, FLAIR, and gadolinium enhanced [GE] T1W axial, coronal, and sagittal sequences), and biological data (serum MOG and AQP-4 antibody, antinuclear antibody [ANA], cerebrospinal fluid [CSF] cells, CSF biochemistry [protein, sugar], CSF oligoclonal bands).[21] Additionally, RT PCR nasopharyngeal swab for COVID-19 was performed for all patients included after the onset of COVID-19 pandemic from March 2020 onwards as per the policy of the department.

Statistical analysis
The clinicoradiologic features of both groups were compared. The SPSS package version 20 was used for data analysis. The significance of difference between percentage of patients in two groups was tested by applying Chisquare test. For comparing numerical parameters like “age at onset”, etc., nonparametric Mann-Whitney U-test was used. The significance level considered was \( P < 0.05 \).

RESULTS
Demographic and clinical presentation
In our study, total 47 patients were included, amongst which 25 (53%) patients were AQP-4 antibody positive and 22 (47%) patients were MOG antibody positive.

Our observations on demographic and clinical features of both the groups are depicted in Table 1. Mean age at onset, onset in first decade, and number of relapses were similar in two groups. However, there was female preponderance (80%) in AQP-4 antibody positive group \(( p = 0.005)\) while preceding infectious prodrome and onset <18 years of age were more frequent in MOG antibody positive group.

AQP-4 ANTIBODY POSITIVE GROUP - Myelitis was the commonest manifestation in 18 (72%) patients, 9 (36%) patients presented with paraparesis, 6 (24%) with quadriplegia and 1 (4%) with quadriplegia (left hemiparesis and right upper limb weakness). One (4%) patient presented with quadriplegia with recurrent vomiting with bilateral ON and 1 (4%) patient presented with quadriplegia with recurrent vomiting.

Optic neuritis was presenting feature in 5 out of 25 (20%) patients. Unilateral ON was present in 2 (8%) patient and bilateral ON was present in 3 (12%) patient. Interestingly, there were two (8%) patients who presented with hemiparesis, of which 1 (4%) patient had isolated hemiparesis and other patient presented with hemiparesis along with intractable vomiting.
One patient (4%) presented with respiratory distress, recurrent vomiting, and altered sensorium. Recurrent vomiting was presenting feature in 4 (16%) patients.

**MOG ANTIBODY POSITIVE GROUP** - Disease most commonly began as myelitis in 13 patients (59%). Eight (36%) patients presented with paraparesis and 5 (23%) had quadriparesis. ON was presenting feature in 4 (18%) patients. Unilateral and bilateral ON was present in 2 (9%) patients each. Other presentations included isolated brainstem syndrome with ataxia, hiccups and vomiting in two patients (9%); and two patients (9%) presented with cortical involvement in the form that one patient had seizure along with limb weakness and one had multiple seizures only. One patient (4.5%) had ON-ADEM like presentation (unilateral vision loss, seizures, drowsiness).

**Laboratory investigations**

CSF pleocytosis of >5 WBCs/HPF (lymphocytic predominance) and proteins >45 mg % were found in 7 out of 25 (28%) patients with AQP-4 and 6 out of 22 (27%) with MOG antibody positive patients. There was no patient with positive oligoclonal bands in CSF. ANA positivity was found in 4 out of 25 (16%) patients with AQP-4 and none in MOG antibody positive patient. VEP was prolonged in 20 out of 25 (80%) patients (bilaterally in 70% and unilaterally in 30%) with AQP-4 and 12 out of 22 (54.4%) (bilaterally in 75% and unilaterally in 25%) with MOG antibody positive patients. So except ANA positivity in AQP-4, there was no appreciable difference in features in both groups. [Table 2]

No patient tested positive for both AQP-4 and MOG antibody in our study.

**Neuroimaging features**

MRI of brain, orbit and spine with or without contrast was done to study distribution and characteristics of lesions and findings are shown in Table 3.

