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Original Research Article

Analysis of Risk Factors, Clinical Features and Visual Outcome in Cases of Non Arteritic Anterior Ischemic Optic Neuropathy (Na-Aion) At Teaching Govt Hospital in South India

Harshitha Sai R.[1], Sreedevi K.V.N.[2], Chandra Sekhar B.[3], Srinivas Y.[4]

[1]Junior Resident, Department of Ophthalmology, Guntur Medical College, Guntur, Andhra Pradesh, India

[2,3]Assistant Professor, Department of Ophthalmology, Guntur Medical College, Guntur, Andhra Pradesh, India

[4]Associate Professor, Department of Ophthalmology, Guntur Medical College, Guntur, Andhra Pradesh, India

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Corresponding Author: Dr. Srinivas. Y
Conflict of interest: Nil

Abstract:

This prospective observational study aimed to identify potential risk factors, clinical features, and visual outcomes associated with non-arteritic anterior ischemic optic neuropathy (NA-AION). Conducted over a twelve-month period (February 2023 - January 2024) at the Ophthalmology OPD of a government hospital in South India, the study evaluated 24 patients diagnosed with NA-AION based on Hayreh's criteria. The investigation assessed the prevalence of risk factors like diabetes, hypertension, dyslipidaemia, sleep apnoea and smoking. Clinical features such as visual acuity, pain, and disc oedema were documented. Visual outcomes were measured at the final follow-up visit. This study will contribute to a better understanding of the clinical profile and risk factors associated with NA-AION in the South Indian population.

Keywords: Ischemic Optic Neuropathy, Non Arteritic Anterior Ischemic Optic Neuropathy.

Introduction

Ischemic optic neuropathies (IONs) are a major cause of blindness or severe vision impairment in middle-aged and elderly individuals, resulting from ischemic damage to the optic nerve (ON)[1]. Clinically IONs are categorized into anterior (AION) and posterior (PION) forms, distinguished by the presence or absence of optic disc (OD) oedema, respectively. Additionally, IONs are classified as arteritic (A-ION), caused by arteritis, or non-arteritic (NA-ION), the latter of which is idiopathic with debated etiology and pathophysiology. [2]

Non-arteritic anterior ischemic optic neuropathy (NA-AION) is the leading cause of acute optic neuropathy in patients over 50 and the second most common form of optic neuropathy after glaucoma. NA-AION affects the optic nerve, leading to sudden and often painless vision loss, typically noticed upon awakening. The most important clinical finding at the onset of visual loss is optic disc oedema, which usually resolves spontaneously within several weeks, resulting in generalized atrophy of the optic disc. Common risk factors for NA-AION include systemic hypertension, diabetes, hyperlipidaemia, small cup-to-disc ratio or crowded disc, nocturnal hypotension, sleep apnoea, smoking, migraines, certain medications, and various coagulopathies. Early diagnosis and management are crucial to mitigate vision loss in affected individuals.

Aim and Objective:

1. To evaluate the risk factors, clinical characteristics and visual outcome in patients with NAION.
2. To evaluate NAION's response to treatment.

Patients and Methods

This prospective observational study included 24 patients with NAION diagnosed at teaching government hospital in South India from February 2023 to January 2024. The diagnosis of NAION was made on the basis of criteria used by Hayreh and Zimmerman[3].

The study was approved by the institutional ethics committee and written informed consent was obtained from all of the patients before inclusion in

the study. The inclusion and exclusion criteria for the study are given below.

Case 1:

