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Utility of optical coherence tomography in patients of central immune mediated demyelinating diseases – A prospective study

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ABSTRACT

Optical coherence tomography (OCT) is a non-invasive tool to measure thickness of various layers of retina. Recently, retinal nerve fibre layer (RNFL) and ganglion cell and inner plexiform layer (GCIP) thinning has been observed in OCT in patients with multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD), This study compared OCT profile, along with visual acuity (VA), color vision (CV), contrast saturation (CS) and visual evoked potentials (VEP) in two main cohorts of MS and NMOSD and with controls, during acute episode of optic neuritis (ON), at 3 and 6 months.

We found that changes of ON were present in 75% of MS eyes and in 45% of NMOSD patients. Of these, subclinical involvement was present in 56.25% of MS eyes and only in 5% of NMOSD eyes suggesting frequent subclinical involvement in the former. Mean RNFL was 95.23 ± 15.53 in MS and 66.14 ± 43.73 in NMOSD after 6 months of ON episode. Thinning of NQ and IQ was observed in NMOSD eyes in the immediate period after ON attack. At 6 months relative sparing of RNFL in TQ was observed in NMOSD ON eyes and MS ON showed predilection for involvement of TQ.

1. Introduction

Immune mediated demyelinating disorders of the central nervous system include multiple sclerosis (MS), neuromyelitis optica (NMO), acute demyelinating encephalomyelitis (ADEM), acute haemorrhagic leukoencephalopathy (AHLE) and idiopathic inflammatory demyelinating disorder [1]. Optic neuritis (ON), an acute inflammatory demyelinating disorder of the optic nerve, is characterized by sudden loss of vision occurring over a period from one to eight days [2]. This may occur either in isolation or in combination with other clinical manifestations in immune mediated central demyelination. Optic atrophy and pallor may subsequently develop in 4–6 weeks [3].

MS is the prototype and most common among immune mediated central demyelinating diseases, characterized by the presence of focal demyelinated plaques within the central nervous system in the optic nerves, spinal cord, brainstem, cerebellum, and the juxtacortical and periventricular white matter, accompanied by variable degrees of inflammation and gliosis, partial preservation of axons [4]. ON in MS usually presents as acute or subacute unilateral eye pain accentuated by ocular movements with variable degree of visual loss affecting mainly central vision. Bilateral simultaneous ON is rare in MS as compared to neuromyelitis optica spectrum disease (NMOSD). When bilateral ON occurs in patients with MS, the impairment begins asymmetrically and is usually more severe in one eye.

NMOSD with aquaporin-4 (AQP4) autoantibody is associated with florid demyelination and inflammation, involve multiple spinal cord

Abbreviations: ADEM, Acute Demyelinating Encephalomyelitis; AHLE, Acute Haemorrhagic Leukoencephalitis; AQP4, Aquaporin- 4; CS, Contrast Saturation; CV, Color Vision; FC, Finger Counting; GCL, Ganglion Cell Layer; GCL+/ GCIPL, Ganglion Cell Layer + Inner Plexiform Layer; GCL++/ GCC, Ganglion Cell Complex (Ganglion Cell Layer + Inner Plexiform Layer + Macular RNFL); HM, Hand Movement; Ig G, Immunoglobulin G; IQ, Inferior Quadrant; MRI, Magnetic Resonance Imaging; mRNFL, Macular Retinal Nerve Fibre Layer; MS, Multiple Sclerosis; MS ON, Multiple Sclerosis related Optic Neuritis; NMO, Neuro Myelitis Optica; NMOSD, Neuro Myelitis Optica Spectrum Disorder; NMOSD ON, Neuro Myelitis Optica Spectrum Disorder related Optic Neuritis; NPL, No Perception of Light; NQ, Nasal Quadrant; OCT, Optical Coherence Tomography; ON, Optic Neuritis; PL, Perception of Light; pRNFL, Peripapillary Retinal Nerve Fibre Layer; RNFL, Retinal Nerve Fibre Layer; SQ, Superior Quadrant; TQ, Temporal Quadrant; VA, Visual Acuity; VEP, Visual Evoked Potential.

