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ORIGINAL PAPER

Baseline demographics, clinical features, and treatment protocols of 240 patients with optic neuropathy: experiences from a neuro-ophthalmological clinic in the Aegean region of Turkey

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Abstract

Purpose To analyze the demographic patterns, clinical characteristics, and treatment protocols of optic neuropathies.

Materials and methods The hospital data of patients with optic neuropathy admitted to the Department of Neuro-ophthalmology in a tertiary referral center in Turkey between January 2010 to January 2017 were retrospectively analyzed. Demographic patterns, clinical features, treatment protocols, and the natural disease courses were assessed.

Results The total number of patients with optic neuropathy seen over this period was 240, which consist of 43 with idiopathic optic neuritis (17.9%), 40 with multiple sclerosis-related optic neuritis (16.7%), 12 with chronic relapsing inflammatory optic neuritis (5.0%), 12 with atypical optic neuritis (5.0%), 11 with neuromyelitis optica spectrum disorders-related optic neuritis (4.6%), 90 with non-arteritic ischemic optic neuropathy (37.5%), 4 with arteritic ischemic optic neuropathy (1.7%), 10 with traumatic optic neuropathy (4.1%), 6 with compressive optic neuropathy (2.5%), and 12 with mitochondrial optic neuropathy [9 with toxic optic neuropathy (3.7%) and 3 with Leber's hereditary optic neuropathy (1.2%)]. There were 101 males (42%) and 139 females (58%). The mean age was 43.34 ± 15.86 years.

Conclusion This study reported the demographics, clinical characteristics, and treatment protocols of optic neuropathies in a neuro-ophthalmology specialty clinic at a tertiary referral center in Turkey during the past decade. The data may be useful in assessing the global status of optic neuropathies.

Keywords Color vision · Optic nerve · Optic neuropathies · Relative afferent pupillary defect · Visual field defect

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Introduction

Optic neuropathy is a frequent cause of vision loss encountered by neuro-ophthalmologists. The major causes of optic neuropathy include inflammatory or demyelinating optic neuritis (ON), and ischemic, compressive, infiltrative, post-traumatic, and

mitochondrial (hereditary, metabolic, and toxic) optic neuropathies [1]. The diagnosis is based on clinical observations, and the disease history often suggests possible etiologies of the optic neuropathy. A rapid onset is typical of demyelinating, inflammatory, ischemic, and traumatic causes [1, 2]. A gradual course suggests compressive, toxic/nutritional, and hereditary causes. One feature generally shared by acute optic neuropathies, regardless of the cause, is deterioration of visual functions, which may be subjectively perceived as decreases in visual acuity, visual field, and/or color vision. Ancillary investigations such as neuro-imaging of the brain or orbit and visual field testing can support a diagnosis and are critical in its diagnosis [3–10].

There are insufficient data on optic neuropathies in Turkey, and there have been no previous reports comparing the demographic patterns, clinical features, and natural courses of optic neuropathies. This study was performed to evaluate the demographic and clinical features, etiology, treatment protocols, and natural courses of optic neuropathies presenting at the Department of Neuro-ophthalmology, Ege University, Izmir, Turkey.

Materials and methods

The individual case notes of 267 patients coded as having optic neuropathy, idiopathic optic neuritis (ION), multiple sclerosis (MS)-related optic neuritis (ON), neuromyelitis optica spectrum disorders (NMOSD)-related ON, chronic relapsing inflammatory optic neuritis (CRION), atypical optic neuritis (AON)], ischemic optic neuropathy (non-arteritic [NION] and arteritic [AION]), traumatic optic neuropathy, mitochondrial optic neuropathy (Leber's hereditary optic neuropathy [LHON], toxic/metabolic optic neuropathy), and compressive/infiltrative optic neuropathy) in Ege University Hospital from January 2010 to January 2017 were systematically reviewed retrospectively. Subjects whose records were incomplete, did not confirm a diagnosis of clinically definite optic neuropathy or lost on follow-up were excluded. The patients with inflammatory retinal or uveal signs, except those with mild vitritis, were also excluded. Of these, sufficient clinical and diagnostic information was available on 240 patients to be included in the analysis. All patients had a minimum follow-up of 12 months. These patients had been assessed by two experienced neuro-ophthalmologists (N.C and F.G). Demographic and clinical data were recorded. The data on patient age, gender, laterality, the presence of pain, clinical findings, onset and duration of the symptoms, recurrence, recurrence interval, and treatment protocols of optic nerve disease were collected. Neuro-ophthalmological examination included the evaluation of ocular movements, swinging flashlight test to record relative afferent pupillary defect [RAPD], best corrected visual acuity (using refraction and Snellen's chart) test, color vision test with Ishihara's pseudoisochromatic color vision chart (inability to read any one of the Ishihara test plates was considered abnormal), fundus evaluation under mydriasis and visual field test (in cooperative patients with visual acuity over 1/10).