**AQP-4 POSITIVE GROUP** - MRI of the spinal cord was abnormal in all 18 (72%) patients who presented with myelitis and it was LETM [Figure 6]. Dorsal cord was involved in 9 (36%) patients, cervical cord in 7 (28%) patients, 1 (4%)...
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1 patient had cervicodorsal involvement and 1 (4%) patient had dorsal cord to conus involvement. Cervical cord lesions extending into the medulla were seen in 16% (4/25) patients. Distribution of brain lesions in AQP-4 patients included subcortex, periventricular region, thalamus, hypothalamus, corpus callosum, brainstem, and cerebellum. Most commonly involved structure was brainstem found in 20% (5/25) patients and area postrema was involved in all of them. Cerebellum and middle cerebellar peduncle involvement, subcortical periventricular and corpus callosum atypical white matter lesions, bilateral thalamic, and hypothalamic involvement was seen in 1 (4%) patient each [Figure 5].

Total 5 (20%) AQP-4 positive patients presented with ON, out of which 2 (8%) patient had bilateral optic nerve affection, 2 (8%) patient had unilateral optic nerve affection, and in 1 (4%) patient MRI orbit was normal. Longitudinally extensive optic nerve involvement was seen mainly in the posterior segment of optic nerve.

MOG POSITIVE GROUP - MRI of the spinal cord was abnormal in all 13 (59%) MOG patients who presented with myelitis in the form of longitudinally extensive transverse myelitis (LETM). Dorsal cord involvement was seen in 5 (23%) patients, while 4 (18%) patients had cervicodorsal involvement, and four (18%) patients had conus involvement [Figure 4].

Distribution of brain lesions in MOG patients included cortex, caudate nucleus, thalamus, brainstem, and cerebellum. Most commonly involved structure was brainstem. Brainstem lesions were found in 7 (32%) patients of which pons was involved in 6 (27.3%) patients and midbrain was involved in 4 (18.2%) patients [Figures 1 and 3].

Total 4 (18%) MOG positive patients presented with ON, out of which 1 (4.5%) patient had bilateral optic nerve affection, 1 (4.5%) patient had unilateral optic nerve affection, and in 2 (9%) patient MRI orbital section was normal. Longitudinally extensive optic nerve involvement was seen mainly in the anterior segment of optic nerve [Figure 2].

Table 2: CSF, serological, and vep study results of the aqp4 and mog antibody positive patients

| Investigation          | Components                                           | AQP4 antibody positive patients (n=25) | MOG antibody positive patients (n=22) | P (significance: P<0.05) |
|------------------------|------------------------------------------------------|---------------------------------------|---------------------------------------|--------------------------|
| CSF                    | CSF pleocytosis (>5 WBCs/HPF)                        | 7 (28%)                               | 6 (27%)                               | P=0.96                   |
|                        | (i) Lymphocytic predominance                         | 5/7 (71.5%)                           | 4/6 (66.6%)                           | P=0.96                   |
|                        | (ii) Neutrophilic predominance                       | 2/7 (28.5)                            | 2/6 (33.3)                            | -                        |
| CSF proteins (>45 mg %)|                                                      | 7 (28%)                               | 6 (27%)                               | P=0.96                   |
| CSF OCB                |                                                      | 0                                     | 0                                     | P=0.96                   |
| ANA positive           |                                                      | 4 (16%)                               | 0                                     | P=0.96                   |
| VEP                    | Bilateral prolonged VEP                              | 20                                    | 12                                    | P=0.96                   |
| Prolonged P 100 latency| Unilateral prolonged VEP                            | 14/20                                 | 9/12                                  | P=0.96                   |
|                        |                                                      | 6/20 (30%)                            | 3/12 (25%)                            | P=0.96                   |

Table 3: Radiological features of aqp4 antibody and mog antibody positive patients