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segments and the optic nerves with associated astrocyte death, axonal loss, perivascular lymphocytic infiltration, and vascular proliferation [5]. Hallmark features of NMOSD include acute attacks of bilateral or rapidly sequential ON (leading to severe visual loss) or transverse myelitis with a typically relapsing course [6]. Individual ON attacks in NMOSD are indistinguishable from isolated syndromes of ON or those related to MS, though visual loss is generally more severe in NMOSD [7]. Sequential ON in rapid succession or bilateral simultaneous ON is highly suggestive of NMOSD.

A minority of AQP4-seronegative patients with a phenotype of NMOSD has serum antibodies against Myelin oligodendrocyte glycoprotein (MOG). Patients with MOG associated demyelination (MOGAD) are more likely to involve the optic nerve than spinal cord, mostly simultaneous bilateral ON. The course of MOGAD is more likely to be monophasic, has fewer relapses and it is less likely to be associated with other autoimmune disorders. MOGAD causes proportionally more brainstem and cerebellar lesions, and fewer supratentorial lesions with spinal cord lesions mainly in the lower portion of spinal cord [8]. Optic nerve involvement in MOGAD is bilateral where optic nerves become oedematous, enlarged, and tortuous with optic disc edema [9]. One third of ON shows inflammation and enlargement of *peri* optic nerve sheath which is not present in MS and NMO. Optic nerve involvement in MOGAD is bilateral or unilaterally anterior whereas NMO involves posterior part of the optic nerve with chiasmal involvement [9]. Studies of MOGAD in India has shown relapsing ON as the most common phenotype [10].

Differentiating the ON between NMOSD-related ON (NMOSD ON) and MS-related ON (MS ON) can be difficult. Early discrimination between NMOSD ON and MS ON is crucial to provide appropriate and timely management. Optical Coherence Tomography **(**OCT) is a non-invasive, affordable and easily available tool used to measure thickness of various layers of retina. OCT gives an in-vivo cross sectional view of retina. It is an optical analogue of ultrasound imaging. It captures optical scattering from tissue to decode spatial details of tissue microstructures. Retinal ganglion cell axons, lacking myelin sheath, constitute the retinal nerve fibre layer (RNFL) which gives rise to the optic nerve that becomes myelinated after passing through the lamina cribrosa. This anatomical privilege of the RNFL allows the assessment of the retrograde effects of the demyelination process on the anterior optic pathway, providing a diagnostic window for monitoring neurodegeneration. Retinal involvement in patients with MS and NMOSD is mainly seen in the form of changes in the peri-papillary retinal nerve fibre layer (RNFL), ganglion + inner plexiform layer (GCIPL) thickness and the thickness of macula. The frequent involvement of the optic nerve in MS and NMO may be caused by a more reduced blood-brain barrier (BBB) function. Because there is no myelin in the retina, RNFL measurements done through OCT are independent of myelin diseases and may only reflect axonal thinning or loss.

The aim of our study was to compare the OCT and visual profile comprising of RNFL thickness, GCIPL thickness, visual acuity (VA), color vision (CV), and contrast saturation(CS) in patients of central immune mediated demyelinating diseases, immediately during acute episode and subsequent follow up.

2. Methods

This is a prospective, observational, cohort study, carried out among patients of immune mediated central demyelinating diseases admitted in the department of Neurology, during 18 months period from January 2020–June 2021, at a tertiary care hospital in western Rajasthan in India. The study was cleared by institutional ethics committee (AIIMS/IEC/2019–20/973). Patients were recruited during the acute phase of demyelinating disease, either first episode or a relapse of the disease. All the patients regardless of clinical ON status were taken in the study. These were followed up at 3 and 6 months. Patients with past history of ON were not included as this study evaluated changes in the first 6 months of patients with ON. Patients with history of familial, infectious, vascular or compressive optic neuropathy as well as congenital or acquired condition/pathology of eyes that may lead to interference with visualization of retina such as cataract, glaucoma, cystoid macular oedema, retinal detachment, vitreal haemorrhage or vitreal detachment were excluded. Refractive errors >5 dioptres of spherical equivalent refractive error or 3 dioptres of astigmatism were also excluded.

The initial evaluation constituted MRI brain and spine and cerebrospinal fluid (CSF) analysis. CSF examination for cell cytology and biochemistry, serum and CSF oligoclonal bands (OCB), CSF IgG index, serum AQP4 antibody, serum MOG antibody was done as per the clinical and radiological characteristics of the disease.