Diagnosis of optic nerve disorders

1. Optic neuritis (ON) was diagnosed according to the following findings: Painful acute/subacute unilateral visual loss, dyschromatopsia, the presence of RAPD, normal or swollen optic disk on fundus examination in an otherwise healthy young adult without any other identified cause.
   (a) MS-related ON: Diagnosis was made by following criteria:
      (i) The presence a history of MS.
      (ii) Magnetic resonance imaging (MRI) features supporting MS according to Barkhof criteria during the first optic neuritis attack [3].
   (b) NMOSD-related ON was diagnosed according to the following findings: In the absence of AQP4-IgG seropozitivity, the presence of longitudinal transverse myelitis extending 3 segments, area postrema syndrome, acute brainstem syndrome, acute diencephalic or systematic cerebral syndrome with NMOSD-typical MRI lesions accompanying optic neuritis. Optic neuritis associated with AQP4-IgG seropozitivity was diagnosed as NMOSD [5].

(c) CRION was diagnosed in patients with recurrent ON, steroid responsive/dependent and normal brain MRI, normal cerebrospinal fluid (CSF) and serological testing for other autoimmune or infectious diseases and no evidence of systemic illness on long-term follow-up [6].

(d) ION: No previous history of neurological attack and normal neurological examination and cranial and spinal MRI [11].

(e) AON was considered in patients with features inconsistent with the classical ON such as lack of pain, simultaneous or near-simultaneous bilateral onset, lack of response to steroids, and optic nerve head or peripapillary hemorrhages [11].

2. Ischemic optic neuropathy [8, 12]

(a) NION was diagnosed in elderly patients with vascular risk factors defining acute vision loss in one eye with RAPD, altitudinal visual field defects (usually inferior), unilateral optic disk swelling and a fellow eye with a small cup-to-disk ratio, normal levels of c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and no other etiology being found (structural lesion compressing the orbital optic nerve, infiltrative process).

(b) AION was diagnosed in acute unilateral or bilateral vision loss, dyschromatopsia associated with systemic features such as painful jaw muscle spasms, scalp tenderness, unintentional weight loss, fatigue, myalgias and loss of appetite with increased levels of CRP and ESR and temporal artery ultrasonography revealing signs of temporal arteritis and temporal artery biopsy when necessary.

3. Traumatic optic neuropathy: The diagnosis was made by the presence of vision loss after direct or indirect head or ocular trauma with dyschromatopsia and the presence of RAPD and could not be explained by other causes [7, 12, 13].

4. Compressive optic neuropathy comprised the following features: decreased visual acuity, color vision loss, the presence of RAPD, if one eye involved; a compatible visual field defect and optic nerve impairment caused by compression of the anterior visual pathway by a tumor or aneurysm, confirmed by cranial MRI [12, 14].

5. Mitochondrial optic neuropathy

(a) Toxic/metabolic optic neuropathy was diagnosed in progressive, painless, bilateral visual loss and dyschromatopsia after usage of known toxic agents with compressive/infiltrative and infective etiologies ruled out by MRI and CSF examination if necessary [12, 15].

(b) Leber's hereditary optic neuropathy (LHON) diagnosis was based on bilateral visual loss with the fellow eye becoming affected either simultaneously or sequentially, with a median inter-eye delay of 6–8 weeks mainly in young males with a positive genetic testing and compressive/infiltrative and infective etiologies ruled out by MRI and CSF examination if necessary [12, 16].

