Original research

Clinical characteristics of patients presenting with the first-episode optic neuritis in a South Asian population: A study from Sri Lanka

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Abstract

The clinical profile of optic neuritis in caucasian European populations is well-documented, and those findings form the basis for current treatment strategies. Limited evidence from Asian samples suggests a lower prevalence of multiple sclerosis and a significant proportion of patients having bilateral optic neuritis. This study describes the clinical characteristics of optic neuritis in Sri Lankans, a South Asian population, and compares the clinical picture with those of other Asian and caucasian European populations.

We consecutively recruited 90 adults (age 18-75 years, 50 women) who presented with first-episode optic neuritis to a tertiary care ophthalmology centre in Sri Lanka. The clinical and ophthalmological findings are described.

The patients presented within a median of 5 (Interquartile range, IQR:2-10; range: 1-20) days following the onset of symptoms. Fifty-three (59%) patients had unilateral optic neuritis, and 37 (41%) had bilateral optic neuritis. In the total sample, 60% had peri-ocular pain and 67% had optic disc oedema. In the subsample with unilateral optic neuritis, 58% had peri-ocular pain, while 80% had optic disc oedema.

Our findings indicate that a significant proportion of first-episode optic neuritis is bilateral: a presentation common in Asia but rare in people of Caucasian European descent. Unilateral optic neuritis in Sri Lankans has a different presentation compared to the caucasian European population: peri-ocular pain is less common, but almost 4 in 5 patients had optic disc oedema. The significance of these differences in the diagnosis and management of patients is yet to be investigated.

Keywords: optic neuritis, Asia, unilateral, bilateral, clinical characteristics, disc oedema, peri-ocular pain

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Introduction

The typical form of demyelinating optic neuritis is usually associated with multiple sclerosis[1, 2]. Typical optic neuritis, which is commonly seen in caucasian European people, presents with sub-acute onset unilateral visual impairment, peri-ocular pain and dyschromatopsia [2]. The management of optic neuritis is largely based on the recommendations of the Optic Neuritis Treatment Trial, which is a major study carried out on a cohort of unilateral optic neuritis patients, of whom 85% were caucasian Europeans [3]. These management recommendations have been widely adopted in the rest of the world, including Asia.

The patients with acute optic neuritis who subsequently develop multiple sclerosis in Asian countries are fewer compared to people of caucasian European descent [4], and diseases other than multiple sclerosis have been implicated in optic neuritis in the former populations [5, 6]. Neuromyelitis optica and chronic relapsing inflammatory optic neuropathy have been identified as some of the causative factors for optic neuritis in different regions around the world by now [7, 8]. Limited evidence from East Asian ethnic groups has shown differences in clinical presentation and prognosis of optic neuritis compared with the caucasian European population [9]. This form of atypical optic neuritis prevalent in East Asian countries can present bilaterally with the absence of pain [10], and this is considered to be a different entity from unilateral optic neuritis [11]. Consequently, the management protocols developed based on caucasian European samples may not be uniformly applicable to the patient populations of Asian and African ethnic origin. In addition to the geographical region, ethnic background is an important factor to be taken into consideration in the diagnosis and management of patients with optic neuritis [7]. Given the above constraints, and the scarcity of literature on the clinical profile of acute optic neuritis, particularly in South Asia, we aimed to investigate the clinical characteristics of optic neuritis in a cohort of adult patients in Sri Lanka, a South Asian country. We also aimed to compare their clinical profile with those reported in other Asian and caucasian European countries.

Methods

Study design

This study was a part of a larger research project which was conducted to study the pattern of clinical and visual electrophysiological parameters in patients presenting with the first-episode optic neuritis [12].

Study setting

The study was carried out from February 2017 to October 2019 at the Ophthalmology Centre of the National Hospital, Kandy and the Clinical Neurophysiology Department of the Teaching Hospital Peradeniya, two tertiary care referral centres of Sri Lanka.

Ethics

The study design and protocols complied with the code of ethics of the World Medical Association Declaration of Helsinki [13]. Ethical clearance for the study was granted by the Ethical Review Committee, Faculty of Medicine, University of Peradeniya, Sri Lanka. Informed written consent was obtained from the participants recruited in the study.