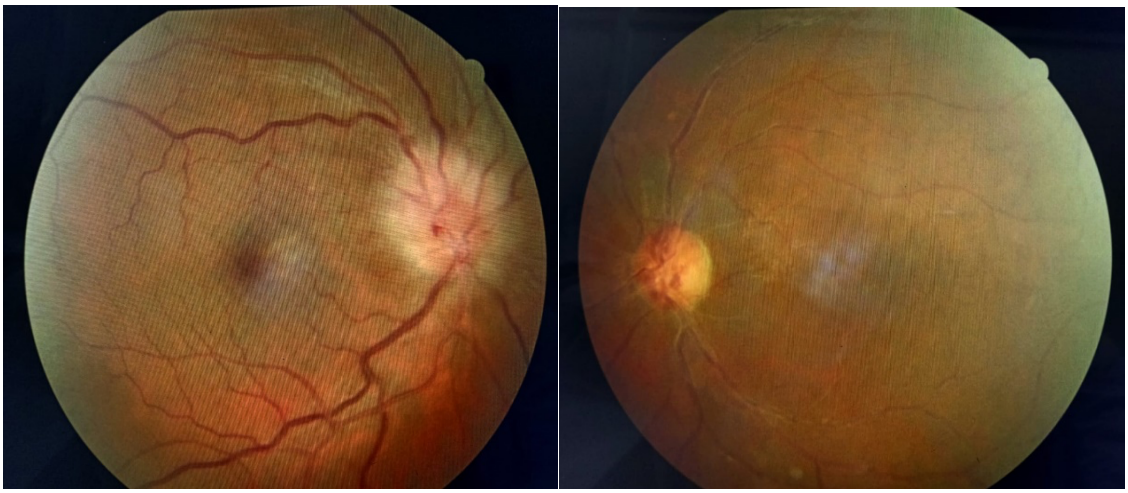

Figure 1: (a) **Figure 1: (b)**

Figure 1: (a & b) 68-year-old woman with acute diminution of vision in the right eye and a past history of a similar event in the left eye. a) Fundus photograph showing optic disc oedema with peripapillary haemorrhages in the right eye and with b) collaterals on the disc and attenuation of the vessels in the left eye.

Case 2:

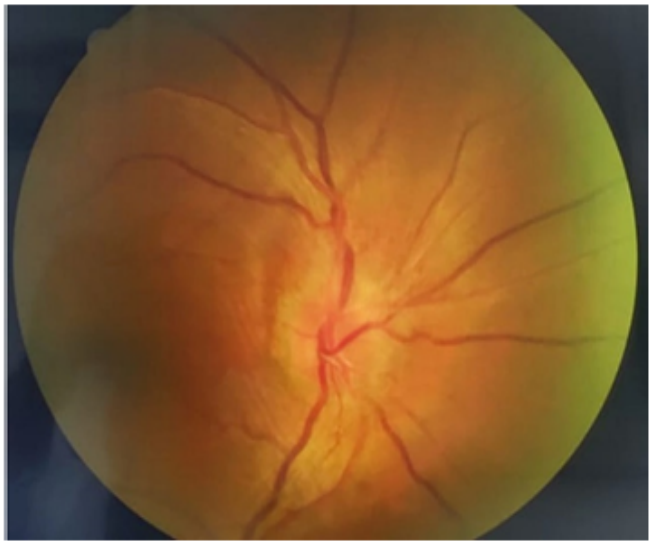

Figure 1: (c)

Figure 1(c): 64-year-old man with acute diminution of vision in the left eye upon waking. Best corrected visual acuity of Left eye is 6/18p. Fundus photograph showing optic disc oedema.

Inclusion Criteria:

1. Patients with acute unilateral NA-AION who presented within the first 2 weeks of symptom onset.
2. Diagnosis of NA-AION based on the criteria used by Hayreh and Zimmerman [3].
3. No evidence of systemic, neurological, or ocular disorders other than NA-AION that could account for vision loss.

Exclusion Criteria:

1. Patients who are not willing for study.
2. Patients with history of other ocular surgeries, ocular injuries.
3. Patients with history of uveitis or active eye inflammation;
4. Patients with history or evidence of glaucoma
5. Patients with media opacity hindering posterior pole examination;

6. Patients with retinal and optic nerve pathologies in the affected eye.
7. Patients with AAION are excluded, through appropriate examination and investigations.
8. Congenital optic disc anomalies are excluded.

A detailed clinical history was obtained from all patients, including age at presentation, duration and pattern of visual loss, and history of systemic conditions such as diabetes mellitus, hypertension, obesity, coronary artery disease, cerebrovascular events, sleep apnoea, and migraines. The history also included smoking habits and details on the duration and dosage of steroids and other medications.

