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ORIGINAL RESEARCH

Non-Arteritic Anterior Ischemic Optic Neuropathy Before and During the COVID-19 Pandemic: A Retrospective Comparative Study

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Purpose: Non-arteritic anterior ischemic optic neuropathy (NAION) is an ischemic disorder of the optic nerve head often associated with systemic vascular risk factors. While COVID-19 is primarily a respiratory disease, it has been linked to vascular and thromboembolic complications. This study compared the incidence, clinical characteristics, and outcomes of NAION diagnosed before and during the COVID-19 pandemic.

Patients and Methods: A retrospective review was conducted of new NAION cases at a tertiary neuro-ophthalmology clinic diagnosed between May 2017–May 2019 (Pre-COVID) and March 2020–March 2022 (During-COVID). Data collected included demographics, vascular risk factors, clinical presentation, visual acuity, optical coherence tomography–derived retinal nerve fiber layer (RNFL) thickness, and visual field mean deviation (VF MD). Statistical analyses employed Chi-square, Fisher's exact test, *t*-test, and Mann–Whitney *U*-test.

Results: Among 1,543 clinic patients, 46 were diagnosed with NAION (Pre-COVID: 27; During-COVID: 19). The relative frequency of NAION increased during the pandemic (3.7% vs 2.6%). Patients in the During-COVID group had significantly higher rates of hypertension (84.2% vs 40.7%, p=0.003), atherosclerotic cardiovascular disease (15.8% vs 0%, p=0.033), suspected sleep apnea (36.8% vs 0%, p=0.001), obesity (21.1% vs 0%, p=0.013), and smoking history (42.1% vs 3.7%, p=0.001). Subacute onset was more frequent during the pandemic (36.8% vs 0%, p=0.001), suggesting delayed presentation. At three months, visual acuity was worse in the During-COVID group (logMAR 1.34 vs 0.72, p=0.014). Baseline RNFL thickness and VF MD did not differ significantly. Only 31.6% of During-COVID cases had documented SARS-CoV-2 infection.

Conclusion: During the COVID-19 period, NAION was proportionally more frequent and associated with increased vascular comorbidities, delayed presentation, and worse visual outcomes. Both direct viral and indirect pandemic-related factors may contribute.

Keywords: COVID-19, NAION, SARS-CoV-2 infection, optic nerve ischemia, visual outcome

Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV- 2), emerged in late 2019 and has since resulted in widespread global morbidity and mortality.[1] While COVID-19 is primarily known for its respiratory symptoms, accumulating evidence indicates that the disease can also lead to significant systemic complications, particularly involving vascular and thromboembolic events. These include ischemic stroke, myocardial infarction, pulmonary embolism, and deep vein thrombosis (DVT), largely attributed to COVID-19-associated endothelial dysfunction, inflammation, and hypercoagulability.[2–6]

The virus gains entry into host cells via angiotensin-converting enzyme 2 (ACE-2) receptors, which are widely expressed in lung alveolar cells, cardiac myocytes, and vascular endothelial cells. This interaction can result in

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endothelial injury and immune-mediated inflammation, promoting a prothrombotic state. These pathophysiological changes have been implicated in a wide range of ischemic complications.[7]

Recent evidence underscores this risk specifically within the ocular vasculature; for instance, a systematic review by Tzamalis et al highlighted a significant association between COVID-19 and other retinal vascular occlusions (retinal vein occlusion and retinal artery occlusion), further illustrating the virus's potential to induce thromboembolic episodes in the eye.[8]

Non-arteritic anterior ischemic optic neuropathy (NAION) is one such ischemic event. It results from reduced perfusion to the optic nerve head, most commonly due to occlusion of the short posterior ciliary arteries. NAION typically presents as sudden, painless, monocular vision loss, often in individuals with systemic vascular risk factors such as hypertension, diabetes mellitus, or atherosclerosis.[9] Given the vascular pathogenesis of NAION and the systemic thrombotic effects of COVID-19, a possible link between the two has been proposed.[10]

Although there have been several case reports describing NAION occurring after COVID-19 infection,[11–14] comprehensive data comparing the characteristics and frequency of NAION before and during the COVID-19 pandemic are lacking. Understanding whether COVID-19 has influenced the incidence or clinical profile of NAION could provide important insights into its pathophysiology and guide future diagnostic and management strategies.

