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Optic neuritis in the era of biomarkers – the Sri Lankan experience

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Introduction to optic neuritis

The optic nerve, a direct extension of the diencephalon, contains the axons of retinal ganglion cells, that are wrapped by myelin derived from oligodendrocytes, and is peripherally ensheathed by all the three meningeal layers. The total length of the nerve is typically 50-60 mm, and can be divided into four main parts: intraocular (1mm), intraorbital (25-30 mm), intracanalicular (4-10 mm), and intracranial (10 mm). One can consider it to be a communication cable between the eye and the brain. Invariably diseases affecting the optic nerve results in significant visual morbidity.

Optic neuritis, the inflammation of the optic nerve is the commonest cause of optic neuropathy in the young. It results from autoimmune, infective or inflammatory aetiologies. It carries the risk of poor visual outcomes and even blindness, particularly when treatment is initiated late. It should be emphasised that "time-is-nerve" in optic neuritis, making it a neuro-ophthalmological emergency!

The diagnosis of optic neuritis can be suspected with careful history and examination. Patients often present with subacute monocular or binocular (simultaneous or sequential) loss of vision progressing over 3 to 7 days. It is associated with diminished colour perception, decreased contrast sensitivity, seeing scotomas and flashes/photopsia (30%). Another pertinent symptom at presentation is ocular pain evoked by eye movements, related to inflammatory irritation of the adjacent extraocular muscles. The Optic Neuritis Treatment Trial (ONTT) found that 92.2% of patients had ocular pain[1]. The pain was constant and worse with eye movements in 51.3% and present with eye movements only in 35.8%. Absence of ocular pain, or ocular pain persisting beyond 7 days should raise concern for another diagnosis.

The presence of disc oedema denotes the inflammation of the optic nerve head. Hence it may not be seen with retrobulbar involvement. In the ONTT, 35.3% of patients had optic disc oedema[1]. The term "typical optic neuritis", as what is commonly seen with multiple sclerosis (MS), has no or mild disc oedema, and no features of intraocular inflammation, optic disc haemorrhages, retina haemorrhages or retinal vasculitis. "Atypical optic neuritis" is the term given when the individual concerned is younger (<15y) or older (>50y), the visual loss being painless, sudden, bilateral or severely reduced (e.g.no light perception), and when fundoscopy reveals severe optic disc oedema, along with vitreous cells, retinal vasculitis or peripapillary haemorrhages. Disc or peripapillary hemorrhages were found in only 5.6% of patients in the ONTT[1]. These features were associated with a absolutely no risk of developing MS in the ONTT when the brain MRI was normal. After the acute phase of optic neuritis, optic disc pallor is expected in both eyes regardless of the initial appearance of the optic nerves. This becomes apparent approximately 6-8 weeks after the onset of vision loss.

Almost every type of visual field pattern can be seen in optic neuritis. The ONTT found that the most common visual field defects were diffuse (48.2%), altitudinal (14.9%), three quadrant (7.1%), quadrant (6.0%), cecocentral (4.5%), and hemianopic (4.2%) defects[1]. The presence of a relative afferent pupillary defect (RAPD/ Marcus Gunn pupil) denotes an abnormality in the anterior visual pathway proximal to the of the lateral geniculate body. It gives an idea of severity of involvement of one side in comparison to the other. Monocular optic neuritis, therefore, results in ipsilateral RAPD. Altered colour perception is a also feature of inflammatory optic neuritis.

With advances in modern medicine, several investigational tools aid in confirmation, aetiological diagnosis, monitoring and prognostication of optic neuritis. The optical coherence tomography (OCT) is a non-invasive clinical tool that can be used to measure the Retinal Nerve Fibre Layer (RNFL) and the Ganglion Cell Complex (GCC) thickness. However, in patients with acute optic neuritis and no optic disc edema, the RNFL and GCC are approximately normal thickness assuming there is no prior history of an optic neuropathy. The RNFL and GCC will start to decrease in thickness a few weeks after the onset of vision loss.

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The Visual Evoked Potentials measures the cortical activity in the visual system to flash or pattern stimulus. A delayed latency of the P100 wave (the first positive peak in the VEP waveform) can last for a significant period after clinical improvement in optic neuritis due to demyelinating aetiologies.

