ORIGINAL RESEARCH PAPER

Ophthalomology

SEROPREVALENCE OF BIOLOGICAL MARKERS IN PATIENTS WITH OPTIC NEURITIS

KEY WORDS: optic neuritis, biomarkers, atypical, NMO, Aqp 4, MOG

Dr. Mathew Savio Post PG Doctor, Under Directorate of Medical Education, Assam

Dr. Moushumi Majumder* Associate Professor, Department of Ophthalmology, Assam Medical College, Dibrugarh, Assam *Corresponding Author

ABSTRACT

Optic neuritis is inflammation of the optic nerve. There are usually a variety of causes leading to optic neuritis and it is usually difficult to find the exact cause from the local signs and symptoms. There are many cases of optic neuritis that is unrelated to MS. Two novel biomarkers, Aquaporin-4 (AQP4-IgG) and Myelin oligodendrocyte glycoprotein (MOG-IgG), have been found in the past that were found to be linked to be linked to atypical optic neuritis. The present study was carried out in 56 eyes of 43 consecutive patients who presented to the outpatient department of Assam Medical College & Hospital, Dibrugarh during the period of July 2020 to June 2021. These patients were examined for various signs as well as microbiological tests were done to detect these antibodies. Antibody against Aquaporin-4 was positive in 3 patients in the present study accounting to 6.98%. The patients who were seronegative for Aquaporin-4 were tested for antibody against MOG and none of the patients were found to be seropositive for the same.

INTRODUCTION

Much of our current knowledge about acute demyelinating optic neuritis derives from the Optic Neuritis Treatment Trial (ONTT). [1] During a 10-year follow-up of the Optic Neuritis Treatment Trial (ONTT), 56 percent of individuals with normal baseline MRIs did not develop clinically or radiologically diagnosed MS. This led to the assumption that there are many cases of optic neuritis that is unrelated to MS. The identification of antibodies (Abs) that selectively recognize aquaporin-4 (AQP4) and myelin oligodendrocyte glycoprotein (MOG) has recently enhanced the management of optic neuritis patients that are not related to multiple sclerosis.[2]

Rationale Of The Study

The prognosis for seropositive optic neuritis is very different as it involves more neurological risks as well as long term effects like hemiparesis. Thus, it's crucial to distinguish between the two. We are trying to assess the proportion of these antibodies in patients who presented with optic neuritis to our department who did not have any prior neurological defect.

AIM OF THE STUDY

To assess the prevalence of anti-Aquaporin-4 (AQP4) and anti-Myelin Oligodendrocyte Glycoprotein (MOG) in patients with optic neuritis.

Relevant Anatomy

1. Antibody against Aquaporin-4 (AQP-4)

The AQP4 gene in humans encodes the water channel protein aquaporin-4, also known as AQP4. The aquaporin channel in the CNS is found in the peri microvascular astrocyte foot processes, glia limitans, and ependyma.[3–5]

Neuromyelitis Optica (NMO) is an uncommon demyelinating, inflammatory central nervous system condition that mostly affects human optic nerves and spinal cord. In two-thirds of instances of Neuromyelitis Optica, aquaporin-4 is the most prevalent autoimmune target, and higher AQP4 autoantibody levels are associated to optic neuritis (ON).[6,7]

2. Antibody Against Myelin Oligodendrocyte Glycoprotein (MOG)

The glycoprotein, myelin oligodendrocyte glycoprotein (MOG) is thought to play a role in the myelination of nerves in the central nervous system (CNS). The MOG gene encodes this protein in humans. It is thought to be an essential "adhesion molecule" for the myelin sheath's structural integrity, and is known to form late on the oligodendrocyte.[8,9]

METHODOLOGY

This is a hospital based cross sectional study consisting of 43 patients of optic neuritis attending the Outpatient Department of Ophthalmology, Assam Medical College & Hospital, Dibrugarh during the period from July 2020 to June 2021.

1) Inclusion Criteria

- Age group between 15 and 70 years of either sex
- Clinically diagnosed cases of unilateral/bilateral optic neuritis.
- No current evidence of any systemic illness other than multiple sclerosis.