Evaluating potential shifts in NAION characteristics may elucidate the broader vascular effects of systemic infections. This study aims to retrospectively compare the number of NAION cases before and during the COVID-19 pandemic, and to analyze differences in demographic characteristics, clinical presentation, and disease progression between the pre-COVID era and during-COVID era.

Material and Methods

We reviewed the medical records of new cases of non-arteritic ischemic optic neuropathy (NAION) in patients who visited the Neuro-ophthalmology Clinic at Rajavithi Hospital between May 1, 2017, and March 1, 2023. This study was approved by the Institutional Review Board of Rajavithi Hospital (approval no. 230/2567). The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective nature of the study, the requirement for informed consent for all participants was waived by the Institutional Review Board. Patient confidentiality was strictly maintained, and all data were anonymized prior to analysis.

Inclusion criteria consisted of newly diagnosed NAION cases evaluated at the neuro-ophthalmology clinic during the study period. Exclusion criteria included patients with arteritic anterior ischemic optic neuropathy, optic neuropathy from other identifiable causes (eg, optic neuritis, compressive, hereditary, or toxic etiologies), or incomplete clinical data. All diagnoses of NAION were established and confirmed by a neuro-ophthalmologist. In cases where the initial differential diagnosis was between optic neuritis and NAION, confirmation was obtained by MRI, and in some instances, intravenous steroid injection was administered prior to establishing the final diagnosis.

The records were categorized into two groups: the Pre-COVID-19 Group (May 1, 2017, to May 1, 2019) and the During-COVID-19 Group (March 1, 2020, to March 1, 2022), with each group spanning an equal duration of two years. Records from June 1, 2019, to February 29, 2020, were excluded due to the absence of clear evidence of COVID-19 transmission in Thailand during that period.

Data collected included age, gender, underlying medical conditions, presenting signs and symptoms, findings from ophthalmic examinations, and treatment details. Retinal nerve fiber layer (RNFL) thickness was assessed using optical coherence tomography (OCT) with the Spectralis OCT system (Heidelberg Engineering, Germany), and visual field mean deviation (VFMD) was obtained using the Humphrey Visual Field Analyzer (Carl Zeiss Meditec) with the 24–2 program. Visual examinations and investigation were collected in all cases at disease onset (within 2 weeks of diagnosis) and at follow-up of at least 3 months.

Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Visual acuity was converted to logarithm of the minimum angle of resolution (logMAR) units. Categorical variables were summarized as frequencies and percentages, and continuous variables as means with standard deviations. Comparisons between groups were performed using the chi-square test or Fisher's exact test for categorical variables, as appropriate, and paired or independent t-tests for continuous variables. Fisher's exact test was applied when expected cell counts were small or

included zero values. A p-value < 0.05 was considered statistically significant. No formal sample size calculation or power analysis was performed due to the retrospective, exploratory nature of the study.

Results

Out of 1,543 total patients who visited the Neuro-ophthalmology Clinic during the study period, 46 (3.0%) were newly diagnosed with non-arteritic anterior ischemic optic neuropathy (NAION). These cases were categorized into the Pre-COVID-19 group (N = 27) and the During-COVID-19 group (N = 19). The overall characteristics of NAION patients are summarized in Table 1.

The prevalence of diabetes or prediabetes (63.2% vs 55.6%; p = 0.606) and dyslipidemia (73.7% vs 66.7%; p = 0.611) was slightly higher in the During-COVID-19 group, though not statistically significant. However, hypertension was significantly more common during the pandemic (84.2% vs 40.7%; p = 0.003). Similarly, there was a significantly higher prevalence of atherosclerotic cardiovascular disease (ASCVD; 15.8% vs 0%; p = 0.033), suspected sleep apnea (36.8% vs 0%; p = 0.001), obesity (21.1% vs 0%; p = 0.013), and smoking history (42.1% vs 3.7%; p = 0.001) in the During-COVID-19 group. Gender distribution (p = 0.261) and mean age of onset (56.33 ± 8.09 years vs 59.58 ± 10.38 years; p = 0.387) were also not significantly different between groups.

