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Original Research Paper

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RETINAL NERVE FIBER LAYER THICKNESS IN PATIENTS WITH MIGRAINE: A COMPARATIVE OCT STUDY

Dr. S. Naresh kumar	Assistant professor, Department of General medicine
Dr. Thummathati Sivapriya*	Senior resident, Department OF Ophthalmology*Corresponding Author
Dr. Gadumuru Hepsiba	Junior resident, Department OF Ophthalmology

ABSTRACT

Purpose To evaluate peripapillary retinal nerve fiber layer (RNFL) thickness in patients with migraine using spectral-domain optical coherence tomography (SD-OCT) and compare it with healthy controls. **Methods** This hospital-based cross-sectional comparative study included 120 participants comprising 60 patients diagnosed with migraine according to the International Classification of Headache Disorders-3 criteria and 60 age- and sex-matched healthy controls. All participants underwent comprehensive ophthalmic examination and SD-OCT imaging. Average RNFL thickness and quadrant-wise RNFL measurements (superior, inferior, nasal, temporal) were recorded. Statistical analysis was performed using independent t-test and Pearson correlation analysis.**Results**The mean age of migraine patients was 34.5 ±8.1 years and controls was 33.9 ±7.6 years (P=0.68). Mean average RNFL thickness was significantly lower in migraine patients compared to controls (96.2 ±8.4 μm vs 101.5 ±7.2 μm, P=0.001). Superior, inferior, and nasal quadrant RNFL thicknesses were significantly reduced in migraine patients. Patients with migraine with aura demonstrated greater RNFL thinning than those without aura (92.4 ± 7.2 μm vs 98.5 ± 8.0 μm, P=0.003). Significant negative correlations were observed between migraine duration and average RNFL thickness (r=-0.41, P=0.002).**Conclusion** Migraine patients exhibit significant thinning of the RNFL, suggesting chronic neurovascular and neurodegenerative changes. OCT may serve as a valuable non-invasive biomarker for assessing retinal involvement in migraine.

KEYWORDS : Migraine, Optical Coherence Tomography, Retinal Nerve Fiber Layer, Neurodegeneration, Retina

INTRODUCTION

Migraine is a common neurological disorder characterized by recurrent episodes of headache associated with various sensory and autonomic symptoms. It affects approximately 15% of the global population and is more prevalent among females during the productive years of life.

The exact pathophysiology of migraine remains incompletely understood. Current evidence suggests a complex interaction between vascular dysfunction, cortical spreading depression, trigemino vascular activation, and neuroinflammatory mechanisms. Recurrent cerebral hypoperfusion and vasospastic episodes have been implicated in neuronal injury and neurodegeneration.

The retina and optic nerve are considered extensions of the central nervous system. Advances in optical coherence tomography (OCT) have enabled non-invasive quantification of retinal nerve fiber layer (RNFL) thickness, allowing assessment of neuronal integrity. Increasing evidence indicates that migraine may be associated with retinal structural alterations, particularly thinning of the RNFL.

Identification of retinal biomarkers in migraine could provide valuable insights into disease pathogenesis and facilitate monitoring of neurodegenerative changes. Therefore, this study aimed to evaluate RNFL thickness in migraine patients and compare it with healthy controls using SD-OCT.

Materials and Methods

Study Design

Hospital-based cross-sectional comparative study.

Study Duration

January 2025 to December 2025.

Study Population

Patients attending general medicine and Ophthalmology outpatient departments of a tertiary care center.

Sample Size

120 participants.

- Migraine group: 60
- Control group: 60

Inclusion Criteria

Cases

- Age 18 – 50 years
- Diagnosed migraine according to ICHD-3 criteria
- Best corrected visual acuity ⩾6/9

Controls

- Healthy age- and sex-matched volunteers
- No history of migraine

Exclusion Criteria

- Diabetes mellitus
- Hypertension
- Glaucoma
- Optic neuropathy
- Retinal pathology
- Previous ocular surgery
- High myopia (>6D)
- Neurological disorders other than migraine

Ophthalmic Examination

All participants underwent:

- Visual acuity assessment
- Refraction
- Slit-lamp examination
- Intraocular pressure measurement
- Dilated fundus examination

OCT Imaging

Spectral-domain OCT was performed.

Measured parameters:

- Average RNFL thickness
- Superior RNFL

- Inferior RNFL
- Nasal RNFL
- Temporal RNFL

Statistical Analysis

Statistical analysis was performed using SPSS version 26.