Data collection and analysis

One of the co-authors (SS) who is a specialist ophthalmologist clinically examined and conducted fundoscopic examination of the potential participants. Patients who were included into our study fulfilled the following criteria: (a) having acute onset visual impairment with or without peri-ocular pain in one or both eyes within 3 weeks, and (b) having at least one of the following abnormalities;a positive relative afferent pupillary defect (RAPD), a visual field defect, pathognomonic fundoscopic changes, or abnormal visual evoked potentials [14-16]. Those who complained of visual impairment in one eye were classified as having unilateral optic neuritis, whereas those who complained of visual impairment in both eyes were classified as having bilateral optic neuritis. If the patient had bilateral optic neuritis, the eye that was more affected according to the patient presentation and ophthalmologic assessment was denoted the affected eye [17]. The less affected eye in patients with bilateral optic neuritis or normal eye in patients with unilateral optic neuritis was denoted as the fellow eye [16]. According to the above inclusion criteria, we recruited 90 patients aged more than 18 years and presenting with the first-episode of optic neuritis with no previous history of eye diseases. We excluded those who were previously diagnosed with multiple sclerosis, neuromyelitis optica spectrum disorder or myelin oligodendrocyte glycoprotein antibody-associated disease and those who presented with a recurrence of ocular symptoms (even if there was no pre-existing diagnosis). We also excluded those with previously diagnosed vascular, toxic, nutritional,

infiltrative, infectious and alcohol-induced optic neuropathies and other ophthalmic conditions including, but not limited to, diabetic or hypertensive retinopathy, glaucoma, pre-existing optic atrophy, or cataracts. Patients with optic chiasmal or optic tract lesions were also excluded based on the visual field examination findings as well as clinical features. Even if the patient did not have ocular symptoms, we also excluded those who had other neurological illnesses, including epilepsy, meningitis, movement disorders and sarcoidosis. None of the recruited participants had fundoscopic features of other ophthalmic diseases that might confound our results.

All participants underwent a neuro-ophthalmological assessment which included measurements of visual acuity, colour vision with Ishihara chart (24 plates edition, 1993), pupillary reflexes, fundoscopy and visual fields tested with 30-2 Humphrey automated perimetry in each eye separately. Visual acuity was best corrected for both eyes in all the patients. Demographic and clinical information was collected using an interviewer-administered structured datasheet. Visual acuity of distant vision measured with a Snellen chart was converted and is reported in Logarithm of the Minimal Angle of Resolution (LogMAR) units [18]. Since we have not done the serological investigations in all the patients, samples were not stored. Age, duration of symptoms and visual acuity showed skewed distributions; and therefore, are reported as medians and interquartile ranges (IQR). SPSS (IBM SPSS Statistics for Windows, version 22.0.) was used for statistical calculations.

Results

Ninety patients with a clinical diagnosis of optic neuritis were recruited during the study period. The median age of the sample was 47 (IQR: 22.3-54; range: 18-75) years. Fifty (55%) were females. Of the total sample, 33 patients had diabetes mellitus, 18 had hypertension, but none of them had ophthalmic complications of those diseases.

All had a clinical history of sub-acute onset of visual impairment, most frequently blurred vision in one or both eyes. The median duration of onset of visual impairment was 5 days (IQR: 2-10; range: 1- 20) before the date of their presentation. Fifty-three (59%) patients had unilateral optic neuritis, with the right eye involved in 29 patients and left eye in 24. The remaining 37 (41%) had bilateral optic neuritis.

The clinical characteristics (viz. peri-ocular pain, RAPD, pattern reversal visual evoked potentials (PRVEP), visual acuity and visual field defects) of the sample, dichotomized for the affected eye and the fellow eye are summarized in Table 1. In the affected eye, 54 (60%) had peri-ocular pain at presentation, 45 (50%) had a positive RAPD, 83 (92%) had a prolonged P100 PRVEP latency, 83(92%) had impaired visual acuity, 60 (67%) had optic disc oedema, and all had some form of visual field defect (central, peripheral, temporal, whole field or lower half). In the fellow eye, 24 (27%) had peri-ocular pain at presentation, 45 (50%) had a prolonged P100 PRVEP latency, 47 (52%) had impaired visual acuity, 18 (20%) had optic disc oedema, and 37 (41%) had some form of visual field defect (central, peripheral or whole field).

Although all patients complained of unilateral visual impairment in the clinical interview were classified having unilateral optic neuritis, 29 (55%) of them showed at least one abnormality in the fellow eye in further ophthalmological examination: 20 had reduced visual acuity, 4 optic disc oedema, 14 prolonged P100 latencies in PRVEP and 1 had peri-ocular pain. However, in all those patients classified as having unilateral optic neuritis, ophthalmological findings in the fellow eye were less severe than those in the affected eye.