All the patients were evaluated in detail regarding the ocular complaints. All patients underwent assessment for VA, CV, CS, Visual evoked potential (VEP) analysis for P100 latency and amplitude and OCT analysis. Patients were evaluated for visual acuity by Snellen's chart at 6 m. Ishihara charts with 19 plates were used for color vision analysis. Contrast saturation was measured in all the patients using Pelli-Robson chart. VEP response were elicited in all patients by 48 checker board pattern of black and white squares at 1 Hz on television monitor with patient sitting 1 m away from the screen in dark room. 3D spectral domain OCT machine (NIDEK RS 3000 – Advance 2) was used for scanning the inner retinal layers. All OCT scans were performed by experienced technicians. If patients' pupils were of adequate size for obtaining OCT scans, mydriatic agent was not used. In those requiring it, 1% tropicamide eye drops were used. Scan quality was measured in terms of scan strength. Scan with strength ≥7 (Scan strength ranges from 0 to 10, with 0 being poorest and 10 being best) were used for analysis.

OCT parameters studied were RNFL (papillary RNFL, pRNFL), GCL+ [ganglion cell layer (GCL) and inner plexiform layer (IPL)] and GCL++ [macular RNFL (mRNFL) + GCL+)], also called as GCC. RNFL was measured in superior quadrant(SQ), inferior quadrant (IQ), nasal quadrant (NQ) and temporal quadrant (TQ). The normal range for RNFL considered is 122 ± 12.09 for SQ, 136 ± 14.46 for IQ, 90.5 ± 14.73 for NQ and 81.62 ± 11.76 for TQ and average RNFL is 107.84 ± 7.96 [11]. However, there is difference in RNFL thickness in normal eyes observed based on the race and ethnicity. A study done to measure RNFL in Indian eyes showed, 140 ± 22 for SQ, 131 ± 26 for IQ, 85 ± 21 for NQ and 67 ± 17 for TQ as standard RNFL parameters and average RNFL was 104 ± 39 [12]. The reference for average GCL+ was taken as 63 ± 9.0 and average GCL++ as 100 ± 11.23. In our study, non ON eyes were used as control group.

Eyes with or without clinical optic nerve involvement but showing impairment of VEP, RNFL thickness and/or VA were considered in ON group. Eyes without clinical or subclinical involvement were grouped under non ON group. MS and NMOSD were the main subgroups in the study. Differences between VA,CV,CS and OCT parameters were assessed between ON vs. non ON group, MS ON vs. MS non ON group, NMOSD ON vs. NMOSD non ON group. A longitudinal analysis was carried out to see the change in RNFL over 6 month period in ON, MS ON and NMOSD ON group. All the collected data was analysed using SPSS 27.0.1. A value of $P < 0.05$ was considered significant for all statistical tests. Descriptive statistics and univariate analysis was performed. CV and CS were compared between the ON and non ON group by Fisher exact test. VAwas compared between ON and non ON group by chi square test. The difference in the RNFL thickness and GCL thickness in various quadrants was calculated using *t*-test, following which *P* value was derived.

3. Results

This study was carried out at a tertiary health care center over 18 months from January 2020 to June 2021 with major part of the data collection falling during the period of SARS COVID-19 global pandemic. The study focused on the role of OCT in the evaluation of central demyelinating disorders. We studied the changes in OCT in the first six

months after acute episode of ON. A total 20 patients were recruited for the study, of which 8 patients were MS and 10 patients were NMOSD. Of these 8 MS patients, 6 were OCB+ and remaining 2 were diagnosed on the radiological and clinical features. Of the 10 NMOSD patients, 3 had AQP4 antibodies and 2 had MOG antibodies. The remaining 5 were diagnosed based on radiological and clinical features. All the patients were on treatment without defaulting during the entire course of the study.

Details of patient demographics and patient characteristics is shown in Table 1. Gender distribution showed female predominance (female to male ratio 9:1). Of the 2 male patients, one each had MS and ADEM. The MS cohort had female to male ratio of 7:1. Mean age of presentation for MS and NMOSD in our cohort was 34.25 ± 8.7 years and 39.9 ± 15.13 years respectively. The third decade was the most common presenting age of immune mediated demyelinating disorders.