Ocular Examination: Visual acuity (VA) was assessed using Snellen charts. During follow-up visits, any improvement or deterioration in VA was defined as a change of more than three lines in either direction. Colour vision was evaluated using the Pseudo Ishihara chart. Intraocular pressure was measured by Goldmann applanation tonometry.

A slit lamp examination with a 90D or 78D lens was preferred over direct ophthalmoscopy (DO) or indirect ophthalmoscopy (IO) for assessing the optic disc, following standard examination procedures for optic disc disorders. Colour fundus photographs were taken for all patients at the initial visit and during follow-up visits using the Canon CX-1 Digital Retinal (MYD/NM) Camera. Visual fields were assessed using the confrontation method and Humphrey Field Analyzer.

Relevant biochemical and haematological tests were conducted to check for giant cell arteritis, vasculitis, or other comorbidities. When necessary, colour Doppler and MRA were used to rule out AAION. All patients received treatment according to standard guidelines and were followed up with detailed neurological and ophthalmological evaluations for at least six months.

Observation and Results

During the trial, 82 individuals reported to neurology or ophthalmology departments with acute visual impairment. The study excluded fifty-eight patients with alternate diagnoses (17 with demyelinating optic neuritis, 12 with idiopathic intracranial hypertension, seven with branch retinal vein occlusion, ten with AAION, eight with toxic optic neuropathy, three with associated diabetic retinopathy, and one with optic nerve meningioma). Thus, 24 eyes were included in this study.

Demographic Features: The study group includes the patients of age >50 years which comprised of 14 (58.33%) men and 10 (41.6%) women.

Clinical Profile: For analysing clinical profile, the denominator was the number of eyes (n = 24) (right – 10, left -14). The median time from onset of visual symptoms to visual assessment was two weeks.

Relationship with Sleep: Vision loss was noticed at awakening only in 7 (29.16%) eyes while there was no relationship between vision loss and sleep in 17 (70.83%) eyes (Table 1).

Headache/Ocular Pain: Fifteen (68.1%) patients did not have any headache or ocular pain. Eight (33.3%) patients had headache while three (12.5%) patients had retro-orbital pain at the time of onset of vision loss. (Table 1).

Comorbidities: The most common comorbidities were diabetes mellitus, hypertension, and smoking, coronary artery disease, sleep apnoea, cerebrovascular accident (Table1). Only 1/24 (4.16%) patient had had a prior cerebrovascular event.

Past History of Similar Events: A past history of NAION was present in 6/24 (25%) patients (same eye –one, other eye – five). The duration between the two events may range between 6 months to 30 months.

Influence of Various Demographic and Clinical Factors on Recurrence: We investigated how different demographic characteristics and existing medical conditions affect the likelihood of NAION recurrence. Upon analysis, we found that none of these demographic factors or comorbidities was linked to a higher risk of NAION recurrence (Table1).

Table 1: Demographic profile of patients with NAION

Parameter	NAION (n=24 patients)
Duration of visual loss 2 weeks	12(50%)
Vision loss noticed on awakening	7 (29.16%)
Retro-orbital pain	3 (12.5%)
Headache	8 (33.3%)
No headache/retro-orbital pain	15 (68.1%)
Treatment received before presentation	
Oral steroids	3 (12.5%)
Intravenous + oral steroids	3 (12.5%)
Steroids + aspirin	4 (16.6%)
Aspirin alone	2 (8.3%)
None	12 (62.5%)

Comorbidities	**NAION (n=24 patients)**
Diabetes mellitus	15 (62.5%)
Hypertension	13 (54.16%)
Coronary artery disease	4(16.6%)
Obesity (body mass index > 30 kg/m2)	5(20.83%)
Sleep apnoea	4(16.6%)
Cerebrovascular event	1(4.16%)
Migraine	2 (8.3%)
Smoking	9 (37.5%)
Past history of similar event	6 (25%)
Neuroimaging	**NAION(n=24patients)**
Abnormal	4 (16.6%)
Right middle cerebral artery territory chronic infarct	1
Microangiopathic changes	3
Vascular imaging	NAION (n=24 patients)
Abnormal (stenosis of right MCA)	1(4.16%)

Visual acuity (VA): VA was divided into five grades (grades I–V) ranging from best to worst (Grade I – 6/6–6/9; Grade II – 6/12–6/18; Grade III – 6/24–6/36, Grade IV – 6/60–3/60; and Grade V – counting fingers or worse). (Table2).