As shown in Table 2, there were no statistically significant differences in the laterality of the affected eye between groups (p = 0.765). In the Pre-COVID-19 group, right-eye involvement was noted in 14 patients (51.8%) and left eye

Table 1 Demographic and Systemic Characteristics of Non-Arteritis Ischemic Optic Neuropathy Patients Before and During COVID-19

	Pre-COVID-19	During COVID-19	p-value
	N = 27	N = 19	
Gender [n (%)]			0.261[a]
Female	13(48.2)	6(31.6)	
Male	14(51.8)	13(68.4)	
Age of onset(year) [Mean ± SD]	56.33 ± 8.09	59.58 ± 10.38	0.387[c]
Underlying disease [n (%)]			
Diabetes or Prediabetes	15(55.6)	12(63.2)	0.606[a]
HT	11(40.7)	16(84.2)	0.003[a]
DLP	18(66.7)	14(73.7)	0.611[a]
ASCVD (Stroke, CAD, PAD)	0(0)	3(15.8)	0.033[a]
Sleep apnea suspect	0(0)	7(36.8)	0.001[b]
Obesity (BMI >30) [n (%)]	0(0.0)	4(21.1)	0.013[a]
Smoker (Current smoker or >30 pack year history) [n (%)]	1(3.7)	8(42.1)	0.001[a]

Notes: [a]p-value from Pearson Chi-square test; significant at p<0.05; [b]p-value from Fisher's Exact test; significant at p<0.05; [c]p-value from independent *t*-test; significant at p<0.05.
Abbreviations: HT, Hypertension; DLP, Dyslipidemia; ASCVD, Atherosclerotic cardiovascular disease; CAD, Coronary artery disease; PAD, Peripheral artery disease; BMI, Body Mass Index.

Table 2 Signs and Symptoms of Non-Arteritis Ischemic Optic Neuropathy Patients at Presentation

	Pre-COVID-19	During COVID-19	p-value
	N = 27	N = 19	
Affected eye [n(%)]			0.765[a]
Right eye	14(51.8)	9(42.1)	
Left eye	13(48.2)	10(57.9)	
Days between symptoms onset and diagnostic of NAION [Mean ± SD]	20.89 ± 19.64	31.11 ± 45.12	0.652[d]
Headache or eye pain at onset /prodromal	4(14.8)	2(10.5)	0.671[a]

(*Continued*)

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Table 2 (Continued).

	Pre-COVID-19	During COVID-19	p-value
	N = 27	N = 19	
Onset [n(%)]			0.001[a]
Acute	27(100.0)	12(63.2)	
Subacute (worsening >48 hr.)	0(0.0)	7(36.8)	
Disc edema [n(%)]	23(85.2)	15(78.9)	0.583[a]
Type of disc edema [n(%)]			0.744[a]
Total edema	15(65.2)	9(60.0)	
Segmental edema	8(34.8)	6(40.0)	
Disc hemorrhage [n(%)]	2(7.4)	4(21.1)	0.176[a]
Crowded disc in another eye [n(%)]	6(22.2)	10(52.6)	0.033[a]

Notes: [a]p-value from Pearson Chi-square test; significant at p<0.05. [d]p-value from Mann–Whitney *U*-test; significant at p<0.05.
Abbreviation: NAION, Non arteritic anterior ischemic optic neuropathy.

involvement in 13 patients (48.2%). One patient experienced sequential bilateral NAION (right eye followed by left eye); this case was included as two separate entries for analysis. In the During-COVID-19 group, the left eye was more frequently affected (57.9%, 10 patients), followed by the right eye (42.1%, 9 patients).