Prior to the era of biomarkers, optic neuritis was almost always thought to be linked only with MS. But with several breakthroughs in the field serological and CSF biomarkers, distinct clinical entities causing optic neuritis are being discovered. In 2004, IgG antibodies against Aquaporin-4 (AQP-4) were identified and found to be positive in patients previously diagnosed to be having Neuromyelitis Optica or Asian Optic-Spinal Multiple Sclerosis[2]. It a specific marker autoantibody of Neuromyelitis Optica Spectrum Disorder (NMOSD and binds at or near the blood-brain barrier. In 2007, IgG antibodies against Myelin oligodendrocyte glycoprotein (MOG) was identified in a group of patients with distinct clinical phenotypes including optic neuritis, leading up to new entity called Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOGAD) in 2020[3,4]. Currently we have sufficient understanding that MS, NMOSD and MOGAD have distinct differences in pathophysiology, clinical presentation and response to immuno-modulatory treatment. It is now known that if a patient is positive for AQP4-IgG or MOG-IgG, this suggests a worse visual prognosis compared to MS, and a high chance of a relapsing course and intravenous methyl-prednisolone in combination with immuno-suppressive medications are usually initiated. I feel that for this very reason, all patients with optic neuritis should undergo screening for these biomarkers. On the contrary, optic neuritis in multiple sclerosis has favourable response to treatment, with only 3% will have 20/200 vision or worse (i.e. legal blindness).

All patients should undergo a dedicated Magnetic Resonance Imaging (MRI) of the orbits (T1 weighted sequences with fat suppression, pre and post contrast) within a week of diagnosis. The presence of a swollen optic nerve with contrast enhancement (due to break-down of the blood-optic nerve barrier) consolidates the diagnosis, and the pattern and extent of optic nerve involvement will give clue to the underlying aetiology. MS, results in unilateral short segment optic neuritis, whereas AQP4 positive NMOSD results in posterior long-segment optic neuritis extending to the chiasm and optic tracts. Imaging is also important to diagnose alternative diagnoses, such as compressive optic neuropathy. MOGAD classically causes bilateral anterior long-segment optic neuritis and perineural enhancement. In a patient with optic neuritis, investigations should be directed towards assessing for any evidence of white matter lesions elsewhere in the central nervous system. This would be best evaluated with an MRI of the brain and spine with contrast. The presence of lesions disseminated in time and space would support a diagnosis of multiple sclerosis. Both AQP4-NMOSD and MOGAD have characteristic pattern of involvement in MRI brain and spine.

The landmark Optic Neuritis Treatment Trial (ONTT) was a 3-year, multicentre RCT from the USA compared treatment with intravenous methylprednisolone (1g/d for 3 days), oral prednisone (1mg/kg), and oral placebo for 457 patients presenting with first ever episode of monocular optic neuritis[1]. It found that intravenous methylprednisolone hastened the recovery of vision (end points of visual field, contrast sensitivity, visual acuity and colour vision) by approximately 4-6 weeks if started within 8 days of onset. The ONTT showed that spontaneous visual recovery begins within 3 weeks and continues up to 1 year, even though there was no difference in visual acuity at 6 months in the intravenous methylprednisolone compared to the placebo or oral prednisone group. Visual acuity improved to at least 20/40 in over 90% of patients at 6 months. There were slightly better visual fields, contrast sensitivity and colour vision in the intravenous methylprednislone group at 6 months, but this was not seen at 1 year. Intravenous methylprednisolone also reduced the risk of developing clinically definite multiple sclerosis for two years in the intravenous methylprednisolone group, although this beneficial effect appeared to lessen after the first two years of follow-up. The ONTT showed that the overall risk of recurrence at 10 years was 35%. The recurrence risk was higher in the oral prednisone group (44%) when compared with the intravenous methylprednisolone group (29%; p=0.03).

Follow-up data of the ONTT showed that for patients with a normal MRI of the brain, the risk of developing clinically definite multiple sclerosis was 25% at 15 years[5]. If there was at least 1 white matter lesion > 3 mm in diameter, the risk of clinically definite multiple sclerosis was 72% at 15 years. The overall risk of multiple sclerosis was 50% at 15 years.