Statistical analyses

All statistical analyses were performed using the Statistical Program for Social Sciences (SPSS) statistical software for Windows version 11.5 (SPSS Inc.Chicago, Illinois). A descriptive statistical analysis was performed for including means for continuous variables and percentage for categorical ones. The paired *t* test and Wilcoxon signed-rank test were used to compare the means of the two samples of related data. P values of < 0.05 were considered to be statistically significant.

Results

Demographic characteristics of study participants are listed in Table 1. The total number of patients diagnosed with optic neuropathy during the study period was 240, consisting of 43 with ION (17.9%), 40 with MS-related ON (16.7%), 12 with CRION (5.0%), 12 with AON (5.0%), 11 with NMOSD-related ON (4.6%), 90 with NION (37.5%), 4 with AION (1.7%), 10 with traumatic optic neuropathy (4.1%), 6 with compressive optic neuropathy (2.5%) [optic nerve

Table 1 Demographics of patients with optic neuropathy

	No. of patients	Gender (F/M)	Age at onset years (mean ± SD)
Optic neuritis			
MS-related	40 (16.7%)	30/10	33.02 ± 10.1
NMOSD	11 (4.6%)	7/4	38.27 ± 8.6
CRION	12 (5.0%)	8/4	36.14 ± 7.3
ION	43 (17.9%)	23/20	34.74 ± 10.4
AON	12 (5.0%)	8/4	30.25 ± 10.3
Anterior ischemic optic neuropathy			
NION	90 (37.5%)	54/36	57.06 ± 13.9
AION	4 (1.7%)	1/3	70.50 ± 10.2
Traumatic optic neuropathy			
	10 (4.1%)	1/9	33.40 ± 12.4
Compressive optic neuropathy			
	6 (2.5%)	2/4	47.50 ± 15.3
Mitochondrial optic neuropathy			
LHON	3 (1.25%)	1/2	37.66 ± 12.0
Toxic optic neuropathy	9 (3.75%)	4/5	50.60 ± 15.4

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sheath meningioma in four and craniopharyngioma in two], and 12 with mitochondrial optic neuropathy [9 (3.7%), with toxic optic neuropathy ethambutol in two, amiodarone in three, cisplatin in two, and methanol in two and 3 (1.2%) with LHON]. Of these 101 were male (42%) and 139 patients were female (58%). The mean age was 43.34 ± 15.86 years.

Clinical findings of patients with optic neuropathy are summarized in Table 2. Among the 240 patients, four-sixths presented with unilateral involvement (163, 67.9%), one-sixth presented with bilateral involvement (38, 15.9%), and one-sixth presented with sequential involvement (39, 16.2%). Bilateral and sequential presentations were more often seen in toxic optic neuropathy, LHON and NMOSD-related ON. MS-related ON cases were predominantly female (30, 75%) and were younger than other types of optic neuropathies (33.02 ± 10.1). The presence of pain was mainly seen in MS-related ON (60%). The presence of RAPD was more common in patient with ON, traumatic optic neuropathy and AION than in other neuropathies. Recurrence rates were 12.5, 18.1, 100, 9.3, 16.7, 3.3, 25.0% in patients with MS-related ON, NMOSD-related ON, CRION, ION, AON, NION, AION, respectively. Recurrence was recorded from 1 to 42 months after the initial attack.

Optic nerve appearances of patients with optic neuropathy are shown in Table 3. Fundus examination revealed normal, swollen, pale, or atrophic optic disks. The optic disk was swollen in 75% of patients with NION and AION. In ON, however, optic disks were normal in 55.0% of cases with MS-related ON. Temporal pallor was seen in 55 and 50% of patients with toxic and compressive optic neuropathies, respectively. Atrophic optic disk was seen in 66% of patients with LHON.

Details of visual fields evaluation in affected eyes at the first examination are elaborated in Table 4. The commonest visual field defects in patients with MS-related ON, NMOSD-related ON, CRION, ION, AON, and mitochondrial optic neuropathy were central–centrocecal scotoma. Altitudinal, total, and peripheral scotomas were frequently seen in patients with NION/AION, traumatic and compressive optic neuropathy, respectively.