Based on the provisional diagnosis made after ophthalmologic assessment and availability, 27 patients (16 with bilateral optic neuritis and 11 with unilateral optic neuritis) underwent magnetic resonance imaging (MRI). Of them, 5 showed features of multiple sclerosis. We followed up 44 patients. Among them, 29 patients have been treated with optic neuritis treatment trial combined corticosteroid regimen, while 15 patients have been conservatively managed [20].

The diagnosis of multiple sclerosis was confirmed only in 6% in our sample; however, this could be an underestimation given the MRI was done only in 30% of the sample.

Table 1. Clinical characteristics of the study sample (90 patients)

Clinical parameter n(%)		Affected eye	Fellow eye
Positive peri-ocular pain		54 (60%)	24 (27%)
Positive colour vision abnormalities		35 (39%)	5(6%)
Positive RAPD		45 (50%)	-
PRVEP prolonged P100 latency		83 (92%)	45 (50%)
Visual acuity by LogMAR median (IQR)		+ 0.50 (IQR:0.2-1.0)	+ 0.20 (IQR: 0.0-0.3)
Disc oedema fundoscopy		60 (67%)	18 (20%)
Visual field defect			
	Central field	15 (17%)	2 (2%)
	Peripheral field	3 (3%)	2 (2%)
	Temporal field	1 (1.%)	0 (0%)
	Whole field	62 (69%)	33 (37%)
	Lower half	9 (10%)	0 (0%)
	Normal	0 (0%)	53 (59%)

IQR =Inter quartile range, n = number of patients

Discussion

This is the first study which was carried out to characterize the clinical profile of patients presenting with the first-episode optic neuritis in Sri Lanka. Our findings indicate that a significant proportion of first-episode optic neuritis is bilateral (41%) like in most of the other countries in Asia. This presentataion is different from the populations of caucasian European descent who mainly present with unilateral optic neuritis. With regard to the patients with unilateral optic neuritis (59%) in our sample, peri-ocular pain is less common and almost 4 in 5 patients have disc oedema. This clinical presentation of unilateral optic neuritis is also similar to the pattern observed in the Asian region, but different to the patients with caucasian European descent.

Although cases of bilateral optic neuritis have been reported in the population of caucasian European descent, simultaneous bilateral acute optic neuritis has been considered rare among the adults [23]. Unilateral optic neuritis has been the most commonly encountered and researched entity in populations of caucasian European descent, and has been comprehensively described in the optic neuritis treatment trial, in which the patients with bilateral optic neuritis have been excluded [16]. Clinical and demographic characteristics of the present sample, other caucasian European samples [16, 23] and Asian samples [4, 9, 14, 15, 17, 21, 22, 24-27] are summarized in Table 2. In each study, we calculated the 95% confidence intervals (CIs) around the reported percentages for different clinical features (Tables 2, 3 and 4), so that their findings could be compared with better accuracy and precision. As in populations of caucasian European descent, the Asian countries also seem to have a higher prevalence of unilateral optic neuritis than bilateral involvement. However, the percentages of patients with bilateral optic neuritis in the Asian samples (ranging from 16 to 41%, pooled estimate across studies = 28%, 95% CI: 25, 32)[4, 14, 15, 17, 21, 22, 24, 26, 27] seem to be higher than the percentage of bilateral involvement (i.e. 7%, 95% CI: 4, 11) in a predominantly caucasian European sample [23].

Table 2. Clinical findings of the affected eye of patients with optic neuritis in the present study, other Asian countries and the caucasian European countries