Of 16 MS eyes, 3 (18.75%) had clinical ON and 9 (56.25%) had subclinical involvement, leading to a frequency of 75% ON in MS (Table 2). Unilateral ON was present in 3 patients contributing to 3 eyes, all belonging to MS patients. The NMOSD cohort had 8 clinical ON eyes constituting 40% and remaining one (5%) had subclinical involvement leading to a frequency of 45% ON in NMOSD.

Our NMOSD cohort showed CV and CS impairment in 33.33% eyes as compared to no CV and CS impairment in MS patients. We could not find any patients with VA 6/60 or low in our MS ON cohort whereas in NMOSD cohort VA impairment with vision <6/60 was present in 33% patients. Our findings show that higher degree of VA impairment is more frequent in NMOSD patients as compared to MS patients. Table 3 shows OCT, VA, CV, CS and VEP findings at 0, 3 and 6 months. VEP analysis in our MS and NMOSD cohort showed prolonged P100 latency in both the groups with a mean value of 122 ms in NMOSD and 125 ms in MS. Our RNFL analysis in MS and NMOSD patients revealed significant thinning of RNFL in NQ (*P* value 0.044) and IQ (P value 0.012) in NMOSD acute episode, with that in IQ being statistically significant when compared with MS cohort (P value 0.039, Table 4). When followed for 6 months, it showed significant thinning in SQ, NQ, IQ and average RNFL with less thinning of TQ in NMOSD (Table 5). The MS patients did not show any significant thinning during acute episode of ON, mean thickness being 121 μm, 124 μm, 80 μm, 63 μm and 97 μm at 0 month in SQ, IQ, NQ, TQ and average RNFL, respectively. However, the RNFL thickness in TQ at 6 months was 55 μm, being selectively reduced as compared to other quadrants.

GCL analysis revealed significant thinning of GCL+ and GCL++ at the time of acute attack in NMOSD as compared to controls (*p* value for GCL+, 0.003; p value for GCL++, 0.001). Such thinning was not observed in MS patients. Mean GCL+ at 6 months in MS was 60.56 ± 4.64 where as it was 52.00 ± 16.67 in NMOSD. Mean GCL++ at 6 months was 94.36 ± 12.63 in MS whereas it was 78.00 ± 28.87 in NMOSD.

Comparison of RNFL changes between MS ON and NMOSD ON group at 6 months (Table 5) showed a significant difference between thinning in MS ON and NMO ON group with NMOSD ON showing more thinning than MS ON in SQ (*P* value 0.045), IQ

(P value 0.047), NQ (P value 0.039) with no significant difference in TQ (Table 5). Mean RNFL in TQ in MS ON was 55 ± 16.1 and that in NMOSD ON was 51.67 ± 42.81, with no significant difference between the two. Though average RNFL did not show a statistically significant change, average RNFL in MS ON was 95.23 ± 15 and average RNFL in NMOSD ON was 66.14 ± 43.13. This showed a difference of approximately 30um in both groups indicating a significant difference in thinning, in favor of NMOSD.

Table 1
Patient demographics.

No.	Patient characteristics	MS	NMOSD	ADEM	Total
1.	No. of patients	8	10	2	20
2.	OCB + MS	6	–	–	6
3.	OCB- MS	2	–	–	2
4.	AQP4 + NMOSD	–	3	–	3
5.	MOG + NMOSD	–	2	–	2
6.	Seronegative NMOSD	–	5	–	5
7.	No. of Eyes	16	20	4	40
8.	ON eyes	12	9	2	23
9.	Non ON eyes	4	11	2	17
10.	Male	1	0	1	2
11.	Female	7	10	1	18
12.	Age,				
	21–30 Years	4	4	1	9
	31–40 Years	2	1	1	4
	41–50 Years	2	2	–	4
	51–60 Years	–	2	–	2
	61–70 Years	–	1	–	1
13.	Socio-economic status				
	Upper	2	1	–	3
	Upper- middle	3	5	1	9
	Lower-middle	3	2	1	6
	Upper-lower	–	1	–	1
	Lower	–	1	–	1
14.	Clinical features				
	Unilateral ON	3	–	–	3
	Bilateral ON	–	4	–	4
	Paraparesis	3	3	–	6
	Quadriparesis	–	2	–	2
	Hemiparesis	4	1	1	6
	Bladder involvement	2	5	–	7
	Bowel involvement	2	5	–	7
	Sensory involvement	7	6	1	14
	Other cranial nerves	1	2	–	3
	Altered mental status	–	–	2	2
15.	EDSS				
	0–3	6	1	0	7
	4–5	1	3	0	4
	6–8	1	1	0	2
	>8	0	5	2	7

Table 2
Clinical and subclinical ON in study groups.