Table 2: ophthalmological profile of patients with NAION

Visual acuity (VA) at presentation	**NAION (n = 24 eyes)**
6/6-6/9 (Grade I)	6 (25%)
6/12-6/18 (Grade II)	4(16.6%)
6/24-6/36 (Grade III)	3 (12.5%)
6/60-3/60 (Grade IV)	4 (16.6%)
Counting fingers- worse (Grade V)	7 (29.1%)
Relative afferent pupillary defect	23 (95.8%)
Low cup-to-disc ratio (< 0.3)	13 (54.16%)
Visual field assessment **Pattern of defects**	
Diffuse	12 (50%)
Superior	2(8.3%)
Inferior	6 (25%)
Inferonasal	3 (12.5%)
Temporal	1 (4.16%)
Severity of field deficit	
Normal (0)	0
Minimal 0.5)	0
Mild (> 0.5-1.5)	2 (8.3%)
Moderate (1.5-2.5)	8 (33.33%)
Marked (2.5-3)	4 (8.3%)
Severe (3.5-4)	10 (41.6%)

Relative afferent pupillary deficit (RAPD): Twenty-three (95.8%) eyes showed RAPD. One patient had simultaneous vision loss the pupillary reaction was better in the less severely affected eye. VF analysis revealed inferior altitudinal defect in that eye.

Fundus evaluation: On fundus evaluation, 21 (87.5%) eyes had optic disc oedema. while 3 eyes (12.5%) had sectoral pallor alone. Fundus evaluation of the fellow eyes (n = 24) revealed sectoral pallor in two (8.3%) and disc atrophy in three (12.5%) eyes.

The cup-to-disc ratio was low (<0.3) in 13 (54.16%%) eyes (table2).

VF testing: Amongst the 24 eyes, 12 (50 %) had diffuse while remaining 12 (50%) had sectoral VF defects. Among the eyes with sectoral defects, an inferior altitudinal defect was the most common (n = 6) (Table2).

Influence of various demographic and clinical features as well as comorbidities on Visual Acuity: We examined how different demographic factors, clinical features, and comorbidities affect visual acuity (VA) in patients with Non-Arteritic An-

terior Ischemic Optic Neuropathy (NAION) at the time of presentation. Various comorbidities such as diabetes mellitus, hypertension, coronary artery disease (CAD), obesity, sleep apnoea, cerebrovascular events, migraine, and smoking habits, as well as factors like severity of visual field deficit, sudden versus gradual onset of vision loss, and low cup-to-disc ratio in the fellow eye, did not correlate with the number of eyes presenting with VA worse than 6/60**.**

However, we observed a significant positive association between poor VA at presentation and severe optic disc edema. Additionally, there was a noticeable trend suggesting a correlation between poor VA and the presence of more than one vascular risk factor.

Investigations: For the majority of our patients who were sent to higher centers, we advised fundus fluoresceine angiography (FFA) and visual evoked potential (VEP).In addition to the ocular investigations, we performed other systemic investigations related to their comorbidities.

Neuroimaging: Four of the twenty-four patients had aberrant imaging results; one patient had a persistent infarct located in the right middle cerebral artery area, and the other three had microangiopathic alterations.

Treatment and follow up: A daily dosage of 75 mg aspirin was given to each patient in our trial. Ten patients were administered steroids; three were to get methylprednisolone intravenously, followed by oral prednisone, and the other seven were to receive oral steroids exclusively. The patients were monitored for 6 months on average (with a range of 2 to 9 months). Two eyes (8.3%) of a patient receiving steroid treatment showed an improvement in visual acuity on the Snellen chart of more than three lines at the follow-up (see Table 3). Furthermore, five eyes (one with aspirin alone and four with steroids) showed improvement in their visual field defects (see Table 3). There was no significant difference in visual outcome between patients who got steroids versus those who did not.