The Mayo Clinic USA – Sri Lankan collaboration

There was a time in Sri Lanka, when optic neuritis was misdiagnosed and late diagnosed, under-standably so when medical school curricula at the time did not include optic neuritis as a subject. Lack of knowledge and unavailability of diagnostic tools along with comparatively deficient neurology services resulted in many affected young people suffering in silence with extremely poor mobility and visual outcomes[6].

Fortunately, this field has undergone tremendous advances. In the year 2013, we established a collaborative link with pioneering researchers at Mayo clinic, Minnesota, USA. This highly acclaimed centre is the point of many discoveries in diagnostics and precision medicine, including the AQP4 antibody in 2004. Through this link, a total of 2164 Sri Lankan patients have been sero-tested between 2013 to 2023 for serum AQP4-IgG and MOG-IgG-antibodies using highly specific live cell-based assays.

In 2016, with the objective of describing the epidemiology, clinical characteristics, treatment responses and outcomes of patients with inflammatory demyelinating disorders (IDDs) of the central nervous system (CNS) in Sri Lanka, a registry of all patients with CNS-IDDS was initiated. After obtaining approval from the Ethics Review Committee of the University of Kelaniya, the registry was initiated at the Institute of Neurology, NHSL, the island's premier centre for care and final point of referral for patients with CNS-IDDs. The registry is being continually updated with data collection performed by the medical officers under my direct supervision.

Each month, we see approximately 300 new and follow-up patients of all types of Central Nervous System – Inflammatory Demyelinating Disorders (CNS-IDDs), majority of whom had optic neuritis. They are managed and specific disease modifying therapies (DMTs) are issued. This was a result of an advocacy program with the Ministry of Health, which I spearheaded over 15 years ago, to convince authorities to make these therapies available.

In December 2018, the SLCTRIMS (Sri Lanka committee for the treatment and research in multiple sclerosis and related disorders), was founded in together with four of my colleagues. Modelled after similar organizations like ECTRIMS (European) and PACTRIMS (Pan-Asia), it functions to facilitate communication and create synergies among clinicians and eminent scientists to promote and enhance research and to improve clinical outcomes.

We have published three cross sectional studies jointly with the Mayo Clinic, retrospectively analysing the data from consecutive cohort of patients with CNS IDDs in Sri Lanka[7,8,9]. These papers were widely cited by internationally. At the time of analysis our registry included 2053 patients, including 239 cases of MOGADs (11%), 82 cases of AQP4 NMOSDs (4%), 261 cases of clinically definite MS (13%), 27 cases of seronegative NMOSD (1%) and 27 cases of CRION (1%). The other cases remained unclassified.

Epidemiology of optic neuritis in Sri Lanka

A total of 998 patients with optic neuritis were referred to the Institute of Neurology from 2013 to date, and all underwent comprehensive clinical, imaging and serological evaluation. We estimated a crude annual incidence of 1.7 cases of optic neuritis per 100,000 population of Western Province. These estimates have limitations as they are hospital-based data, and the referral rates may vary across the country. In comparison to a retrospective population-based study of 110 patients in Olmsted County Minnesota, lesser proportion of patients with optic neuritis had MS, and higher proportion had MOGAD[10] (Table 1).

Multiple sclerosis related Optic Neuritis in Sri Lanka
Our data shows that, optic neuritis was the commonest presenting complaint in MS occurring in 47%

Table 1. Categorisation of patients with optic neuritis in our cohort, compared with a similar study

Category	*Sri Lanka Number (%)*	*Olmsted County Minnesota (3%)*
AQP4 NMOSD with optic neuritis	49 (5%)	3%
MOGAD presenting with optic neuritis	180 (18%)	5%
Multiple sclerosis with optic neuritis	132 (13%)	57%
Seronegative NMOSD with optic neuritis/ single episode ON	18 (2%)	1%
CRION (Chronic Relapsing Inflammatory Optic Neuropathy)	27 (3%)	34%
Aetiology undetermined	592 (59%)	