| Structure                  | Pattern of involvement | AQP-4 positive patients n=25 | MOG positive patients n=22 | P (significance: P<0.05) |
|----------------------------|------------------------|-----------------------------|---------------------------|--------------------------|
| Optic nerve/chiasmal abnormalities | Total patients with ON | 5 (20%)         | 4 (18%)                     | P=0.87                   |
| 1. Normal                  |                        | 1 (4%)                      | 2 (9%)                     | P=0.34                   |
| 2. Bilateral               |                        | 2 (8%)                      | 1 (4.5%)                   | P=0.64                   |
| 3. Unilateral              |                        | 2 (8%)                      | 1 (4.5%)                   | P=0.64                   |
| Cortex                    | Bilateral              | 0                           | 2 (9%)                     | -                        |
| Periventricral/callosal white matter |                  | 1 (4%)                      | 0                          | -                        |
| Basal ganglia              | Bilateral caudate nucleus |                          | 0                           | 1 (4.5%)                 | -                        |
| Thalamus                  | Bilateral              | 1 (4%)                      | 2 (9%)                     | -                        |
| Hypothalamus              | Bilateral              | 1 (4%)                      | 0                          | -                        |
| Brainstem involvement     | Midbrain               | 1 (4%)                      | 4 (18%)                    | -                        |
|                            | Pons                   | 2 (8%)                      | 6 (27%)                    | -                        |
|                            | Medulla                | 5 (20%)                     | 2 (9%)                     | -                        |
| Cerebellum/peduncles      | LETM                   | 18 (72%)                    | 13 (59%)                   | P=0.54                   |
| Spinal cord               |                        | 7 (28%)                     | 0                          | -                        |
|                            | Cervical cord          | 9/36%                       | 5/23%                      | -                        |
|                            | Cervical to conus      | 1 (4%)                      | 2 (9%)                     | -                        |
Management

AQP-4 POSITIVE GROUP - In the AQP-4 positive group, 21 out of 25 (84%) patients were treated with injection methylprednisolone (MPS) 1 gm daily for 5 days. Two (8%) patients were treated with 3 cycles of plasmapheresis, 1 (4%) patient was treated with 5 cycles of plasmapheresis and 1 (4%) patient was treated with 2 cycles of plasmapheresis followed by injection rituximab.

MOG POSITIVE GROUP - In the MOG antibody positive group, all 22 patients were treated with injection MPS 1 gm daily for 5 days.

Discussion

We have attempted to find differentiating features in 25 patients with AQP-4 vs. 22 patients with MOG antibody positive group. We also reviewed the literature and data from various studies on NMOSD vs. MOG are presented in Table 4 along with our observations.

In most of the NMOSD reported series the mean age of onset was in the 4th decade [23,24] while in our study, it was 29.52 years, with a wide range of 10-52 years matching with another Indian study. [22] A strong female preponderance has been reported for NMOSD in various studies in different patient populations. [23,24] Our study also found a high female: male ratio of 4:1. The mean age of onset in our MOG antibody patients was 23.32 years, whereas in other studies it was on higher side. [21,22,25-27] The larger studies of MOG antibody disease reported a high incidence in paediatric age group and no gender bias, similar to our study. [21,22,25-27] Preceding clinical events were more frequent in MOG positive group while number of patients with relapse were similar in both the groups.

In our AQP-4 antibody positive patients, myelitis was most common presenting clinical feature followed by ON. Previous larger studies also showed similar presentation. [28,29] We encountered a wide spectrum of MOG antibody disease, with myelitis being the commonest phenotype followed by ON, brainstem syndrome, cerebral syndrome, and ADEM-ON. However, in the previous larger studies ON was found to be more common than myelitis. [21,22,25-27] The spinal cord involvement in all myelitis cases in both the groups of our study was in the form of LETM and we did not find any short segment spinal cord lesions.

In MOG antibody disease anterior segment of optic nerve was more involved and in AQP-4 antibody disease posterior segment and optic chiasma was more involved as reported in other larger studies. [21,22,25-29]

Hemiparesis as a presenting feature has not been described in NMOSD or MOG antibody disease in earlier studies. However, two of our patients presented with hemiparesis in AQP-4 group. Seizures were observed in two patients in the MOG group, but not in the AQP4 group. Isolated cortical encephalitis presenting with seizures has been seen in MOG antibody disease, but not in AQP4 antibody disease. [17,18,21] Most of the demographic and clinical features were not significant statistically in two groups we studied.

CSF studies were almost same in both the groups. In AQP-4 positive group ANA was found to be positive in 4 (16%) patients, however further work up could not be done due to financial constraints. Prolonged VEP was seen more frequently in AQP-4 positive patients (80%) as compared to MOG positive patients (54.4%) but it was not significant statistically.