No.	Disease	Total no. of patients	Total no. of eyes N (%)	ON status	Clinical N (%)	Subclinical N (%)
1	MS	8	16(100)	12 (75)	3 (18.75)	9 (56.25)
2	NMOSD	10	20(100)	9(45)	8(40)	1(5)
3	ADEM	2	4(100)	2(50)	0	2(50)

4. Discussion

This study has brought to fore the importance of OCT in assessment of patients with central demyelinating disorders, notably MS and NMOSD. Some of the findings are consistent with the clinical and radiological observations of the same. However, a new dimension is provided by OCT in these disorders. In addition, serial assessments of OCT may show some key pointers favoring one against the others.

The demographic characteristics of the study population was similar to previous observations from the Indian subcontinent. A clear female predilection was observed with female to male ratio 7:1 for MS and > 10:1 for NMOSD. Female predominance in MS has increased from 1.4:1in 1955 to 2.3:1in 2000 [13]. Previous Indian studies have shown ratio of 4.2:1 and 7.8:1 [14,15]. Mean age of presentation for MS and NMOSD in our cohort was 34.25 ± 8.7 years and 39.9 ± 15.13 years respectively and was consistent with existing studies [16]. However, some studies show early onset of NMOSD in Indian population [14]. All patients in our MS cohort belonged to either upper or middle class which is commensurate with higher SE status shown by Wadia et al. in the Parsi community centered around Mumbai and Pune in India who have high literacy rate and higher income [17]. Additionally, the relationship between SE status and occurrence of MS is debatable as varying

Table 3
VA, CV, CS, VEP p100 latency, RNFL, GCL+, GCL++ parameters in MS and NMOSD at 0,3 and 6 months.

No.	Parameters	MS ON eyes					NMOSD ON eyes				
		0 Month	P value (as compared to control)	3 Month	6 Month	P value (as compared to controls)	0 Month	P value (as compared to controls)	3 Month	6 Month	*P* value (as compared to controls)
1.	RNFL, SQ	121.58 ± 17.79	0.774	121.11 ± 17.3	123.09 ± 20.45	–	112.89 ± 31.46	0.055	81.78 ± 43.32	81.33 ± 51.57	**0.022**
2	RNFL, IQ	124.74 ± 19.17	0.791	131.56 ± 35.98	122.18 ± 22.18	–	97.67 ± 31.02	**0.012**	94.33 ± 31.27	81.11 ± 50.6	**0.044**
3	RNFL, NQ	80.25 ± 12.12	0.561	82.89 ± 19.69	80.64 ± 11.49	–	72.78 ± 27.26	**0.044**	63.33 ± 28.81	50.44 ± 36.07	**0.013**
4	RNFL, TQ	63.17 ± 20.35	0.33	68.44 ± 18.22	55 ± 16.1	–	66.67 ± 38.02	0.652	41.89 ± 21.55	51.67 ± 42.81	0.139
	RNFL, Average	97.46 ± 13.9	0.818	100.97 ± 20.31	95.23 ± 15.53		87.5 ± 21.93	**0.039**	70.33 ± 21.98	66.14 ± 43.73	**0.032**
5	GCL+, Average	63.31 ± 6.04	0.702		60.56 ± 4.64	–	55.00 ± 11.20	**0.003**		52.00 ± 16.67	
7	GCL++, Average	95.45 ± 10.33	0.351		94.36 ± 12.63	–	82.22 ± 23.17	**0.001**		78.00 ± 28.87	
9	CV impairment	0 (0%)		0 (0%)	0 (0%)	–	5 (55.56%)	**0.008**	5 (55.56%)	3 (33.33%)	**0.150**
10	CS impairment	0 (0%)		0 (0%)	0 (0%)	–	5 (55.56%)	**0.008**	5 (55.56%)	3 (33.33%)	**0.150**
11	VA impairment LogMAR >1	0 (0%)		0 (0%)	0 (0%)	–	3 (33.33%)	**0.115**	2 (22.22%)	2 (22.22%)	
12	Mean VEP p100 latency	121.41	0.221	128.33	125.91	–	124.77	**0.001**	135.71	122.85	**0.014**

Table 4
Comparison of RNFL between MS ON and NMO ON group at 0 month.