(123/260). 62% (104/167) had clinically evident optic neuritis at some point. Additionally, we found that 29 (17%) had delayed VEP on evaluation without clinically evident visual impairment[7]. Overall, four out of five patients with MS (79%; 132/167) had clinical or subclinical optic neuropathy at some point of their illness. International data suggest clinically evident ON occurs in around 25% of MS at presentation; and around 70% at some point. However, at autopsy it is estimated to be close to 100%[11,12]. Literature says that out of all patients who present with optic neuritis 20% have evidence of MS at presentation, while another 40% go on to develop MS in due course[13]. Also in our cohort, one in five patients presented with isolated optic neuritis (22%; n=42/167) while others had optic neuritis in combination with transverse myelitis and/or brainstem syndrome and/or cortical syndrome. Of those who had optic neuritis, 25% had bilateral optic neuritis while 30% had recurrent optic neuritis. While one third of them complained of painful visual impairment (37/117; 32%) two thirds presented with painless visual impairment (80/117; 68%). All of the patients had abnormal MRI Brain at presentation. 75 patients had undergone CSF-OCB performed through iso-electric focusing (IEF) method; 45% (34/75) had positive OCB. 17% (18/104) patients went on to have three or more episodes of optic neuritis during the illness. All patients were treated with IV methyl prednisolone pulses during the episodes. Disease modifying treatment was given in the form of beta interferon - parenteral in 71% (74/104) and finglimod - oral in 15% (16/104). Visual outcome data available in 89 out of 104 patients with clinical optic neuritis. Outcomes were measured in visual functional system score of EDSS (Expanded Disability System Score). Normal vision gets a score of 0; worst vision is disabling visual impairment of bilateral eyes which gets a score of 6. Median disease duration in this population was 6 years (SD 7.2y; range 1-45y). Patients were followed up over a median duration of 6y (Range 1-45y; SD 6.5y). Median Visual FSS was 0 (Range 0-5); mean score of 1.14. 62% had completely normal vision at last follow up. Only 12% (12/104) had disabling visual impairment (Visual FSS 4 or more). Low CSF-OCB positivity and better outcomes are possibly regional phenomena.

AQP4-NMOSD and optic neuritis

In 2022, we conducted a cross-sectional study retrospectively analyzing the epidemiological, clinical and treatment related data of patients with AQP4-antibody associated neuromyelitis optica spectrum disorder (NMOSD)[8]. Serological confirmation was made based on cell-based assays performed at the Mayo-Clinic, USA. We had 59 patients with AQP4-NMOSD by the time of publication. AQP4-NMOSD was diagnosed based on the 2015 revised International Panel for Neuromyelitis-Optica Diagnosis (IPND) criteria after exclusion of infectious, granulomatous and neoplastic aetiologies[14]. We found that, 44% of the patients had optic neuritis at initial presentation (n=26/59) while 59% had optic neuritis at some point of the illness (n=48/82). One patient had delayed VEP without any clinically evident episode of optic neuritis. Optic neuritis is reported in around 84% of cases of NMOSD worldwide[15]. Subclinical optic neuropathy is rare in NMOSD as opposed to MS[15]. One in three patients had isolated optic neuritis (n=18/59; 31%) as the presenting symptom while around 13% (n=8/59) had optic neuritis in combination with other symptoms. Around One in five patients (13/59; 22%) had either single or recurrent episodes of optic neuritis as the only clinical symptom during the entire period of follow up. Of those who had optic neuritis, 33% (12/36) had bilateral optic neuritis while 29% (17/59) had recurrent episodes of optic neuritis. Of the patients with isolated optic neuritis five out of thirteen (39%) had abnormalities in MRI brain and three out of thirteen (23%) had abnormality in MRI spine in the form of short segment myelitis. All patients with optic neuritis were treated with IV methyl prednisolone during the acute episode followed by plasma exchange in around 50% (19/56; 53%). Patients have been in follow up for a median duration of 8.5y (Range 1-16y). At the last follow up visual status assessment using visual FSS showed a mean FSS of 3.3 (Range 0-6; SD 2.3). Around 22% (8/30) had completely normal vision while up to half the population had disabling visual impairment (16/30; 44%).