Treatment protocols of patients with optic neuropathy during the acute attack are listed in Table 5. Pulse steroid treatment (1 g intravenously for 3–7 days) was used in 95% of patients with MS-related ON and ION. Pulse steroid followed by oral steroid treatment was used in all patients with AION and AON, in around 91% of patients with NMOSD-related ON and CRION. In patients with NION, Acetylsalicylic acid was used alone (34%) or in combination with oral steroids (21%).

On admission, visual acuity in the affected eyes ranged from 0.9 to light perception. Initial visual

Table 2 Clinical findings of patients with optic neuropathy

	The presence of pain	The presence of RAPD	Color vision impairment	Laterality			Recurrence rate	Recurrence interval (months)
				Unilateral	Bilateral	Sequential		
Optic neuritis								
MS-related	24 (60.0%)	31 (77.5%)	31 (77.5%)	33 (82.5%)	3 (7.5%)	4 (10.0%)	5 (12.5%)	19.0
NMOSD	5 (45.4%)	6 (54.5%)	8 (72.7%)	5 (45.5%)	2 (18.2%)	4 (36.3%)	2 (18.1%)	5.0
CRION	5 (41.6%)	8 (66.6%)	8 (66.6%)	10 (83.4%)	1 (8.3%)	1 (8.3%)	12 (100.0%)	13.2
ION	19 (44.1%)	28 (65.1%)	29 (67.4%)	33 (76.8%)	7 (16.2%)	3 (7.0%)	4 (9.3%)	13.0
AON	5 (41.6%)	8 (66.6%)	8 (66.6%)	6 (50.0%)	2 (16.7%)	4 (33.3%)	2 (16.7%)	1.0
Anterior ischemic optic neuropathy								
NION	25 (27.7%)	53 (58.8%)	66 (73.3%)	61 (67.8%)	8 (8.9) %	21 (23.3%)	3 (3.3%)	42.5
AION	0 (0.0%)	3 (75.0%)	3 (75.0%)	3 (75.0%)	0 (0.0%)	1 (25.0%)	1 (25.0%)	1.0
Traumatic optic neuropathy								
	5 (50.0%)	8 (80.0%)	9 (90.0%)	8 (80.0%)	2 (20.0%)	0 (0.0%)	0 (0.0%)	–
Compressive optic neuropathy								
	1 (16.6%)	3 (50.0%)	3 (50.0%)	4 (66.6%)	1 (16.7%)	1 (16.7%)	0 (0.0%)	–
Mitochondrial optic neuropathy								
LHON	0 (0.0%)	2 (66.6%)	2 (66.6%)	0 (0.0%)	3 (100. 0%)	0 (0.0%)	0 (0.0%)	–
Toxic optic neuropathy	0 (0.0%)	3 (33.3%)	9 (100.0%)	0 (0.0%)	9 (100.0%)	0 (0.0%)	0 (0.0%)	–

MS multiple sclerosis, *NMO* neuromyelitis optica, *CRION* chronic relapsing inflammatory optic neuritis, *ION* idiopathic optic neuritis, *AON* atypical optic neuritis, *NION* non-arteritic anterior ischemic optic neuropathy, *AION* arteritic anterior ischemic optic neuropathy, *LHON* Leber's hereditary optic neuropathy

Table 3 Optic nerve appearance of patients with optic neuropathy

	Optic nerve appearance			
	Normal	Swollen	Pallor	Atrophic
Optic neuritis				
MS-related	22 (55.0%)	4 (10.0%)	11 (27.5%)	3 (7.5%)
NMOSD	3 (27.3%)	5 (45.4%)	3 (27.3%)	0 (0.0%)
CRION	7 (58.3%)	3 (25.0%)	2 (16.7%)	0 (0.0%)
ION	22 (51.1%)	14 (32.6%)	7 (16.3%)	0 (0.0%)
AON	6 (50.0%)	3 (25.0%)	3 (25.0%)	0 (0.0%)
Anterior ischemic optic neuropathy				
NION	0 (0.0%)	68 (75.6%)	21 (23.3%)	1 (1.1%)
AION	0 (0.0%)	3 (75.0%)	1 (25.0%)	0 (0.0%)
Traumatic optic neuropathy				
	3 (30.0%)	2 (20.0%)	3 (30.0%)	2 (20.0%)
Compressive optic neuropathy				
	2 (33.3%)	1 (16.7%)	3 (50.0%)	0 (0.0%)
Mitochondrial optic neuropathy				
LHON	0 (0.0%)	0 (0.0%)	1 (33.3%)	2 (66.7%)
Toxic optic neuropathy	3 (33.3%)	1 (11.1%)	5 (55.6%)	0 (0.0%)