The neuroimaging involvement of upper brainstem (midbrain and pons), cortical lesions and conus was found more commonly in MOG antibody group, on the other hand involvement of medulla mainly area postrema, cervicodorsal spinal cord and extension of cervical lesion up to brainstem was more commonly found in the AQP4 antibody group, similar to earlier studies. [12,13,21] However, the neuroimaging features did not have a statistical significance on comparing both the groups in our study. In AQP-4 group, though the number is too small, 1 (4%) patient had left subcortical white matter, periventricular and callosal involvement presenting as hemiparesis; and 1 (4%) patient had bilateral thalamic and hypothalamic involvement who presented with hypersomnolence. Cortical and basal ganglia involvement was not seen in AQP-4 group.

We did not find any difference between males and females in terms of clinical presentation and radiological findings.

Figure 1: (a-d): MRI brain T2 FLAIR axial sequences showing large fluffy cortical, and subcortical hyperintensities in patients with MOG antibody positive disease
### Table 4: Various studies published on NMOSD vs MOG - review of literature

| Features | AQP4 + antibody group | MOG + antibody group |
|----------|------------------------|----------------------|
|          | Kitley et al.[13] 2014 n=20 | Sato et al.[12] 2014 n=139 | Höftberger et al.[14] 2015 n=59 | van Pelt et al.[14] 2016 n=41 | Ojha et al.[22] 2020 n=27 | Our study 2022 n=25 | Kitley et al.[13] 2014 n=9 | Sato et al.[12] 2014 n=16 | Höftberger et al.[14] 2015 n=17 | van Pelt et al.[14] 2016 n=20 | Ojha et al.[22] 2020 n=21 | Our study 2022 n=22 |
| Demographic | | | | | | | | | | | | |
| 1. Mean age of onset (years) | 44.9 | 37 | 40.5 | 42 | 28.6 | 29.5 | 32.3 | 37.5 | 27 | 36.2 | 32.2 | 23.3 |
| 2. Females | 18(90%) | 122 (88%) | 53 (90%) | 35 (85%) | 18 (67%) | 20 (80%) | 4 (44%) | 6 (38%) | 9 (53%) | 9 (45%) | 11 (52%) | 9 (41%) |
| 3. Onset in 1st decade (years) | >18 y only | >18 y only | >18 y only | >18 y only | >18 y only | >18 y only | >18 y only | >18 y only | >18 y only | >18 y only | >18 y only | >18 y only |
| 4. Paediatric patients (age <18 years at onset) (%) | 8 (40%) | 116 (83%) | 53/57 (93%) | 29 (71%) | 14 (52%) | 4 (16%) | 0 | 8 (50%) | 10 (59%) | 6 (30%) | 9 (43%) | 4 (18%) |
| 5. Number of patients with relapses (%) | 6 (30%) | 16 (10%) | 6 (4%) | 4 (16%) | 0 | 7 (41%) | 4 (18%) |