MOGAD related optic neuritis in Sri Lanka

In 2019, we published our cross-sectional study retrospectively analyzing the epidemiological, clinical and treatment related data of 126 patients with MOG antibody associated disorders (MOGAD), whose serological confirmation was made based on cell based assays performed at the Mayo-Clinic, USA[9]. These patients fulfill the current criteria, and infectious, granulomatous and neoplastic aetiologies excluded[16]. The MOGAD cohort consisted of a paediatric population of 30% (44/126). In both adults (57%) and children (37%), optic neuritis was the commonest presenting feature affecting 67% of the patients (n=111/167) while 72% had optic neuritis at some point of the illness (n=171/239). Additionally, 90% of patients with isolated optic neuritis had a normal MRI brain outside of the optic nerve. Nine patients had delayed VEP without any clinically evident episode of optic neuritis. Altogether three out of four patients with MOGAD had clinical or subclinical optic

neuropathy at some point of the illness (180/239; 75%). One half the patients had isolated optic neuritis (n=92/167; 55%) as the presenting symptom while around 11% (n=19/167; 11%) had optic neuritis in combination with other symptoms. One half the patients (82/167; 52%) had either single or recurrent episodes of optic neuritis as the only clinical symptom during the entire period of follow up to date. Of those who had optic neuritis, 60% (67/111) had bilateral optic neuritis while 29% (32/111) had recurrent episodes of optic neuritis. ON is known to be the presenting symptom in upto 55% of MOGADs MOGAD-ON are known to be more bilateral, recurrent and are more likely to have disc oedema[17,18]. We continued to follow the patients with MOGAD up for a median duration of 3y (Range 1-20y). Around 33% (34/101) had completely normal vision while 58% (59/101) had mild visual impairment [Visual FSS = 3 or less] and only 8 patients had disabling visual impairment [Visual FSS = 4 or more] (8/101; 8%).

Seronegative NMOSD related optic neuritis

Out of the 28 patients satisfying the 2015 International consensus diagnostic criteria for NMOSD with serostatus negative for AQP4 and MOG antibodies, 18 (64%) had optic neuritis. 11 of them had bilateral optic neuritis (61%). 4 had sequential episodes; 7 had simultaneous episodes. One half of them had painful visual impairment (6/13) while others had painless visual impairment (7/13). Around two out of three (11/18; 61%) had associated transverse myelitis in the form of long segment myelitis. 8 had lesions noted in MRI Brain involving the optic nerve including one with a lesion in the optic chiasm. One patient had positive CSF-oligoclonal bands. Two patients had positive Anti-nuclear antibodies (ANA) without any other features to suggest an autoimmune disease. All were treated with IV methylprednisolone pulses followed by plasma exchange in four. Longterm treatment was with steroids in combination with Azathioprine in 11; with mycophenolate mofetil in 3; and rituximab in one patient. Five patients had recurrent episodes of ON despite treatment. All except 2 patients claimed to have subjective improvement in vision with treatment. Assessment of visual acuity at the last follow up revealed 2/8 (25%) with normal vision [Visual FSS=0]; 4/8 (50%) with non disabling visual impairment [Visual FSS= 3 or less]; 2/8 (25%) with disabling visual impairment [Visual FSS= 4 or more].

Chronic Relapsing Inflammatory Optic Neuritis

Chronic Relapsing Inflammatory Optic Neuritis (CRION) is a condition characterized by steroid dependent recurring episodes of optic neuritis, and negative serology. 27 of our patients satisfying the proposed diagnostic criteria for Chronic Relapsing Inflammatory Optic Neuropathy (19). 13 of them had bilateral optic neuritis (48%); 4 had sequential episodes; 9 had simultaneous episodes. 63% had painful visual impairment (17/27) while others had painless visual impairment (10/27). All of them lesions involving the optic nerve in the MRI Brain. One patient had positive CSF-oligoclonal bands. All were treated with IV methylprednisolone pulses followed by plasma exchange in six and rituximab in four. Longterm treatment was with steroids in all in combination with Azathioprine in 20; with mycophenolate mofetil in 5; and rituximab in one patient. Number of relapses ranged from 2-6. All except 2 patients claimed to have subjective improvement in vision with treatment. Assessment of visual acuity at the last follow up revealed 3/18 (17%) with normal vision [Visual FSS=0]; 8/18 (44%) with non disabling visual impairment [Visual FSS 3 or less]; 7/18 (39%) with disabling visual impairment [Visual FSS 4 or more]. Cases of CRION are increasingly being detected in Sri Lanka, and tend to have a visual ourcome better than AQP4-NMOSD but worse than MS or MODAD.