All patients in the Pre-COVID-19 group presented with an acute onset, whereas only 63.2% in the During-COVID-19 group did; the remaining 36.8% had a subacute onset (p = 0.001). The average time from symptom onset to diagnosis was longer during the pandemic (31.11 ± 45.12 days) compared to the pre-pandemic period (20.89 ± 19.64 days), but this was not statistically significant (p = 0.652). Other presenting features—including the presence of disc edema (p = 0.583), type of disc edema (p = 0.744), and disc hemorrhage (p = 0.176)—did not differ significantly between groups. However, crowded optic disc in the contralateral eye was significantly more common in the During-COVID-19 group (52.6% vs 22.2%; p = 0.033).

Some patients with NAION did not have documented visual field defects, as chart review revealed only notes of vision loss without any documentation of visual field testing or CTVF 24–2 results. Visual field defect patterns were similar between groups, with altitudinal defects being the most frequent. There were no statistically significant differences in the side or presence of visual field defects (Table 3).

Most patients in both groups were managed conservatively with observation: 66.7% in the Pre-COVID-19 group and 89.5% in the During-COVID-19 group. Steroid therapy, including intravenous methylprednisolone (IVMP), was used more frequently before the pandemic, although the difference in treatment approach was not statistically significant (p = 0.172) (Table 4).

Visual acuity outcomes, assessed using log MAR at presentation, one month, and three months, are summarized in Table 5. At presentation, patients in the During-COVID-19 group had worse visual acuity (1.59 ± 1.06) compared to the

Table 3 Type of Visual Field Defect of Non-Arteritis Ischemic Optic Neuropathy Patients at Presentation

	Pre-COVID-19	During COVID-19	p-value
	N= 21	N = 14	
Types of visual field defect [n(%)]			0.749[b]
Altitudinal defect	11(52.4)	7(50.0)	
Arcuate defect	2(9.5)	1(7.1)	
Generalized defect	6(28.6)	6(42.9)	
Unspecified	2(9.5)	0(0.0)	

Notes: [b]p-value from Fisher's Exact test; significant at p<0.05.

Table 4 Acute Treatment for Non-Arteritis Ischemic Optic Neuropathy Patients in Both Groups

	Pre-COVID-19	During COVID-19	p-value
	N = 27	N= 19	
Acute treatment[n(%)]			0.172[a]
Observation	18(66.7)	17(89.5)	
Oral steroid	2(7.4)	0(0.0)	
Intravenous methylprednisolone	7(25.9)	2(10.5)	

Notes: [a]p-value from Fisher's Exact test; significant at p<0.05.

Table 5 Functional Outcomes Comparison Between Pre COVID-19 and During COVID-19 of Non-Arteritis Ischemic Optic Neuropathy Patients

Subgroup		Mean ± SD	P-value
Log MAR worst eye at presentation	Pre COVID-19 During COVID-19	1.01 ± 0.98 1.59 ± 1.06	0.066[a]
Log MAR worst eye at 1 month later	Pre COVID-19 During COVID-19	0.84 ± 0.76 1.13 ± 0.84	0.190[a]
Log MAR worst eye at 3 months later	Pre COVID-19 During COVID-19	0.72 ± 0.68 1.34 ± 0.97	0.014[a]
OCT RNFL within 2 weeks of onset	Pre COVID-19 During COVID-19	211.95± 109.59 149.41 ± 81.75	0.094[a]
OCT RNFL at least 3 month follow up	Pre COVID-19 During COVID-19	62.22 ± 13.40 51.83 ± 15.82	0.126[a]
VF MD within 2 weeks of onset	Before COVID-19 During COVID-19	−18.77 ± 8.03 −22.15 ± 8.05	0.855[b]
VF MD at least 3 month follow up	Before COVID-19 During COVID-19	−16.47 ± 6.83 −21.07 ± 5.93	0.873[b]

Notes: [a]p-value by Mann–Whitney *U*-test; significant at p<0.05. [b]p-value by independent sample *T* Test; significant at p<0.05.

Abbreviations: OCT RNFL, Optical Coherence Tomography image of Retinal Nerve Fiber Layer; COVID-19, Coronavirus disease of 2019; VF MD, Visual field mean deviation; COVID-19, coronavirus disease of 2019.

