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Association of migraine with peripapillary retinal nerve fiber layer and macular ganglion cell complex thickness: A cross-sectional study

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ABSTRACT

Background: Migraine is one of the most common neurological disorders worldwide, affecting more than one billion individuals and representing a major cause of disability, particularly among young adults. The thinning of the peripapillary retinal nerve fiber layer and ganglion cell layers in migraine patients, suggesting chronic neuronal injury secondary to repeated ischemic and vasospastic episodes.

Aims & Objectives: To assess the association between migraine and changes in peripapillary retinal nerve fiber layer (pRNFL) thickness and macular ganglion cell complex (GCC) thickness using Optical Coherence Tomography.

Methodology: A cross sectional study was conducted among 56 Patients with Migraine attending out-patient department of Ophthalmology, at R. L. JALAPPA HOSPITAL, Kolar from July 2026 to June 2027.

Results: The mean average pRNFL thickness was lower in migraine patients (98.9 ± 7.9 µm) compared with non-migraine participants (104.7 ± 6.6 µm), and the difference was statistically significant (p=0.004). Migraine patients had significantly reduced pRNFL, GCC and GCC++ thickness in comparison with non-migraine individuals, suggesting measurable retinal structural differences associated with migraine.

Conclusion: The repeated neurovascular alterations, vasospasm, and chronic ischemic episodes associated with migraine may contribute to subclinical retinal neuronal injury and neurodegeneration. Consequently, spectral-domain OCT measurements of pRNFL and GCC thickness hold potential utility as objective structural biomarkers for monitoring ocular involvement and neurodegenerative changes in migraine patients.

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KEYWORDS
Migraine, Retinal Nerve, Macular Ganglion cell complex, Retina, Optical coherence tomography.

1. Introduction

Migraine is one of the most common neurological disorders worldwide, affecting more than one billion individuals and representing a major cause of disability, particularly among young adults. [1,2,3] The disorder is characterized by recurrent headache episodes associated with complex neurovascular mechanisms involving cortical spreading depression, trigeminovascular activation, neurogenic inflammation, and vascular dysregulation.[4]

Recent evidence suggests that migraine-related vascular and inflammatory changes may extend beyond the central nervous system and affect ocular structures, particularly the retina and optic nerve.[5,6] The retina, embryologically derived from the central nervous system, provides a unique opportunity to study neurodegenerative changes occurring in neurological diseases.[7]

Optical coherence tomography (OCT) is a rapid, non-invasive imaging modality capable of providing high-resolution quantitative assessment of the retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC). Several studies have reported thinning of the peripapillary retinal nerve fiber layer and ganglion cell layers in migraine patients, suggesting chronic neuronal injury secondary to repeated ischemic and vasospastic episodes.[8,9]

Evaluation of these retinal structural changes may improve our understanding of migraine pathophysiology and may serve as a potential biomarker for neurodegeneration. Therefore, the present study was undertaken to assess peripapillary retinal nerve fiber layer and macular ganglion cell complex thickness in migraine patients using spectral-domain OCT and compare them with healthy controls. Although previous studies have reported retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) thinning in migraine patients, the findings have been inconsistent due to small sample sizes, heterogeneous study populations, lack of age- and sex-matched controls, and limited evaluation of both peripapillary RNFL and macular GCC together. Furthermore, very few studies have assessed these retinal

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structural changes after correcting for axial length, which can significantly influence OCT measurements. There is also limited evidence from the Indian population regarding OCT-based retinal neurodegenerative changes in migraine patients. Therefore, the present study was undertaken to comprehensively evaluate peripapillary RNFL and macular GCC thickness in migraine patients using spectral-domain OCT and compare them with healthy controls.

Aims & Objectives: To assess the association between migraine and changes in peripapillary retinal nerve fiber layer (pRNFL) thickness and macular ganglion cell complex (GCC) thickness using Optical Coherence Tomography.

Methodology: A cross sectional study was conducted among 56 Patients with Migraine attending out-patient department of Ophthalmology, at R. L. JALAPPA HOSPITAL, Kolar from July 2026 to June 2027. Sample size was estimated using comparison of two independent means. Based on mean pRNFL thickness values of 91.62 ± 15.70 µm in migraine patients and 106.19 ± 10.46 µm in controls, with a two-sided alpha error of 1% and power of 90%, the minimum required sample size was 25 participants per group. After allowing for a 10% non-response rate, the final sample size was 56 participants. The Institutional ethical Committee permission was taken prior to the study. Written Informed consent was taken from all study participants.

Data entry & analysis: Data were entered into Microsoft excel data sheet and analyzed by using SPSS 22 version software. Categorical data were represented in the form of Frequencies and proportions. Continuous data were represented as mean and standard deviation. Bar diagrams was used to represent data graphically. Independent t test to compare mean between two groups p value

<0.05 was considered as statistically significant.