The characteristics of optic neuritis of our patients are summarised in Table 2.

With regards to treatment, acute episodes were treated with pulsed methyl prednisolone and/ or IVIG and/ or plasma exchange in all patients. 37% (27/73) of all cases with AQP4 NMOSD had received plasma exchange at the initial episode or during a relapse. Long term maintenance treatment was given for 74% (141/191) in the case of multiple sclerosis with beta interferon in 86% (121/141) or fingolimod in 14% (20/141). Half the population of MOGADs were given maintenance immunosuppression with prednisolone/ azathioprine/ mycophenolate or combinations thereof. All patients with AQP4 NMOSD were continued on long-term immunosuppression with either prednisolone combined with azathioprine (54/73; 74%) or mycophenolate (4/73; 5%) or with Rituximab in 5/73 (7%).

Plasma exchange as treatment of acute optic neuritis
We analyzed data of 31 patients who underwent plasma exchange (PLEX) for optic neuritis which was either refractory to steroid pulse therapy after excluding other secondary (in 27 cases), Refractory optic neuritis in association with transverse myelitis (4 cases). Median duration from onset of visual impairment to PLEX was 4 weeks (Range 1week to 8 months). With PLEX 19/31 (61%) had improvement in vision while 12/31 (39%) did not. Mean visual FSS prior to PLEX was 4.4 and post PLEX was 3.3 (Figure 1). It is now accepted that early initiation of PLEX even with methyl prednisolone significantly improve visual outcomes[20].

Table 2. Comparison of characteristics of optic neuritis in Sri Lanka

Characteristic	*MS*	*AQP4-NMOSD*	*MOGAD*	*Seronegative NMOSD*	*CRION*
Median age	35	34	27	40	49
Gender (F:M)	68%:32% F>M	89%:11% F>>M	58%:42% F~M	44%:56% F~M	72%:28% F>>M
<u>ON characteristics</u>					
Frequency	79%	66%	75%	64%	-
Bilateral	25% +	33% +	60% +++	61% +++	48% ++
Painful	32% +			46% ++	63% +++
Recurrent	30% +	29% +	29% +	28% +	- -
In isolation	22% +	2%	52% +++	0%	- -
Visual outcome – disabling visual impairment	12% +	44% ++++	8% +	25% ++	39% +++

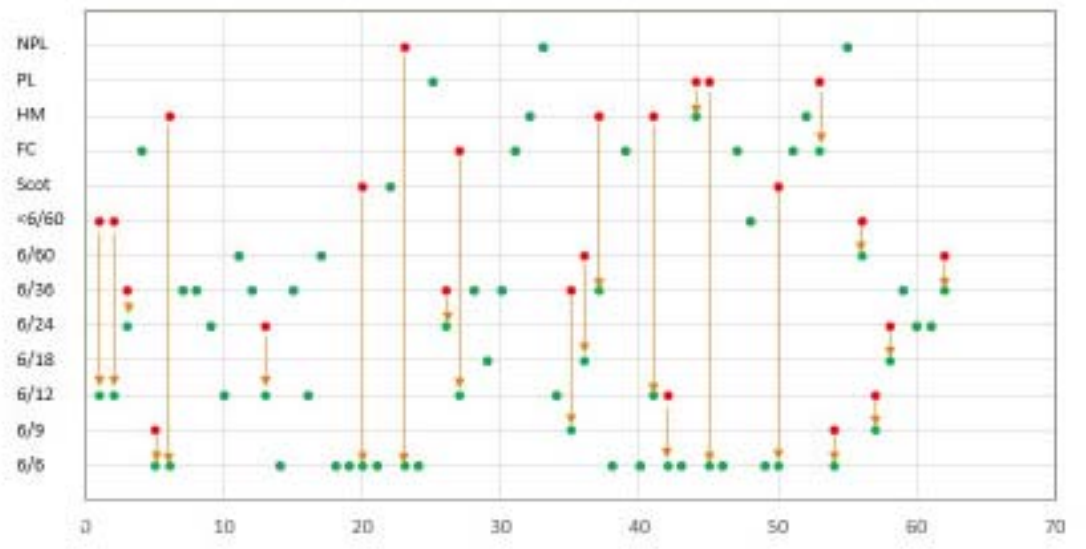

Figure 1. *Individual visual acuities pre and post plex. Red dots – pre PLEX status, Green dots – post PLEX status.*