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Table 4 Visual field defects in patients with optic neuropathy

	Visual field defects				
	Central–centrocecal	Altitudinal	Peripheral	Total	Tubular
Optic neuritis					
MS-related	27 (67.5%)	0 (0.0%)	11 (27.5%)	0 (0.0%)	2 (5.0%)
NMOSD	8 (72.8%)	0 (0.0%)	3 (27.2%)	0 (0.0%)	0 (0.0%)
CRION	8 (66.7%)	0 (0.0%)	4 (33.3%)	0 (0.0%)	0 (0.0%)
ION	22 (51.1%)	7 (16.3%)	11 (25.6%)	3 (7.0%)	0 (0.0%)
AON	7 (58.3%)	0 (0.0%)	3 (25.0%)	2 (16.7%)	0 (0.0%)
Anterior ischemic optic neuropathy					
NION	12 (13.3%)	48 (53.3%)	19 (21.1%)	8 (8.9%)	3 (3.4%)
AION	0 (0.0%)	3 (75.0%)	0 (0.0%)	1 (25.0%)	0 (0.0%)
Traumatic optic neuropathy					
	0 (0.0%)	0 (0.0%)	3 (30.0%)	5 (50.0%)	2 (20.0%)
Compressive optic neuropathy					
	1 (16.6%)	1 (16.7%)	3 (50.0%)	1 (16.7%)	0 (0.0%)
Mitochondrial optic neuropathy					
LHON	2 (75.0%)	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)
Toxic optic neuropathy	5 (55.6%)	0 (0.0%)	0 (0.0%)	3 (33.3%)	1 (11.1%)

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acuity was worse in patients with mitochondrial and traumatic optic neuropathy than in patients with MS-related ON. Visual acuity at last follow-up was the best in patients with MS-related ON, NMOSD-related ON, CRION and ION ($p < 0.05$). The details of visual acuity are given in Table 6.

Discussion

This study was conducted to provide data on the epidemiology of optic neuropathies in Turkey. To the best of our knowledge, this was the first report on the demographics, different subgroups, and characteristic findings of optic neuropathies in a patient population from this country.

Baseline demographics

Our study demonstrated female dominance in all ON subgroups. This is in accordance with Optic Neuritis Treatment Trial (ONTT) [17] and other studies [10, 18–25] though male predominance has been reported in two studies from Asia [26, 27]. On the other hand, a female predominance (60%) recorded in our NION group was inconsistent with Ischemic Optic Neuropathy Decompression Trial (IONDT) (38%) [8]. AION, traumatic, and mitochondrial optic neuropathy patients were more often males, which was similar with the previous published data [12, 13, 28]. In a previous study, no sex predilection was found for compressive optic neuropathy with the exception of Graves' orbitopathy and meningiomas, two conditions mainly affecting women [14]. Though a male predominance seemed to be present in our compressive optic neuropathy group, it is open to question as there were only six patients.

Our results were similar to other ON studies [8, 10, 17–25] in terms of presentation age, which was the third decade, and emphasize the significant impact neuritis has on patients during their most productive working years. Regarding ischemic optic neuropathy, AION, like NION, is almost always seen in older patients with a mean age of near 70 years (the

Table 5 Treatment protocols of patients with optic neuropathy during an acute attack