Table 3: Visual acuity and visual fields at presentation and follow up in study group(n=24)

	Visual acuity at follow up (number of patients)%						
Visual acuity at initial visit (number of patients [%])	**6/6-6/9**	**6/6-6/9**	**6/12-6/18**	**6/24-6/36**	**6/60-3/60**	**Counting fingers-worse**	**Total**
	6/6-6/9	6 (25%)	0	0	0	0	6
	6/12-6/18	0	4 (16.6%)	0	0	0	4
	6/24-6/36	0	0	3 (12.5%)	0	0	3
	6/60-3/60	0	0	2 (8.3%)	2 (8.3%)	0	4
	CF-worse	0	0	0		7 (29.1%)	7

	Visual Field deficit at follow up (number of patients)%						
Visual field deficit at presentation (number of patients [%])		**Minimal**	**Mild**	**Moderate**	**Marked**	**Severe**	**Total**
	Minimal	0	0	0	0	0	0
	Mild	1(4.16%)	1 (4.16%)	0	0	0	2
	Moderate	2(8.3%)	0	6 (25%)	0	0	8
	Marked	0	0	1(4.16%)	3 (12.5%)	0	4
	Severe	0	0	0	1 (4.16%)	9 (37.5%)	10
	Total	3	1	7	4	9	24

Discussion

This study found that NAION was a more common cause of acute optic neuropathy than previously thought. In fact, it was the second most common cause, accounting for 29.26 % of cases. Notably, NAION was three times more frequent than anterior ischemic optic neuropathy (AAION).

Not everyone with NAION wakes up with vision loss: According to this study, only 7 (29.16%) of patients' eyes had visual loss soon after waking up. This is significantly lower than what prior study revealed (73.3% according to Hayreh et al.[11,12]. During 24-hour ambulatory blood pressure monitoring, they noticed a drop in arterial blood pressure at night in a significant proportion of their patients, and they proposed nocturnal arterial hypotension as a cause of NAION. Nonetheless, it underscores the need of examining NAION, particularly in people who do not report visual loss upon awakening.

Our outcomes are comparable to those from the Ischaemic Optic Neuropathy Decompression Trial (IONDT)[3], in which only 42% of all patients showed visual loss after two hours of waking. The authors also proposed that the 42% incidence reflects a more consistent distribution of the onset of NAION throughout the day. Furthermore, five of twenty-four eyes (20.8%) of patients in the study suffered progressive vision loss over 24 hours or more. This demonstrates that NAION can appear

with a gradual deterioration in vision, rather than just rapid visual loss upon awakening.

In short, consider NAION as a possibility even if someone doesn't lose vision right away or wake up with vision problems.

NAION can be painful, even though it's usually described as painless: NAION is often assumed to be painless. However, the results we obtained showed that 33.3% of patients reported headaches, while 12.5% experienced retro-orbital discomfort, or pain behind the eyes. Our results were similar to those of Swartz et al.[4] This shows that NAION should not be dismissed as a possible cause of sudden vision loss owing to migraines or ocular pain.

Recurrence Events: In our study, 6 (25%) eyes out of 24 eyes of patients experienced recurrent NAION events, with an average duration between episodes of 18 months (ranging from 6 to 30 months). Beri et al. [5] reported a 25% risk of fellow eye involvement over three years among 438 patients, while Beck et al [6]. noted a 17% risk over five years in a cohort of 431 individuals. Newman et al [7]. Found that 14.7% of patients developed new NAION in the fellow eye, with a median interval of 1.2 years between events. Factors such as baseline visual acuity of 6/60 or worse, diabetes mellitus, coronary artery disease (CAD), hypertension, stroke, sleep apnoea or transient ischemic attacks (TIAs) were weakly linked to NAION occurrence in the fellow eye in previous studies [7].