Pre-COVID-19 group (1.01 ± 0.98), though the difference was not statistically significant (p = 0.066). At one month, visual acuity remained poorer in the During-COVID-19 group (1.13 ± 0.84 vs 0.84 ± 0.76; p = 0.190). However, at three months, the During-COVID-19 group showed significantly worse visual outcomes (1.34 ± 0.97 vs 0.72 ± 0.68; p = 0.014).

Retinal nerve fiber layer (RNFL) thickness, measured by Heidelberg Spectralis optical coherence tomography (OCT) within two weeks of onset and again at a minimum of three months, showed no statistically significant differences between groups in either eye (Table 5). Similarly, visual field mean deviation (VF MD) values at both initial and follow-up assessments did not differ significantly (Table 5).

Despite a reduced number of clinic visits during the pandemic (511 vs 1,032 patients), the prevalence of new NAION cases was proportionally higher during COVID-19 (3.7%) compared to the pre-pandemic period (2.6%). This corresponds to a higher incidence of new NAION per clinic visit during the pandemic (19/511 vs 27/1,032) (Table 6).

Among patients in the During-COVID-19 group, 6 (31.6%) had a confirmed history of COVID-19 infection, diagnosed by antigen test (ATK). None required hospital admission. Notably, only one patient developed NAION following COVID-19 infection; the remaining patients were diagnosed with COVID-19 after their NAION diagnosis.

Table 6 Prevalence of of Non-Arteritis Ischemic Optic Neuropathy Patients Between Pre-COVID-19 and During COVID-19

Total cases visited Neuro-ophthalmology clinic	1543
Pre-COVID-19 [n(%)] During COVID-19 [n(%)]	1032(66.9%) 511(33.1%)
New NAION	
Pre COVID-19 [n(%)] During COVID-19 [n(%)]	27(58.7%) 19(41.3%)
Ratio of new cases NAION to all patient visited Neuro-ophthalmology clinic	
Pre-COVID-19 [n(%)] During COVID-19 [n(%)]	27:1032(2.6%) 19:511(3.7%)

Abbreviations: NAION, Non-arteritic anterior ischemic optic neuropathy; COVID-19, Coronavirus disease of 2019.

The key findings of the present study reveal a significantly higher prevalence of vascular risk factors, specifically hypertension, atherosclerotic cardiovascular disease, suspected sleep apnea, obesity, and smoking, among patients in During-COVID-19 group. This group also showed a greater proportion of subacute presentations, and significantly poorer visual acuity at 3 months compared with those in the pre–COVID-19 group.

Discussion

This study provides a comparative analysis of non-arteritic anterior ischemic optic neuropathy (NAION) cases diagnosed before and during the COVID-19 pandemic at a tertiary neuro-ophthalmology clinic. Consistent with the study objectives, our findings demonstrate differences between the pre–COVID-19 and during–COVID-19 periods in the proportional occurrence of NAION, associated vascular risk factors, patterns of clinical presentation, and visual outcomes.

Although the absolute number of new NAION cases was lower during the pandemic, the proportion of new NAION diagnoses relative to clinic visits was higher (3.7% vs 2.6%). This indicates a higher relative proportion of NAION cases during the pandemic period, consistent with concerns that COVID-19 may contribute to ischemic vascular events via systemic prothrombotic mechanisms.[3]

Several systemic vascular risk factors, including hypertension, atherosclerotic cardiovascular disease (ASCVD), obesity, suspected sleep apnea, and smoking history, were significantly more prevalent among NAION patients during the pandemic period. These findings align with emerging literature indicating that COVID-19 may exacerbate or unmask underlying vascular comorbidities through endothelial dysfunction, cytokine-driven inflammation, and hypercoagulability.[2,3] In particular, the marked increase in hypertension prevalence (84.2% vs 40.7%, $p = 0.003$) may reflect either a COVID-19–mediated vascular effect or delayed care in patients with poorly controlled chronic diseases.