- Independent t-test
- Chi-square test
- Pearson correlation

P value <0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

Variable	Migraine (n=60)	Controls (n=60)	P value
Age (years)	34.5 ± 8.1	33.9 ± 7.6	0.68
Male	18 (30%)	17 (28.3%)	0.84
Female	42 (70%)	43 (71.7%)	0.84

RNFL Thickness Comparison

Parameter	Migraine	Controls	P value
Average RNFL	96.2 ± 8.4	101.5 ± 7.2	0.001
Superior RNFL	118.3 ± 14.5	124.7 ± 13.8	0.01
Inferior RNFL	121.6 ± 16.1	127.9 ± 14.2	0.02
Nasal RNFL	71.4 ± 9.8	77.3 ± 8.6	0.001
Temporal RNFL	65.9 ± 7.1	68.5 ± 6.8	0.07

Migraine Subgroup Analysis

Parameter	Aura	No Aura	P value
Average RNFL	92.4 ± 7.2	98.5 ± 8.0	0.003

Correlation Analysis

Variable	Correlation Coefficient (r)	P value
Migraine duration vs RNFL	-0.41	0.002
Attack frequency vs RNFL	-0.37	0.005

DISCUSSION

The present study demonstrated significant thinning of the average retinal nerve fiber layer (RNFL) thickness in migraine patients compared with healthy controls. Significant reductions were observed in the superior, inferior, and nasal quadrants, whereas temporal RNFL thickness did not differ significantly between the two groups. These findings are in agreement with previous OCT studies that have consistently demonstrated RNFL thinning among individuals with migraine, suggesting the presence of chronic retinal neuronal damage.[1–3]

The retina is embryologically derived from the neural tube and shares anatomical and physiological characteristics with the central nervous system. Consequently, retinal imaging has emerged as a valuable non-invasive method for evaluating neurodegenerative changes occurring within the brain.[4]

Several mechanisms have been proposed to explain retinal neuronal loss in migraine. One of the most widely accepted hypotheses is recurrent vasospasm affecting retinal and optic nerve circulation. Migraine attacks are associated with transient cerebral and ocular hypoperfusion, and repeated ischemic episodes may produce cumulative axonal injury, ultimately resulting in RNFL thinning.[5]

Another important mechanism is cortical spreading depression, the electrophysiological phenomenon believed to underlie migraine aura. Cortical spreading depression causes transient neuronal depolarization followed by suppression of neuronal activity and alterations in cerebral blood flow. Repeated episodes may contribute to progressive neurodegeneration involving retinal ganglion cells and their axons.[6]

In the present study, patients with migraine accompanied by aura demonstrated significantly greater RNFL thinning than those without aura. This finding supports the hypothesis that aura-related vascular and neuronal disturbances produce greater retinal neuronal injury. Similar observations have been reported by Demircan et al., who demonstrated significant reductions in both RNFL and ganglion cell layer thickness among migraine patients with aura.[7]

The superior and inferior quadrants exhibited the greatest reduction in RNFL thickness. These regions contain the highest density of retinal nerve fibers and may therefore be particularly susceptible to ischemic injury. Similar patterns of preferential superior and inferior RNFL thinning have been reported by Ascaso et al., Gipponi et al., and Martinez et al.[8–10]

A significant negative correlation was observed between migraine duration and RNFL thickness, indicating that longer disease duration is associated with greater retinal neuronal loss. Likewise, increased attack frequency was associated with thinner RNFL measurements, suggesting a cumulative effect of repeated migraine episodes on retinal neuronal integrity. Similar associations have been described by Reggio et al. and Kara et al.[11,12]

Our findings are further supported by the meta-analysis conducted by Feng et al., which included multiple case-control studies and demonstrated a significant reduction in average RNFL thickness among migraine patients compared with healthy controls. The authors concluded that migraine is associated with chronic neurodegenerative retinal changes that can be detected using optical coherence tomography.[13]

Recent neuroimaging studies have also demonstrated structural brain abnormalities in patients with chronic migraine, including reductions in cortical thickness and white matter integrity. These central nervous system alterations may parallel the retinal changes observed in the present study, reinforcing the concept that the retina serves as a readily accessible biomarker of cerebral neurodegeneration.[14]

From a clinical standpoint, optical coherence tomography offers a rapid, reproducible, and non-invasive method for detecting subclinical neuronal injury in migraine patients. Routine OCT assessment may facilitate early identification of retinal neurodegeneration, enable longitudinal monitoring of disease progression, and potentially evaluate treatment response in patients with chronic migraine.[15]

The strengths of the present study include the use of age- and sex-matched healthy controls, standardized spectral-domain OCT imaging protocols, and assessment of clinically relevant disease characteristics including aura status, migraine duration, and attack frequency.

Nevertheless, several limitations should be acknowledged. The cross-sectional design precludes establishment of a causal relationship between migraine and RNFL thinning.

OCT angiography was not performed, preventing assessment of retinal microvascular alterations, and ganglion cell complex analysis was unavailable. Furthermore, the relatively modest sample size and single-center study design may limit the generalizability of the findings.

Future prospective longitudinal studies incorporating OCT angiography, ganglion cell complex analysis, and larger multicenter cohorts are warranted to further elucidate the relationship between migraine, retinal neurodegeneration, and disease progression.

CONCLUSION

Migraine patients exhibit significant thinning of the retinal nerve fiber layer compared with healthy individuals. RNFL reduction is more pronounced among patients with aura and those with longer disease duration. These findings support the concept of migraine as a neurovascular disorder associated with chronic retinal neuronal injury. Optical coherence tomography may serve as a valuable non-invasive tool for detecting and monitoring neurodegenerative changes in migraine.

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