Observations made on Optical Coherence Tomography

We performed a 3-month pilot study in 2021 where we tested 38 patients with at least one prior attack of optic neuritis (n=10 MS and n=12MOGADs) with OCT. We found that both MS and MOGADs showed significant thinning of retinal nerve fiber layer thickness (RNFL), more evident in MOGADs (average 74.8µm vs 78.1µm in MS). Combined Ganglionic Cell Layer (GCL) and Inner Plexiform Layer (IPL) was 64.9 µm in MS group and 66.6 µm in MOG group. The temporal quadrant was the most affected in both diseases. Combined superior and inferior quadrants were affected in 11.25% in MS and 10.57% in MOGADs. Three patients out of MOG group had normal VEP but with OCT changes. We now consider OCT to be integral part of the evaluation of optic neuritis, not only during follow up but also in the acute stage when making a definite diagnosis. Fernandez et al have shown in their study that asymptomatic abnormalities in inter-attack OCT is more common in patients with MOGADs (84%) than AQP4-NMOSD (38%) in those patients with a past history of optic neuritis; while in those patients without any history of ON up to 20% have abnormalities detected in OCT in both groups[21]. Filippatou et al in a systematic review have shown that retinal nerve fibre thinning is more prominent in AQP4 and MOGAD than in MS while visual outcomes are worse in AQP4 patients than MOGADS and MS patients despite the differences in OCT[22].

Visual outcomes of out patients

Outcomes in CNS demyelinating disorders are described in terms of the Expanded Disability System Score (EDSS) which takes into account, history and examination findings and disability at a given point of time and gives an overall score as well as individual functional system score (FSS). Visual scores were calculated in those who had at least one episode of optic neuritis. 87% had a visual FSS score of <4 (normal vision or non-disabling visual impairment). Similarly, 88% of MOGADs had a visual FSS of <4. Better visual outcomes in MOGADs have been reported by other researchers as well[23].

In the AQP4 NMOSD group, Visual outcomes were poor with 50% having disabling visual impairment or blindness at last follow up. In comparison with Caucasian data, although our visual outcomes were poorer, mobility was betterv[24]. This could be a regional phenomenon as observed by Kitley et al who reported that the time to first relapse was longer, annualized relapse rate was lower and median time to disabling mobility end points were longer in Japanese than the Caucasian and Afro-carribean populations[251]. Another contributory factor could be the early initiation of second line immunotherapy, in the form of therapeutic plasma exchange and rituximab in our patients.

Conclusions

Initially marked by diagnostic challenges and limited awareness, Sri Lanka has now developed a robust framework for managing and understanding optic neuritis due to multiple sclerosis and other CNS-IDDs. I am privileged to have played a role in this evolution by the establishment of a dedicated clinic, initiation of comprehensive registries, and significant international collaborations. These efforts have led to more precise diagnostics, and the availability of advanced disease-modifying therapies, leading to better patient outcomes.

Despite progress, challenges remain, particularly in terms of early diagnosis and access to advanced therapies. Continued advocacy, education, and research are essential to further improve outcomes. The dedicated registry initiated in 2016, encompassing various CNS-IDDs, has facilitated numerous studies on prevalence, clinical phenotypes, and treatment outcomes, contributing to the global understanding of these disorders. The demographics and clinical characteristics of our patients reveal patterns similar to global trends, however, unique regional phenomena highlight the importance of localized research and tailored healthcare approaches.

In the future we hope to further characterize the burden of optic neuritis in Sri Lanka, with a focus on specific disease phenotypes and treatment responses.

The journey from the initial cases of MS to the current state of comprehensive care and research exemplifies the significant strides made as a country as well as my ongoing commitment to enhancing patient care in this field.

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Lastly, I would like to acknowledge the courage and resilience of our patients. Their experiences and perseverance inspire us to strive for better treatments and outcomes. It has been a privilege to contribute to this field and witness the progress we have made together.

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