| Clinical | | | | | | | | | | | | |
| 1. Optic neuritis (ON) n (%) | 23 (96) (24%) | 6/16 (37%) | 1 (4%) | 2 (8%) | 8/11 (73%) | 6/8 (75%) | 1 (6%) | 2 (8%) | 1 (11%) | 0 | 1 (6%) | 1 (5%) |
| 1.1 Bilateral ON n (%) | 73 (96) (76%) | 10/16 (63%) | 3 (11%) | 2 (8%) | 3/11 (28%) | 2/8 (25%) | 4 (19%) | 2 (9%) |
| 1.2 Unilateral ON n (%) | 73 (96) (76%) | 10/16 (63%) | 3 (11%) | 2 (8%) | 3/11 (28%) | 2/8 (25%) | 4 (19%) | 2 (9%) |
| 2. Isolated transverse myelitis (TM) n (%) | 12 (60%) | 43 (31%) | 16 (27%) | 20 (49%) | 15 (55%) | 16 (64%) | 3 (33%) | 5 (31%) | 5 (29%) | 4 (20%) | 1 (5%) | 13 (59%) |
| 3. ON + TM n (%) | 0 | 85 (61%) | 37 (63%) | 5 (12%) | 1 (4%) | 1 (4%) | 4 (44%) | 1 (6.3%) | 4 (24%) | 8 (40%) | 2 (9%) | 0 |
| 4. Brainstem syndrome (BSS) n (%) | 0 | 56 (40%) | 3 (11%) | 0 | 1 (6%) | 0 | 4 (19%) | 2 (9%) |
| 5. ADEM like presentation n (%) | 0 | 0 | 0 | 0 | 1 (6%) | 0 | 1 (5%) | 1 (5%) |
| 6. ON + TM + BSS n (%) | 0 | 1 (4%) | 1 (4%) | 0 | 0 | 0 |
| 7. TM + BSS n (%) | 0 | 1 (4%) | 1 (4%) | 0 | 0 |
| 8. Isolated cerebral synd. (seizure) n (%) | 0 | 0 | 1 (4%) | 2 (22%) |
| 9. Isolated hemiparesis | 0 |
| 10. Hemiparesis with intractable vomiting | 0 |
| 11. Respiratory distress, vomiting, altered sensorium | 0 |
| Associated Features | | | | | | | | | | | | |
| 1. Infectious prodrome | 20 (80%) | 20 (80%) | 20 (80%) | 1 (6%) | 20 (80%) | 20 (80%) | 1 (6%) | 20 (80%) | 20 (80%) | 1 (6%) | 20 (80%) | 20 (80%) |
| 2. Paroxysmal tonic spasms | 59 (42%) | 10 (37%) | 1 (6%) | 4 (14%) | 4 (16%) | 4 (19%) | 7 (32%) |
| Laboratory | | | | | | | | | | | | |
| 1. Antibody | 20 (100) | 139 (100) | 59 (100) | 41 (100) | 27 (100) | 25 (100) | 9 (100) | 16 (100) | 17 (100) | 20 (100) | 21 (100) | 22 (100) |
| 2. CSF pleocytosis (>5 WBCs/HPF) | (≥10) 6/12 (50%) | (>50) 4/39 (10%) | 13/26 (50%) | 7/25 (28%) | (≥10) 5/9 (56%) | 6/10 (60%) | 9/16 (56%) | (≥10) 5/9 (56%) | 6/10 (60%) | 9/16 (56%) | (≥10) 5/9 (56%) |
| 3. CSF proteins (>45 mg%) | (≥60 mg%) 3 (25%) | 12/32 (38%) | 17/26 (65%) | 7 (28%) | (≥60 mg%) 2/10 (20%) | 3/16 (19%) | 1/16 (6%) | 2/10 (20%) | 3/16 (19%) | 1/16 (6%) | 0 |
| 4. CSF OCB | 0 | 11/60 (18%) | 5/44 (11%) | 0/10 | 0 | 1 (11%) | 0 | 1 (11%) | 3/16 (19%) | 1/16 (6%) | 0 |
| 5. ANA + | 20 (49%) | 7/24 (29%) | 1 (11%) | 20 (80%) | 6 (35%) | 1/16 (6%) |
| 6. Prolonged VEP | 12 (54%) |

Contd...
### Table 4: Contd..