	Treatment protocols				
	Pulse steroid	Pulse + oral steroid	Acetylsalicylic acid	Combined oral steroid and acetylsalicylic acid	Untreated
Optic neuritis					
MS-related	38 (95.0%)	2 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMOSD	1 (9.1%)	10 (90.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CRION	1 (8.3%)	11 (91.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ION	41 (95.3%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AON	0 (0.0%)	12 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anterior ischemic optic neuropathy					
NION	20 (22.2%)	1 (1.1%)	31 (34.5%)	19 (21.1%)	19 (21.1%)
AION	0 (0.0%)	4 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Traumatic optic neuropathy					
	8 (80.0%)	2 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Compressive optic neuropathy					
	2 (33.3%)	4 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mitochondrial optic neuropathy					
LHON	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (100.0%)
Toxic optic neuropathy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (100.0%)

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mean age for NION is approximately 57 years). Similarly, LHON, compressive optic neuropathy and traumatic optic neuropathy are more often diagnosed in the third and fourth decades, respectively. These results are consistent with published reports [14, 16, 30].

Clinical features

Pain is a variable feature that suggests an inflammatory disorder. The ocular muscle originates from the annulus of Zinn, which closely envelops the optic nerve sheath. Inflammation of the optic nerve causes painful eye movements as a result of its proximity to the extraocular muscles [31]. However, some ischemic lesions can also cause pain [7, 8]. Swartz et al. [9]. reported pain in 12% of patients with anterior ischemic optic neuropathy. In the present study, pain was present in 27% of patients with NION, which was higher than in previous studies [8, 9]. In addition, 75% of patients with AION suffered from headache. Pain was present in 60% of our patients with MS-related ON and 44% of our patients with ION, which differed from the data compiled on 448 patients with ONTT, of whom 92.2% complained of pain [17], and from other studies from the UK reporting pain in approximately 87% of patients [20–22]. There are also studies from Asia, which are consistent with the higher percentage of pain in ONTT patients [10, 32, 33]. However, studies reporting lower percentage of pain, similar to our results, have also been reported [10, 23, 24, 26, 27]. These differences may result from regional disparities. Pain was reported in approximately 42% of patients with CRION and AON and 45% of patients with NMOSD-related ON.

Other common features include RAPD (if the lesion is unilateral or asymmetric), dyschromatopsia, vision loss, and visual field defects [17]. Swinging flashlight test evidences the RAPD and is the most valuable clinical examination in identifying optic neuropathy. We identified lower rates of RAPD in patients with sequential or bilateral optic nerve involvement than in

Table 6 Visual acuity test results in patients with optic neuropathy

	Visual acuity at presentation	Visual acuity at last follow-up	*P* value
Optic neuritis			
MS-related	0.58 ± 0.38	0.91 ± 0.19	0.011*
NMO	0.57 ± 0.43	0.85 ± 0.28	0.018$^{\varphi}$
CRION	0.51 ± 0.35	0.84 ± 0.15	0.009$^{\varphi}$
ION	0.51 ± 0.36	0.76 ± 0.24	0.041*
AON	0.49 ± 0.42	0.52 ± 0.34	0.156$^{\varphi}$
Anterior ischemic optic neuropathy			
NION	0.43 ± 0.38	0.55 ± 0.41	0.084*
AION	0.30 ± 0.40	0.50 ± 0.46	0.593$^{\varphi}$
Traumatic optic neuropathy			
	0.28 ± 0.30	0.35 ± 0.31	0.131$^{\varphi}$
Compressive optic neuropathy			
	0.45 ± 0.44	0.53 ± 0.48	0.102$^{\varphi}$
Mitochondrial optic neuropathy			
LHON	0.15 ± 0.09	0.11 ± 0.06	0.102$^{\varphi}$
Toxic optic neuropathy	0.26 ± 0.12	0.23 ± 0.14	0.518$^{\varphi}$

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*p value visual acuity at presentation vs. last follow-up (paired t test)

$^{\varphi}p$ value visual acuity at presentation vs. last follow-up (Wilcoxon test)

patients with unilateral involvement as expected (Table 2).

Most of optic neuropathic patients have dyschromatopsia. However, patients with some optic neuropathies, especially those with AION, may have normal color vision. Also, dyschromatopsia can also be seen in some macular disorders. However, in these patients, visual acuity tends to be profoundly affected. A mild-to-moderate visual loss that occurs together with dyschromatopsia is a sensitive indicator for optic neuropathy. Also, color vision in optic neuropathy subgroups may be affected to varying degrees. For instance, color vision impairment is more prominent in patients with MS-related ON compared to AION [12]. In our study, color vision was worse in toxic optic neuropathy and traumatic optic neuropathy followed by MS-related ON and AION (Table 2).