Time	RNFL (ON)		t value	p value
	MS (Mean ± SD)	NMO (Mean ± SD)		
SQ	121.58 ± 17.79	112.89 ± 31.46	0.744	0.472
IQ	124.74 ± 19.17	97.67 ± 31.02	2.308	**0.039**
NQ	80.25 ± 12.12	72.78 ± 27.26	0.767	0.46
TQ	63.17 ± 20.35	66.67 ± 38.02	0.25	0.806
AVG	97.46 ± 13.9	87.5 ± 21.93	1.194	0.255

Table 5
Comparison of RNFL between MS ON and NMO ON group at 6 months.

Time	RNFL (ON)		t value	p value
	MS (Mean ± SD)	NMO (Mean ± SD)		
SQ	123.09 ± 20.45	81.33 ± 51.57	2.287	**0.045**
IQ	122.18 ± 22.18	81.11 ± 50.6	2.263	**0.047**
NQ	80.64 ± 11.49	50.44 ± 36.07	2.413	**0.039**
TQ	55 ± 16.1	51.67 ± 42.81	2.211	0.829
AVG	95.23 ± 15.53	66.14 ± 43.73	1.900	0.089

associations have been reported. The association has been found with higher SE status as well as with lower SE status in different studies while a few studies did not show any relation between the two. A study by Kurtzke et al. in 1489 patients in MS showed an odds ratio (OR) of 2.3 for developing MS in patients with higher SE status [18]. On the contrary, the association of MS with lower SE status was shown by Briggs et al. in 1023 patients with OR 0.7 [19]. Among few studies that did not show any correlation between SE status and MS was that by Antonosky et al. in 241 patients with OR 1.0 [20].

Our study showed subclinical ON in 56.25% of MS patients as compared to only 5% of NMOSD patients. Thus, MS had a higher chance of subclinical as well as asymmetric unilateral ON. On the contrary, presentation of ON in NMOSD was mostly clinically detected. Galvin et al. showed that 9 out of 11 patients of MS without history of clinical ON showed changes of subclinical ON [21]. Histological evidence of ON in autopsy findings in MS patients reaches almost 100% [22]. Gartner et al. carried out an autopsy of 14 MS eyes in 10 patients, all of which showed changes of ON [22]. Of these, only 2 patients had history of clinical ON during the lifetime.

Though our MS patients did not show color vision impairment, dyschromatopsia has been described in MS patients mainly for red/green and blue/green [23]. It may be present irrespective of status of ON. However, our findings were contrary to this possibly because most of MS patients in our cohort had low EDSS and subclinical ON but no significant VA impairment. Bukhari et al. compared 101 patients of MS ON and 164 patients of NMOSD ON and found that higher grades of vision impairment like, no perception of light (NPL), perception of light (PL) alone, hand movements (HM) and counting fingers (CF) were more common in NMOSD group compared to MS group [24]. Vision of CF or worse was present in 11% of NMOSD patients whereas in MS it was present in only 0.6%. Likewise, a higher grade of VA impairment was observed in our NMOSD cohort as compared to MS.

The RNFL thickness analysis revealed significant thinning of NQ and IQ at 0 months in NMOSD subgroup. This differential involvement in NMOSD has been noted before. Even though generally NMOSD is considered to be causing widespread and generalized involvement of optic nerves, Naismith et al. showed in 22 NMOSD patients that there was a particular involvement of SQ and IQ in NMOSD as compared to more pronounced TQ involvement in MS [25]. Outteryck et al. showed that nasal to temporal ratio (N/T) in RNFL was 1.3 for MS, 1.2 for NMOSD and 1.1 for healthy controls suggesting selective preponderance of temporal involvement in MS [26]. They also observed more prominent involvement of NQ in NMOSD. MS patients in present study did not show any thinning at 0 months but showed selective temporal thinning at 6 months. The evidence supporting the temporal quadrant involvement in MS has been shown in an autopsy study carried out in 14 MS patients by Gartner et al. showing the atrophy involving considerable portion of the papillomacular bundle but not always being confined to it and extending to nearby fibres as well as peripheral fibres [22].