Study, Country	Sample composition	Number of patients (% females)	Mean age ±SD (range) in years	Bilateral visual impairment at presentation n (%)	Peri-ocular pain n (%)	Optic disc oedema in the patients n (%)	Multiple sclerosis n (%); diagnostic classification	MRI done n (%)
Optic neuritis treatment trial , 1991[16], USA	Only unilateral	448 (77%)	31.8± 6.7 (18-46)	Only unilateral cases	412 patients (92%)	157 patients (35%)	148 (33%); Definite/Probable /Possible)	All (100%)
De la Cruz et al, 2006 [23], USA	Only bilateral	15 (27%)	(18-64)	All (100%)	12 patients (80%)	8 patients (53%)	None	All (100%)
Wakakura et al, 1999 [9], Japan	Only unilateral	70 (69%)	36.3±12 (14-55)	Only unilateral cases	39 (56%) patients	35 patients (50%)	4 (6%); Definite/Probable	66 (94%)
Zhang et al, 2009 [15], China	Unilateral and bilateral	98 (54%)	25.7±24 (6-55)	32 (33%)	42 patients (43%)	52 eyes (40%)	8 (8%); Definite/Probable	All (100%)
Du et al, 2011[25], China	Only unilateral	100 (66%)	40.3±13.3 (18-74)	Only unilateral cases	40 patients (40%)	48 patients (48%)	6 (6%); Definite	64 (64%)
Choy et al, 2018[21], Hong Kong, China	Unilateral and bilateral	38 (79%)	40±14 (18-71)	7 (18%)	NM	20 eyes (39%)	1 (3%); Definite	All (100%)
Bee et al, 2003[22], Taiwan	Unilateral and bilateral	27 (67%)	35.8±11.3 (13-54)	5 (18%)	12 patients (44%)	12 patients (44%)	4 (15%); Definite	All (100%)
Lin et al 2006[17], Taiwan	Unilateral and bilateral	109 (53%)	41.2±17 (7-80)	38 patients (35%)	36 patients (33 %)	58 patients (53%)	Only idiopathic	51 (47%)
Chang et al, 2007[4], Taiwan	Unilateral and bilateral	43 (65%)	34.8±11.9 (18-60)	13(30%)	64% eyes	24 patients (56%)	5 (12%); Definite/Probable	All (100%)
Wang et al, 2001[24], Singapore	Unilateral and bilateral	31 (39%)	39.1±12.9 (11-67)	5 patients (16%)	NM	17 (55%)	2 (6%); Not specified	21 (68%)
Lim et al, 2008 [27], Singapore	Unilateral and bilateral	55 (76%)	NM (12-70)	9 patients (16%)	39 patients (71%)	33 patients (60%)	14 (25%); Not specified	NM
Ismail et al, 2012 [14], Malaysia	Unilateral and bilateral	31 (68%)	NM (3-55)	10 patients (32%)	13 eyes (32%)	29 eyes (71%)	1 (3%); Not specified	All(100%)
Saxena et al, 2014 [26], India	Unilateral and bilateral	83 (70%)	27.6±8.8 (15-58)	16 patients (19%)	61 patients (73%)	53eyes (53%)	(12%); Not specified	32 (38%)
Present study, Sri Lanka	Unilateral and bilateral (total sample)	90 (55%)	44.9±13.7 (18-75)	37 (41%)	54 (60 %)	60 (67%)	5 (6%); Definite/Probable	27 (30%)

Only unilateral	53 (53%)	45.2±13.5 (18-75)	N/A	31 (58%)	42 (79%)	1 (2%); Definite/Probable	11 (21%)
Only bilateral	37(59%)	44.5±14.3 (18-70)	N/A	23 (62%)	18 (49%)	4 (11%); Definite/Probable	16 (43%)

n: Number, NM: Not mentioned, N/A: Not applicable

In our study, peri-ocular pain was found in 60% of the affected eyes, and disc oedema in 67% of the patients. In other Asian studies–in which the samples consisted of a mixed sample of unilateral and bilateral optic neuritis– presence of peri-ocular pain ranged from 32 to 73% and disc oedema ranged from 44 to 71%. The 95% confidence intervals around the point estimates for each clinical feature were largely overlapping (Table 3), indicating no discernible ethnic or geographical distinctions in those clinical features.

Table 3: Peri-ocular pain and optic disc oedema in different Asian samples with optic neuritis.

Study, Country	Peri-ocular pain		Disc oedema	
	Proportion of patients	Percentage (95% CI)	Proportion of patients	Percentage (95% CI)
Zhang et al, 2009[15], China	42/98	43 (33,53)	52/98	53 (43,63)
Choy et al, 2018 [21], Hong Kong	NR	-	20/38	53 (36,69)
Bee et al, 2003 [22], Taiwan	12/27	44 (25,65)	12/27	44 (25,65)
Lin et al 2006 [17], Taiwan	36/109	33 (24,43)	58/109	53 (43,63)
Chang et al, 2007[4], Taiwan	28/43	65 (49,79)	24/43	56 (40,71)
Wang et al, 2001[24], Singapore	NR	-	17/31	55 (36,73)
Lim et al, 2008[27], Singapore	39/55	71 (57,82)	33/55	60 (46,73)
Ismail et al, 2012 [14], Malaysia	13 eyes/41 eyes	32 (18,48)	29 eyes/41 eyes	71 (54,84)
Saxena et al, 2014 [26],India	61/83	73 (63,82)	53/83	64 (52,74)
Present study, Sri Lanka	54/90	60 (49,70)	60/90	67 (56,76)