Table 6 gives information about the visual acuity status at the initial and last visit to our clinic. On admission, visual acuity ranged from 0.2 to 1. A significant improvement in vision was recorded in patients with MS-related ON, NMOSD-related ON, CRION, and ION, whereas no significant improvement in visual acuity was detected in ischemic, traumatic, toxic, compressive optic neuropathy groups as well as LHON and AON patients. Optic neuritis is considered to have good visual prognosis. As per a report of the ONTT, around 93.3% of patients recovered VA of 20/40 or better [34]. In our study, bad visual prognosis was detected in only the AON subgroup which was worse than patients with even NMOSD-related ON. Other ON subgroups, especially MS-related ON, had good visual prognosis when compared with other neuropathies. Previous studies also suggested an overall poorer visual outcome when compared with the ONTT and our population [26, 32]. A study from the Africa reported extremely poor visual outcome of ON in the African population, with only 27% of eyes gaining VA of 20/40 or more [18]. Visual acuity changes in patients with AION and NION during the follow-up period are controversial. Different studies have reported recovery of at least 3 Snellen acuity lines in 13–42.7% of NION patients [35–40]. Hayreh et al. [41] reported detailed

information about visual acuity changes in NION. Though the visual acuity of their patients with mild visual loss did not change, in patients with moderate-to-severe visual loss improvement was noted. Eyes with a visual acuity of $\leq$ 20/70 showed improvement in 41% of patients within the 6 months, followed by stabilization. They emphasized that in NION visual function can continue recovering during the 6 months from the initial visit, but not thereafter. Improvement of visual acuity in AION with corticosteroid therapy is less striking when compared to NION and has been reported in 4%–34% of patients in the largest series [42–47]. In our study, visual acuity in both AION and NION patients increased during the follow-up, but this increase was not statistically significant. However, the number of patients was small, especially in the AION group.

Fundus examination may show normal, swollen, pallor, or atrophic optic disks. The appearance of the optic nerve can sometimes give an idea about the etiology of the disease. For example, optic neuritis usually has normal optic disk appearance. However, sometimes optic disk swelling which is mild and diffuse in nature may also be seen in optic neuritis. Severe optic disk swelling accompanied by hemorrhages and exudates should be considered alternative etiologies such as NION, AON, or infiltrative optic neuropathy. Sectoral or diffuse disk swelling associated with peripapillary hemorrhages may be seen in eyes with NION. In addition, a small cup–disk ratio is seen in the fellow eyes. AION that resulted from giant cell arteritis has usually diffuse pale or "chalky white" swelling with cotton wool spot. Temporal paleness of the optic nerve should be usually considered toxic/nutritional or hereditary optic neuropathies that affect papillo-macular bundle selectively. An optic disk pallor or optic atrophy should be considered long-standing optic neuropathy including toxic/nutritional, hereditary, and compressive optic neuropathies. It may also be a sequel of previous acute inflammatory or ischemic optic neuropathies. In the present study, rates of optic disk swelling among the ON subgroups ranged from 10.5 to 45.4%, lower than the previous studies reporting swollen optic disks in 35.0–57.6% of cases [17, 19–21]. On the other hand, in a study from the South Africa by Pokroy et al. [18] optic disk swelling was seen in 80% of patients with ON.

Visual field testing is an integral component of the neuro-ophthalmic examination. It helps to estimate the possible etiology and is critical in the diagnosis of optic neuropathy. Visual field defects in different patterns including central–centrocecal, altitudinal, peripheral, tubular, and total defect can occur in optic neuropathies. In addition, these patterns are not specific of any etiology and any type of visual field defect may happen in any optic neuropathy. However, some patterns of visual field defect are more commonly associated with some types of optic neuropathies. For instance, central–centrocecal defects are more common in ON, hereditary, toxic, and nutritional optic neuropathies. In addition, altitudinal defect is often accompanied by ischemic optic neuropathies. Optic Neuritis Treatment Trial (ONTT) reported that nearly all types of visual field defects were seen in optic neuritis [17]. Similar to ONTT, we detected that almost all patterns of visual field defects were seen in optic neuritis. But, the most common visual field defect was central–centrocecal scotoma.