The present study demonstrated average RNFL in MS ON of 95.23 ± 15 and average RNFL in NMOSD ON of 66.14 ± 43.13. this observation correlates with established literature that average RNFL shows more thinning in NMOSD as compared to MS. Green et al. has shown an average RNFL loss in MS ON of 17.6 μm compared to an average 31.1 μm reduction in NMOSD [27]. Schneider et al. observed that in 17 patients of MS, NMOSD and control each, mean RNFL was 85.3 ± 13.3 in MS,

58.5 ± 21.2 in NMOSD and 100 ± 10.8 in controls [28]. Outteryck et al. showed that mean RNFL was 77.98 in NMOSD and 86.75 in MS [26]. Likewise, Naismith et al. showed that mean RNFL in NMOSD ranges from 55 to 83 μm as compared to 93–108 μm in MS [25]. Naismith et al. reported that the odds of falling into NMOSD group increases by 8% with every 1 μm decrease in RNFL thickness.

Another frequent alteration highlighted by OCT in NMOSD is the reduced thickness of the GCL [29]. Our study showed a significant thinning of GCL at 6 months but surprisingly, also at 0 months. The decrease in the thickness of the GCL is more pronounced in NMOSD owing to intense inflammation and necrosis, with more prominent neuronal and axonal damage in NMOSD than in MS [28]. Longitudinal analysis over 6 months showed that average RNFL thickness decreased from 97.46 ± 13.9 μm to 95.23 ± 15.53 μm in MS (*P* value- 0.03) and from 87.5 ± 21.93 to 66.14 ± 43.73 in NMOSD (P value- 0.05). This finding, along with more pronounced RNFL, GCL+ and GCL++ thinning at baseline in NMOSD signifies that severity of disease in NMOSD is more at the time of the acute episode with maximum damage to the retinal layers and to optic nerves. However, once the acute episode has occurred in NMOSD, there is further progressive thinning over next 6 months. This is contrary to that observed in MS in which the retinal layer thinning is not as pronounced as NMOSD during acute attack but progresses sub clinically over next 6 months.

There are limited studies evaluating temporal progression of RNFL thinning in NMOSD. Our study is the first longitudinal follow up study of patients for 6 months after the acute attack. Some unique findings observed in our study that has not been previously reported are the significant thinning of NQ and IQ even during the acute episode of ON in NMOSD. This is contradictory to our current knowledge of temporal evolution of RNFL changes after acute episode of ON. GCL thinning was also observed during acute episode. Though the earliest time required for OCT to detect measurable thinning after ON is not known, existing literature suggests that retrograde degradation may take at least 6 months to fully develop and the best time window to detect RNFL thinning is 3–6 months after ON as transient swelling of optic disc and RNFL may require this time to abate [30]. Our study did show significant RNFL thinning in NMOSD at 6 months with average RNFL being 66.14 ± 43.73 mm but average RNFL at 0 month was also 87.5 ± 21.93, much lesser as compared to control value of 103.75 ± 9.64. We could not find any relevant literature studying such changes in RNFL prospectively during the immediate period after acute ON in NMOSD.

5. Conclusions

This study highlights that concomitant with higher mean EDSS at presentation and frequent VA, CV, CS impairment in NMOSD as compared to MS, OCT demonstrated significant differences between the two entities. During the acute episode, NMOSD showed RNFL thinning in NQ and IQ while at 6 months, NMOSD showed significant thinning in SQ, NQ, IQ and MS showed thinning in TQ. Average RNFL at 6 months was significantly less for NMOSD as compared to MS. Significant GCL thinning was observed in NMOSD compared to MS during the acute episode as well at 6 months. The observations of the present study are novel and reiterate the need for large scale evaluation of these parameters specially in NMOSD.

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CRediT authorship contribution statement

Monalisa Vegda: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing. **Samhita Panda:** Conceptualization, Formal analysis, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing. **Kavita R. Bhatnagar:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing – review & editing.

Declaration of Competing Interest

Authors hold no conflict of interest and no grant was taken for the present study. Institutional ethical approval was obtained before carrying out the study.

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