2) Exclusion Criteria

- Patients having other medical conditions that could affect visual outcome such as diabetic retinopathy, glaucoma, cataracts, inflammation of retina or uveal tract.
- Patients on Methyl prednisolone or other steroids.

A thorough investigation of each patient, in respect to the systemic as well as ocular features in relation to optic neuritis was done. It was followed by testing them for both the antibodies.

The following kits were used for the antibody testing-

1) Aquaporin 4-Ab- ELK1468 Human AQP4 (Aquaporin-4) ELISA Kit by ELK Biotechnology

- Sensitivity: 0.056 ng/mL
- Detection range: 0.16-10 ng/mL
- Specificity: This assay has high specificity for detection of Human AQP4

2) MOG-Ab- EH0896 Human MOG ELISA Kit by Fine Biotech

- Mean O.D value of 20 duplicates of the zero standards, multiplied by their three standard deviations, was calculated
- This test exhibits a good sensitivity and specificity

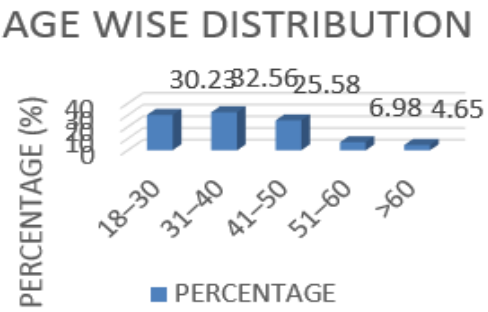
The estimation of antibodies by ELISA was done in the Multidisciplinary Research Unit (MRU) of Assam Medical College & Hospital, Dibrugarh, Assam.

RESULTS AND OBSERVATIONS

Table–1 Age Wise Distribution

Age Group (In Years)	Number (N)	Percentage (%)
15–30	13	30.23
31–40	14	32.56

41–50	11	25.58
51–60	3	6.98
>60	2	4.65
TOTAL	43	100.00
Mean ± S.D.	36.74 ± 12.03 years	
Range	16–62 years	

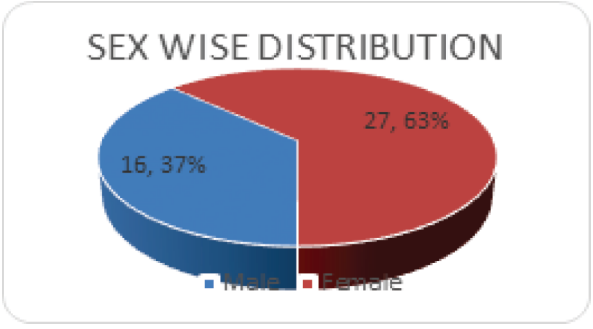


Graph-1

According to Table-1, on analysis of patients in the age group of 15-70 years, the peak age of incidence was found to be in the group 31-40 years (32.56%) closely followed by the group 15-30 years (30.23%).

Table–2 Sex Wise Distribution

Sex	Number (n)	Percentage (%)	Ratio (M:F)
Male	16	37.21	1: 1.69
Female	27	62.79	
Total	43	100.00	

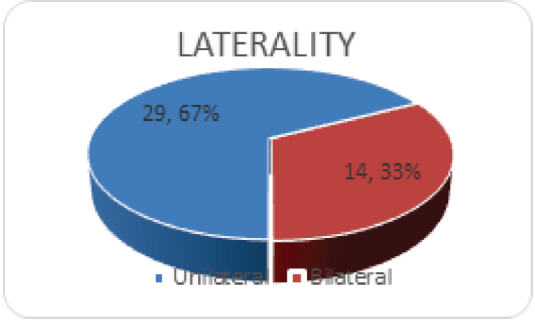


Graph–2

Table–2 shows; in the present study of 43 cases, 16 (37.21%) cases were male and 27 (62.79%) cases were female with a male to female ratio 1: 1.69.