When the clinical features of the ON subgroups were taken into consideration, the most prominent feature of the CRION patients was 100% recurrence rate mainly involving the same side. 83% of the patients had attacks involving the same optic nerve. Sequential involvement of both optic nerves was present in around 36% of patients with NMOSD-related ON and 33% of patients with AON. Visual acuity at presentation did not differ between subgroups of patients with ON. Swollen optic disks were mainly noted in patients with NMOSD-related ON (around 45%). Three of the 11 patients with NMOSD-related ON were seronegative for AQP4-IgG. Two of them had previous longitudinal transverse myelitis attacks, and one was hospitalized because of area postrema syndrome following optic neuritis. Patients with AON were seronegative for AQP4-IgG and did not have previous neurological attacks. However, as myelin-oligodendrocyte glycoprotein antibodies (MOG-Ab) could not be studied in these patients, it is not easy to rule out NMOSD-related ON.

Treatment protocols

Table 6 gives information about the treatment protocol of optic neuropathies. Current approach in optic neuropathy treatment consists of systemic steroids in optic neuritis and AION and oral acetylsalicylic acid in NION. In the present study, most of patients with optic neuritis were treated with high-dose (1 g/day)

intravenous methylprednisolone and responded to therapy, which is in accordance with the ONTT study and studies published from the Asian region [10, 17, 27]. In patients with NMOSD-related ON, CRION, and AON, pulse steroid treatment was generally continued with oral steroids. Similarly, other neuropathies including ischemic, traumatic, and compressive optic neuropathies were also treated with systemic steroids. However, in these neuropathy groups, steroid did not increase visual acuity distinctly when compared with the optic neuritis group. Previous studies already stated that traumatic optic neuropathy and NION did not respond to the steroid adequately [7, 13, 30]. There is no proven treatment for NION at this time [28, 29, 40, 41, 48–51]. However, several studies have stated that oral steroid, acetylsalicylic acid, and intravitreal anti-vascular endothelial growth factor or triamcinolone injections could be effective in treatment. Recently studies have stated that these agents is effective when they were given within the first 14 days of the onset of the disease [28, 29, 40, 41, 48–51]. However, even if they receive these suggested treatments, optic atrophy with poor visual outcome will happen in the majority of these eyes. The use of steroids remains controversial for NION patients. However, high-dose intravenous steroids is compulsory and necessary in patients with AION, especially as a protective against other eye involvement [46, 47, 52].

Within the optic neuritis subgroup, response to steroids was very prominent in patients with CRION, MS-related ON, ION and even NMOSD-related ON patients showed significant improvement in vision after treatment. This contrasts with the previous studies reporting poor visual outcome in patients with NMOSD [53] and CRION [54]. AON group, on the other hand, did not response significantly to systemic steroids.

There are several strengths of our study. First, a comprehensive neuro-ophthalmological examination was performed on all patients. Other causes of vision loss were carefully examined and excluded. Second, to the best of our knowledge, our study was the first to describe the entire optic neuropathy spectrum at the same time, allowing us to make comparisons between optic neuropathy subgroups. In addition, our study had the largest series of consecutive patients, who were evaluated, managed, and followed systematically for optic neuropathies. However, there were some limitations. The major limitation was that it was a retrospective study, and another limitation was that some neuropathy groups included a small number of participants.

In conclusion, this study provided useful information, such as the demographic, clinical characteristics, and the treatment protocols of optic neuropathies in a neuro-ophthalmology specialty clinic at a tertiary referral center in Turkey during the past decade. The results, considering the previously mentioned limitations, will be useful in estimating the worldwide distribution of optic neuropathies.

Author contribution All authors contributed significantly to the creation of this manuscript, each fulfilled criteria as established by the ICMJE.

Compliance with ethical standards

Conflict of interests The authors declare that there is no conflict of interests regarding the publication of this paper.

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