| Features | AQP4 + antibody group | MOG + antibody group |
|----------|------------------------|-----------------------|
|          | Kitley et al. [13]     | Sato et al. [12]      | Höffberger et al. [14] | van Pelt et al. [4] | Ojha et al. [22] | Our study |
|          | (2014) n = 20          | (2014) n = 139        | (2015) n = 59          | (2016) n = 41       | (2020) n = 27    | n = 25     |
|          |                       |                       |                       |                       |                       |            |
|          |                       |                       |                       |                       |                       |            |
| Radiological |                       |                       |                       |                       |                       |            |
| 1. Optic neuritis       | 6                      | 16                     |                       |                       |                       |            |
| 1.1 Normal             | 0                      | 2/16                   |                       |                       |                       | (12%)      |
| 1.2 Bilateral          | 2/6 (33%)              | 2/16                   |                       |                       |                       | (8%)       |
| 1.3 Unilateral         | 4/6 (67%)              | 4/16                   |                       |                       |                       | (5%)       |
| 2. Thalamus            | 2/27 (7%)              | 2/21                   |                       |                       |                       | (9%)       |
| 3. Hypothalamus        | 1                      | 1                      |                       |                       |                       | (4%)       |
| 4. Basal ganglia       | 0                      |                       |                       |                       |                       |            |
| 5. Brainstem           |                       |                       |                       |                       |                       |            |
| 5.1 Midbrain           | 1/7 (14%)              | 1/7 (14%)              | 1 (4%)                | 1/6 (16%)             |                       | (14%)      |
| 5.2 Pons               | 1 (6%)                 | 1/7 (14%)              | 2 (8%)                | 3 (33%)               |                       | (8%)       |
| 5.3 Medulla            | 1 (6%)                 | 1 (4%)                 | 2 (8%)                | 3 (33%)               |                       | (8%)       |
| 6. Cerebellum/Peduncles| 1 (6%)                 | 1/7 (14%)              | 1 (4%)                | 2 (22%)               |                       | (14%)      |
| 7. Periventricular/callosal white matter | 5 (28%) | 1/7 (14%) | 1 (4%) | 2 (22%) | 4/6 (67%) | 3 (14%) |
| 8. Cortex              | 5 (28%)                | 1/7 (14%)              | 1 (4%)                | 2 (22%)               |                       | (14%)      |
| 9. Spinal cord         |                       |                       |                       |                       |                       |            |
| 9.1 Multiple short segments | 14/128 (11%) | 0                     | 0                     | 0                     | 2/6 (33%) | 0 |
| 9.2 LETM               | 114/128 (89%)          | 21/21 (100%)           | 18/21 (100%)          | 6/21 (100%)           |                       | (59%)      |
| 9.2.1 Cervical cord    | 9/11 (82%)             | 89/128 (70%)           | 31/36 (86%)           | 17/21 (81%)           | 7/21 (38%) | 6/9 (66%) |
| 9.2.2 Dorsal cord      | 8/11 (73%)             | 87/128 (68%)           | 30/36 (83%)           | 15/21 (71%)           | 9/21 (36%) | 8/9 (89%) |
| 9.2.3 Conus/lumbar     | 2/11 (18%)             | 5/128 (4%)             | 5/36 (14%)            | 2/21 (10%)            | 1 (4%)    | 6/8 (75%) |
| 9.3 Central cord segments | 9/11 (82%)             | 115/128 (90%)          | 30/36 (83%)           | 21/21 (100%)          | NA        | 6/5 (68%) |
|                     |                       |                       |                       |                       |                       | (67%)      |

synd. = syndrome, NA = not available
We admit that most of the demographic, clinical, laboratory, and neuroimaging differentiating features in both the groups we studied do not carry any statistical significance, however the number studied is small where many features are observed in just single patients. Further larger studies may help in clarification of these issues.

**Conclusion**

MOG and AQP-4 antibody positive cases share many common features though MOG is a very heterogenous disease. We have made an attempt to find out the important differentiating features of patients with AQP4 positive NMOSD and MOG antibody disease. MOG disease should be suspected in patients having ON, brainstem syndrome, myelitis, cerebral syndrome, pediatric ADEM or their combinations. In our study, most common presentation of MOG disease was myelitis in comparison to other previous studies where ON was most common. On the contrary, AQP4 positive NMOSD frequently presents first time as myelitis, area postrema syndrome or their combination with other known manifestations. On neuroimaging, cervical lesion extending to brainstem, area postrema (medulla), subcortical and corpus callosal lesions were more commonly seen in AQP-4 antibody group, on the other hand conus, pons, midbrain, and cortical involvement were more common in MOG antibody group.

These differentiating features may help in early diagnosis of AQP-4 or MOG antibody disease before the antibody test results thereby helping in planning the treatment.
strategy. If the features are suggestive of AQP-4 antibody disease, aggressive treatment will be required while MOG antibody disease is usually monophasic and steroid responsive. Possibly, our comparative series has the largest number of MOG antibody positive cases so far from our country, further larger studies with treatment and long term follow up are needed to explore better differentiating features of statistical significance for planning strategies in future.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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