However, in our current study, none of these factors showed an association with NAION recurrence. This discrepancy may be attributed to the relatively small size of our study group. In this study, we intended to assess if the presence of more than one vascular risk factor affected visual outcome of NAION or the probability of recurrence. We found no correlation between the existence of more than one risk factor and any of these measures. However, the sample size was insufficient to support the observed findings. There were insufficient data available to compare this finding with those of other authors.

Visual Acuity and Visual field testing: In our study, 45.83% of eyes i.e. 11 eyes out of 24 eyes exhibited a visual acuity (VA) of 6/60 or worse. This finding contrasts with Hayreh and Zimmerman's [3] study but aligns with the IONDT cohort [7], where only 23% of eyes had a VA of ≤6/60. Another notable observation was that nearly one third of eyes had a VA ranging from 6/6 to 6/9, indicating that NAION can manifest with both normal or near-normal and severely reduced VA.

Regarding visual field (VF) analysis, our study revealed both diffuse (50%) and sectoral defects, with inferior field defects being the most common. We did not observe a significant correlation between the severity of VF defect and VA. Our finding differs from Hayreh and Zimmerman's study [8], where VFs were normal in 16.6% of cases (all patients in our study exhibited VF defects). Central scotoma was the most common field defect (48.5%), followed by inferonasal (22.4%) and inferior altitudinal (8%) defects. The likely reason for this variation is the more stringent protocol followed in our study.

Optic Disc Changes: In our investigation, 21 (87.5%) of the 24 eyes showed optic disc oedema, whereas three eyes (12.5%) showed just sectoral pallor. The absence of optic disc oedema in these three eyes may be explained by their delayed appearance. After a six-month follow-up, all eyes showed remission of optic disc oedema, with evidence of optic disc pallor. These findings were consistent with those reported by Hayreh and Zimmerman [9]. The low cup-to-disc ratio (< 0.3) of the contralateral eye did not show an association with the risk of recurrence or visual acuity, which aligns with the findings of Fry et al.[10]

Fundus Fluorosceine Angiography: It was the single most prevalent investigation among NAION patients. Our findings suggest that all patients with suspected NAION as well as optic neuropathy of unknown etiology should undergo FFA for confirmation of diagnosis. As a result, we advised the majority of our patients seek further investigations (FFA and also Visually evoked potential) at higher institutional centres.

Neuroimaging and vascular imaging: In the current study, 4 (16.6%) patients had aberrant neuroimaging findings, whereas 1 (4.16%) had aberrant vascular imaging results. Our findings were consistent with those of Fry et al. [10], who found a substantial correlation between carotid artery (large vessel) atherosclerosis and transitory monocular blindness but not AION. Thus, NAION might not be associated with large vessel atherosclerosis, but it can be a symptom of small vessel disease. Further studies of MRI and MRA findings in NAION are required to support this hypothesis.

Treatment

All patients received a daily dosage of 75 mg of aspirin. Ten patients were provided steroids, with three receiving intravenous methylprednisolone followed by oral prednisone and the other seven receiving solely oral steroids.

Patients with diabetes mellitus and hypertension were treated appropriately for hyperglycaemia and hypertension, respectively. Overall, just two eyes (8.3%) exhibited improvement in visual acuity, whereas five (20.8%) showed improvement in visual fields.

This increase in visual acuity was significantly lower than the 41% reported by Hayreh and Zimmerman [3] after six months.

The explanation for the variance in visual results throughout follow-up is unknown; however, it might be due to unexplained genetic or metabolic traits distinct to the Indian population.

In our study, we did not observe any beneficial effects of steroids on visual outcomes in NAION, contrary to the findings of Hayreh and Zimmerman [11], who demonstrated a significant benefit of steroids (n=312) in NAION compared to controls(n=302). This difference might be due to our relatively small sample size and shorter follow-up duration.

Conclusion

In the Indian population, NAION is a prevalent cause of acute optic neuropathy. Given the prevalence of unusual presentations of NAION in the Indian population, it is important to maintain a high degree of suspicion while diagnosing NAION. Larger sample sizes in future research will aid in further elucidating NAION in the Indian population.

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