NR: not reported

There is limited data on clinical characteristics of patients with unilateral optic neuritis in other Asian studies: one in China [25] and the other one in Japan [9]. Comparison of clinical data of our subsample of patients with unilateral optic neuritis with the corresponding Asian samples and the sample of the optic neuritis treatment trial showed some differences (Table 4). Peri-ocular pain in the Asian samples ranged from 40 to 58% whereas it was significantly higher in the caucasian European sample, 9 out of 10 patients having reported peri-ocular pain. Presence of peri-ocular pain indicates involvement of the intra-orbital portion of the optic nerve, while peri-ocular pain does not occur with intracranial optic nerve or chiasm or optic tract involvement. Thus, presence of peri-ocular pain together with the findings of MRI may help to identify the aetiology of acute optic neuritis [28, 29]. In contrast to peri-ocular pain, disc oedema was more prevalent in the Asian samples (48 -79%) and lower in the optic neuritis treatment trial sample from the USA (35%). The disc oedema seems to be even higher in our Sri Lankan sample than in the East Asian samples.

Table 4: Peri-ocular pain and disc oedema in patients with unilateral optic neuritis

Study, Country	Peri-ocular pain		Disc oedema	
	Proportion of patients	Percentage (95% CI)	Proportion of patients	Percentage (95% CI)
Optic neuritis treatment trial ,1991[16], USA	412/448	92(89,94)	157/448	35 (31,40)
Wakakura et al, 1999 [9], Japan	39/70	56(43,67)	35/70	50(38,62)
Du et al, 2011 [25], China	40/100	40(30,50)	48/100	48 (38,58)
Present study (unilateral), Sri Lanka	31/53	58(44,72)	42/53	79 (66,89)

Furthermore, some of our patients with unilateral optic neuritis showed at least one abnormality in the fellow eye in further ophthalmological examination. These abnormal findings are not unexpected, since previous studies on unilateral optic neuritis have shown one or more abnormal ophthalmologic findings in the fellow eye in one-half [9] to two-thirds [19] of the samples.

However, the causation of underlying bilateral optic neuritis observed in the Asian studies has not been reported, except in a few studies. Most of those studies have emphasized the importance of assessing the serological markers viz. serum neuromyelitis optica and myelin oligodendrocyte glycoprotein antibody levels in determining the causation. In a study done in Malaysia it was shown that the prevalence of neuromyelitis optica related optic neuritis as 13% [14]. In a study done in Hong Kong the prevalence of neuromyelitis optica related optic neuritis has been shown as 3% [21]. Another recent study done in India, it has been shown that 10 % patients with optic neuritis have neuromyelitis optica [30]. However, our study is limited in diagnosing the cause of optic neuritis. Although only a small proportion of participants of the sample had undergone MRI at the time of data collection, PRVEPs were done in all subjects to assess the functional integrity of the post-retinal pathways. Nevertheless, it should be noted that even in the Asian patients in whom MRI was done in almost all subjects, the percentages diagnosed with multiple sclerosis (3 - 15%) [4, 9, 14, 15, 21, 22] were lower than that of the populations of 7aucasian European descent. Also. We were unable to investigate the participants using serum neuromyelitis optica or myelin oligodendrocyte glycoprotein antibody testing or lumbar puncture investigations, which we consider as limitations of our study.

Conclusion

This is the first study that decribes the clinical profile of optic neuritis in Sri Lanka. Our findings indicate, like in the rest of Asia, a significant proportion of first-episode optic neuritis is bilateral: a presentation rare in the populations of caucasian European descent. The clinical presentation of unilateral optic neuritis is rather similar to the pattern observed in the Asian region, but seems to have a different clinical picture compared to the populations of caucasian European descent. Specifically, peri-ocular pain being less common. Almost 4 in 5 patients with unilateral optic neuritis have disc oedema in Sri Lanka. Given this distinctive pattern of clinical presentation and lower percentage of multiple sclerosis, further research is warranted in elucidating aetiology and pathology of unilateral optic neuritis in the Asian region.