Interestingly, although most patients in the During-COVID-19 group did not have a documented history of SARS-CoV-2 infection, the observed clustering of vascular risk factors suggests that indirect consequences of the pandemic, including increased sedentary behavior, psychosocial stress, delays in routine care, and reduced access to health services, may have contributed to greater vascular vulnerability.[15] Moreover, one-third of the patients had confirmed COVID-19 infection, though only one developed NAION following infection. This low rate of direct post-COVID NAION may reflect under-testing, retrospective data limitations.

From an ophthalmic standpoint, the During-COVID-19 group had a significantly higher proportion of subacute presentations and longer symptom-to-diagnosis intervals. Delayed presentations may be attributable to fear of viral exposure, lockdown restrictions, or overwhelmed health systems.

Visual outcomes were notably worse in the pandemic group, with significantly poorer visual acuity at three months (logMAR 1.34 vs 0.72; $p = 0.014$), despite comparable baseline structural and functional measurements (OCT-RNFL and

VFMD). These findings suggest that NAION during the COVID-19 period may have a more aggressive or less reversible course. The delay in presentation observed during the pandemic likely led to a poorer visual prognosis. This underscores the critical need for prompt evaluation and meticulous optimization of risk factors, even when healthcare systems face disruption. Other possible explanations include a direct neurovascular impact of COVID-19–associated inflammation and thrombosis.[2]

Despite no statistically significant differences in RNFL thinning or visual field loss progression, the trend toward poorer visual acuity outcomes in the pandemic group underscores the importance of early recognition and management, especially in high-risk patients.

Beyond infection, COVID 19 vaccination could also play a contributory role. During our study period, the majority of Thai adults received inactivated (Coronavac) and adenovirus vectored (AstraZeneca) vaccines.[16] There were several case reports described NAION following various COVID 19 vaccines, implicating transient inflammatory or hemodynamic shifts as hypothetical triggers in predisposed individuals.[17,18] Our retrospective design did not capture vaccination status, so we could not directly assess this factor; however, given the temporal overlap with mass immunization, it remains an important consideration for future prospective research.

Our findings align with previous isolated case reports suggesting an association between NAION and COVID-19 but provide a more systematic comparison of clinical patterns.The elevated proportion of NAION cases, given its restriction to a tertiary neuro-ophthalmology clinic, is not representative of the general population. This observation reflects referral patterns and healthcare-seeking behavior rather than the true population incidence. While the increased proportion may be descriptive of pandemic-related shifts in access to care and case mix within subspecialty clinics, it is insufficient to infer an overall increase in the incidence of NAION in the general population. Other limitations of this study include its retrospective design, small sample size, incomplete visual field data, lack of vaccination status, and possible referral bias due to reduced clinic attendance.

Nevertheless, these results highlight the need for heightened vigilance for NAION in patients with vascular comorbidities, particularly during periods of systemic stress or infection. Although causality cannot be inferred from this retrospective analysis, the temporal association and clustering of vascular risk factors observed during the pandemic support a potential contributory role of COVID-19 and related systemic stressors in NAION pathogenesis. However, the absence of post–COVID-19 data limits assessment of longer-term trends in NAION occurrence. Continued investigation, including larger studies incorporating post-pandemic periods, is warranted to clarify underlying mechanisms and to guide preventive strategies in high-risk populations.

Conclusion

The COVID-19 pandemic appears to be associated with a higher proportional incidence of NAION and a shift in its clinical profile toward subacute onset, greater systemic vascular burden, and poorer visual outcomes. Delayed presentation during the pandemic may have contributed to worse visual prognosis, highlighting the clinical importance of timely evaluation and risk factor optimization even during periods of healthcare disruption. While a direct causal link between COVID-19 and NAION remains to be firmly established, these findings underscore the need for heightened clinical vigilance, particularly among patients with predisposing systemic and anatomical risk factors. Potential mechanisms may include COVID-19–related endothelial dysfunction, inflammation, and hypercoagulability, as well as indirect effects of pandemic-related systemic stressors. Further prospective studies are warranted to clarify the underlying mechanisms and optimize diagnostic and therapeutic strategies for NAION in the context of systemic infections like COVID-19.

Disclosure

The authors report no conflicts of interest in this work.

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