Table–3 Laterality

Laterality	Number (N)	Percentage (%)
Unilateral	30	69.77
Bilateral	13	30.23
Total	43	100.00

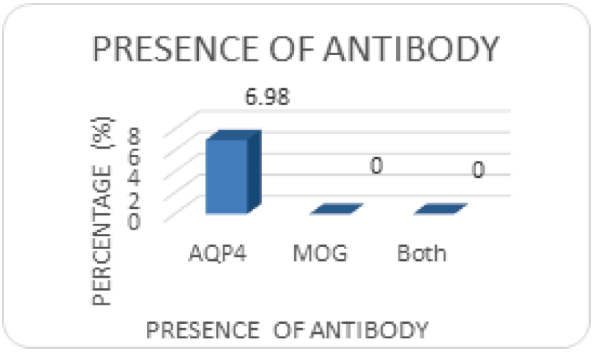


Graph-3

Table-3 shows that unilateral involvement was more common in our study accounting to 30 cases (69.77%). Bilateral involvement was present in 13 cases (30.23%).

Table–4 Presence Of Antibody (n=43)

Antibody	Number (N)	Percentage (%)
AQP4	3	6.98
MOG	0	0.00
Total	3	6.98



Graph-4

Table-4 shows that Aquaporin 4-Ab was detected in 3 cases in our study (6.98%) while MOG-Ab was not detected in any patients.

DISCUSSION

In the present study, on analysis of patients in the age group of 15-70 years, the peak age of incidence was found to be in the group 31-40 years (32.56%) closely followed by the group 15-30 years (30.23%). Together, the peak incidence was found in the age group 15-40 years accounting for 62.79% of total cases.

In our study, 3 cases (6.98%) were found to have presence of AQP4-Ab in their serum on ELISA. Smaller sample size due to the pandemic and lack of follow up in our study might have affected this number.

Pandit L et al (2012)[10] reported similar finding with 3 out of 59 patients in their study (5.01%) being classified as NMO. This was done in South India where patients with ON were evaluated for various etiologies with special mention to NMO. Ambika S et al (2015)[11] did one among the few studies in India regarding seroprevalence of NMO in patients with ON. According to their study, 8 out of 40 patients (20%) came out to be seropositive for AQP4-Ab.

The mean age of presentation in the present study was 35 years. According to literatures, the mean age of presentation of AQP4-Ab seropositive optic neuritis is 40's. In the present study, all the seropositive patients were females. This is in line with many studies which have shown a predominantly female centric disease. In the present study 2 out of the 3 cases (66.67%) presented with a bilateral disease.

All the 3 cases in the present study had a visual acuity less than 6/60 with finger counting at 1 meter being the most common presentation. A follow-up study of these individuals would be ideal, however due to testing restrictions; this was not possible in the present study.

In the present study, no cases were found to have antibodies against MOG. The tests were done on those patients who were seronegative for AQP4-Ab. This may not confirm the absence of this antibody in general population as it will require further studies with a larger study population.

Strengths Of The Study

The study regarding detecting antibodies in optic neuritis patients are very few in India, let alone North -eastern part where this study was done. Further studies can shed some light ob the importance of these tests in suspected individuals to detect early Neuromyelitis Optica.

Limitations Of The Study

1) The sample size was less than expected due to the pandemic
2) The ELISA tests needed to be done together for the samples as it is the case with most enzymatic reagent kits. So, a proper follow up could not be documented.

CONCLUSIONS

1. Considering the typical features of AQP4-Ab positive ON such as female gender in third or fourth decade of life with generally poor visual acuity on presentation, it is important to think about Neuromyelitis Optica (NMO) once other causes of ON like multiple sclerosis has been ruled out.
2. Seropositive optic neuritis has the potential to cause permanent visual impairment as well as features of paresis. Given that treatment approaches differ across these disorders, and medications that are beneficial in MS may aggravate or be ineffective in AQP4- IgG- or MOG-IgG-associated disease, early diagnosis of the underlying etiology of ON has crucial therapeutic implications.

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