Authors contributions

Padmini Dahanayake designed the study, collected data, analyzed data and drafted the manuscript. Tharaka L. Dassanayake designed the study, analyzed data and drafted the manuscript, Manoji Pathirage designed the study, analyzed data, reviewed and edited the manuscript, Saman Senanayake designed the study, collected data, analyzed data, reviewed and edited the manuscript, Mike Sedgwick designed the study, analyzed data, reviewed and edited the manuscript. Vajira S. Weerasinghe designed the study, analyzed the data, reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Ethics approval and consent to participate

Ethical clearance (2016/EC/50) for the study was obtained from the Ethical Review Committee, Faculty of Medicine, University of Peradeniya, Sri Lanka. The study design and protocols complied with the code of ethics of the World Medical Association Declaration of Helsinki. The procedures were explained, and informed written consent obtained from all participants.

Availability of data

All data generated or analysed during this study is available upon a request from the corresponding author.

References

1. Graves J, Balcer LJ. Eye disorders in patients with multiple sclerosis: natural history and management.*Clin Ophthalmol.* 2010;4:1409-22. doi: 10.2147/OPTH.S6383

2. Toosy AT, Mason DF, Miller DH. Optic neuritis. *Lancet Neurol.* 2014;13(1):83-99. doi: 10.1016/s1474-4422(13)70259-x.

3. Beck RW, Trobe JD. The Optic Neuritis treatment trial: putting the results in perspective. *J Neuroophthalmol.* 1995;15(3):131-5.

4. Chang YC, Wu WC, Tsai RK. Prognosis of Taiwanese patients with isolated optic neuritis after intravenous methylprednisolone pulse therapy. *J Formos Med Assoc.* 2007;106(8):656-63. doi: 10.1016/s0929-6646(08)60023-6

5. Horwitz H, Friis T, Modvig S, Roed H, Tsakiri A, Laursen B, et al. Differential diagnoses to MS: experiences from an optic neuritis clinic. *J. Neurol.* 2014;261(1):98-105.

6. Petzold A, Wattjes MP, Costello F, Flores-Rivera J, Fraser CL, Fujihara K, et al. The investigation of acute optic neuritis: a review and proposed protocol.*Nat. Rev. Neurol.* 2014;10(8):447-58. doi: 10.1038/nrneurol.2014.108.

7. Storoni M, Pittock SJ, Weinshenker BG, Plant GT. Optic neuritis in an ethnically diverse population: higher risk of atypical cases in patients of African or African-Caribbean heritage. *J Neurol Sci.* 2012;312(1-2):21-5. doi: 10.1016/j.jns.2011.08.030.

8. Kidd D, Burton B, Plant GT, Graham EM. Chronic relapsing inflammatory optic neuropathy (CRION). *Brain.* 2003;126(Pt 2):276-84. doi: 10.1093/brain/awg045.

9. Wakakura M, Minei-Higa R, Oono S, Matsui Y, Tabuchi A, Kani K, et al. Baseline features of idiopathic optic neuritis as determined by a multicenter treatment trial in Japan. Optic Neuritis Treatment Trial Multicenter Cooperative Research Group (ONMRG).*Jpn. J. Ophthalmol.* 1999;43(2):127-32.

10. Seah BHA, Tow S, Ong KCB Ong, CC Yang, CP Tsai, Lee KH, et al. The natural history of optic neuritis in Asian patients:An observational cohort study. *Neurol Asia.* 2017;22(4):341-8. doi: http://neurology-asia.org/articles/neuroasia-2017-22(4)-341.pdf.

11. Parkin PJ, Hierons R, McDonald WI. Bilateral optic neuritis. A long-term follow-up. *Brain.* 1984;107 (Pt 3):951-64.

12. Dahanayake P, Dassanayake TL, Pathirage M, Senanayake S, Sedgwick M, Weerasinghe V. Electro-oculography in bilateral optic neuropathy. *BMC Res. Notes.* 2020;13(1):287. doi: 10.1186/s13104-020-05131-0.

13. Association WM. World medical association declaration of Helsinki: ethical principles for medical research involving uman subjects. *JAMA.* 2013;310(20):2191-4. doi: 10.1001/jama.2013.281053.

14. Ismail S, Wan Hazabbah WH, Muhd-Nor NI, Daud J, Embong Z. Clinical profile and aetiology of optic neuritis in Hospital Universiti Sains Malaysia--5 years review. *Med J Malaysia.* 2012;67(2):159-64.

15. Zhang X, Wang W, Wang Q, Cui S, Wei W. Clinical features of optic neuritis in China. *Neuro-Ophthalmol.* 2007;31(5-6):133-6. doi: 10.1080/01658100701647506.

16. ONTT. The Clinical profile of optic neuritis: experience of the optic neuritis treatment trial. *JAMA Ophthalmol.* 1991;109(12):1673-8. doi: 10.1001/archopht.1991.01080120057025.

17. Lin YC, Yen MY, Hsu WM, Lee HC, Wang AG. Low conversion rate to multiple sclerosis in idiopathic optic neuritis patients in Taiwan. *Jpn. J. Ophthalmol.* 2006;50(2):170-5. doi: 10.1007/s10384-005-0281-1.

18. Holladay JT. proper method for calculating average visual acuity. *J. Refract. Surg.*1997;13:388-91.

19. Beck RW, Kupersmith MJ, Cleary PA, Katz B. Fellow eye abnormalities in acute unilateral optic neuritis. Experience of the optic neuritis treatment trial. Ophthalmology. 1993;100(5):691-7. doi: 10.1016/s0161-6420(13)31589-9.

20. Dahanayake P, Dassanayake TL, Pathirage M, Senanayake S, Sedgwick M, Weerasinghe VS. The effect of optic neuritis treatment trial (ONTT) combined corticosteroid regimen on pattern reversal visual evoked potentials: a prospective follow-up study. *BMC Ophthalmol.* 2021;21(1):324. doi: 10.1186/s12886-021-02086-z.

21. Choy BNK, Ng ALK, Lai JSM. Clinical characteristics of optic neuritis in Hong Kong population: 10-year review. *Int. ophthalmol.* 2018;38(2):557-64. doi: 10.1007/s10792-017-0491-9.

22. Bee Y, Lin M, Wang C, Sheu S. Optic neuritis: clinical analysis of 27 cases. *Kaohsiung J Med Sci.* 2003;19:105-12.

23. de la Cruz J, Kupersmith MJ. Clinical profile of simultaneous bilateral optic neuritis in adults. *Br J Ophthalmol.* 2006;90(5):551-4. doi: 10.1136/bjo.2005.085399.

24. Wang JC, Tow S, Aung T, Lim SA, Cullen JF. The presentation, aetiology, management and outcome of optic neuritis in an Asian population. Clin. Experiment. *Ophthalmol.* 2001;29(5):312-5. doi: 10.1046/j.1442-9071.2001.00442.x

25. Du Y, Yang J, Li JJ, Zhou RW, He JF. Unilateral optic neuritis in a Chinese population in three centers. *J. Clin. Neurosci.* 2011;18(7):902-4. doi: 10.1016/j.jocn.2010.11.011.

26. Saxena R, Phuljhele S, Menon V, Gadaginamath S, Sinha A, Sharma P. Clinical profile and short-term outcomes of optic neuritis patients in India. *Indian J. Ophthalmol.* 2014;62(3):265-7. doi: 10.4103/0301-4738.121131.

27. Lim SA, Goh KY, Tow S, Fu E, Wong TY, Seah A, et al. Optic neuritis in Singapore. *Singapore Med J.* 2008;49(9):667-71.

28. Storoni M, Davagnanam I, Radon M, Siddiqui A, Plant GT. Distinguishing optic neuritis in neuromyelitis optica spectrum disease from multiple sclerosis: a novel magnetic resonance imaging scoring system. *J Neuroophthalmol.* 2013;33(2):123-7. doi: 10.1097/WNO.0b013e318283c3ed.

29. Kupersmith M, Fazzone H, Lefton D. Optic Neuritis: correlation of pain and MRI. *Investig. Ophthalmol. Vis. Sci.* 2002;43(13):2632.

30. Ambika S, Durgapriyadarshini S, Padmalakshmi K, Noronha V, Arjundas D. Clinical profile, imaging features and short term visual outcomes of Indian optic neuritis patients with and without seromarkers for myelin oligodendrocyte glycoprotein and neuromyelitis optica. *Indian J. Ophthalmol.* 2022;70(1):194-200. doi: 10.4103/ijo.IJO_887_21.