2. Results

Table 1: The thickness of the peripapillary RNFL (µm) in migraine and Non migraine groups

pRNFL thickness (µ)	Migraine (N= 28)			Non-migraine (N=28)			p value
	Mean	Max	Min	Mean	Max	Min	
Average	98.9(7.9)	125	82	104.7(6.6)	122.56	81.01	0.004
Superior	115.5(11.9)	154.6	71.2	121.8(9.4)	153.08	101.32	0.003
Inferior	118.8(11.2)	145.7	83.2	126.8(8.7)	148.8	101.83	0.011
Nasal	80.1(9)	100.4	52.4	84.1(9.2)	104.3	62.83	0.0021
Temporal	73.3(11.1)	96.3	44.1	81.1(8.6)	102.36	58.1	0.0034

Table 2: Ganglion cell layer thickness (µm) in migraine and Non migraine groups

GCC+ (µ)	Migraine patients (N=28)			Non-migra ine (N=28)			p val ue
	Mean	Max	Min	Mean	Max	Min	
Average	75.6(6.6)	91.8	58.3	78.6(4.2)	89.1	65.9	**0.001**
Superior	76.9(7.9)	98.9	59.4	79.6(5.2)	98.4	71.5	**0.001**
Supero- nasal	75.0(6.3)	95.4	60.3	81.7(3.5)	89.5	70.5	**0.004**
Supero- temporal	74.9(8.1)	92.3	58.3	81.3(3.4)	89.6	69.1	**0.002**
Inferior	72.3(7.1)	98.5	57.1	76.6(6.7)	91.3	62.2	**0.001**
Infero-nasal	74.3(7.5)	95.4	59.1	78.6(3.4)	89.4	67.8	**0.003**
Infero -temporal	72.9(7.6)	96.4	60.2	76.9(5.2)	87.6	65.6	0.024

Table 3: GCL++ thickness (µm) in migraine and Non migraine groups

GCC++ (µ)	Migraine patients (N=28)			Non-migraine (N=28)			p value
	Mean	Max	Min	Mean	Max	Min	
Average	102(6.3)	116.6	82.1	108(9)	142.4	86.5	<0.001
Superior	104.6(6.5)	118.5	75.6	111.8(10.6)	168.7	88.7	<0.001
Inferior	102.9(6.6)	118.6	73.7	112.6(12.7)	178.2	88.7	<0.001
Inferio- temporal	98.1(7.1)	119.3	82.1	104.3(8.8)	121.6	85.2	<0.001
Supero- temporal	99.5(7.7)	119.6	80.7	102.9(7.9)	122.6	85.8	<0.001
Infero-nasal	101.8(6.5)	120.7	81.6	107.7(8.1)	124.6	86.9	0.072
Supero-nasal	104.2(6.6)	119.2	84.2	106.5(7.8)	123.6	85.3	0.031

Table 1 compares the peripapillary retinal nerve fibre layer (pRNFL) thickness between migraine and non-migraine groups, with 28 participants in each group. The mean average pRNFL thickness was lower in migraine patients (98.9 ± 7.9 µm) compared with non-migraine participants (104.7 ± 6.6 µm), and the difference was statistically significant (p=0.004). Similarly, the mean superior, inferior, nasal and temporal pRNFL thicknesses were lower in the migraine group than in the non-migraine group, with statistically significant differences for all quadrants (p=0.003, 0.011, 0.0021 and 0.0034, respectively). The greatest reduction in migraine patients was observed in the superior and inferior quadrants, while the temporal quadrant showed the lowest mean thickness in both groups.

Table 2 shows the comparison of ganglion cell complex (GCC) thickness between migraine and non-migraine groups. The mean average GCC thickness was significantly lower among migraine patients (75.6 ± 6.6 µm) compared with non-migraine participants (78.6 ± 4.2 µm, p=0.001). A similar pattern was observed in all individual sectors, including superior, superonasal, superotemporal, inferior, inferonasal and inferotemporal regions. The differences between the two groups were statistically significant in each sector, with p-values ranging from 0.001 to 0.024. Thus, migraine patients demonstrated consistently reduced GCC thickness compared with non-migraine participants.

Table 3 compares GCC++ thickness between the two groups. The mean average GCC++ thickness was lower in migraine patients (102.0 ± 6.3 µm) than in non-migraine participants (108.0 ± 9.0 µm), with a statistically significant difference (p<0.001). Similarly, the superior, inferior, inferotemporal and superotemporal sectors showed significantly lower GCC++ thickness in migraine patients, with p<0.001 for each comparison. The inferonasal and superonasal sectors also showed lower mean thickness in the migraine group; however, the difference was not statistically significant for the inferonasal sector (p=0.072) and was statistically significant for the superonasal sector (p=0.031). Overall, the findings indicate that migraine patients had significantly reduced pRNFL, GCC and GCC++ thickness in comparison with non-migraine individuals, suggesting measurable retinal structural differences associated with migraine.

Figure 1. The thickness of the peripapillary RNFL (µm) in migraine and Non migraine groups

Figure 2: Ganglion cell layer thickness (µm) in migraine and Non migraine groups

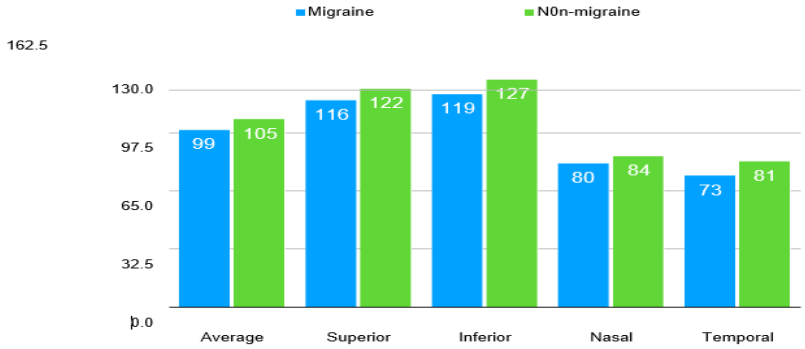
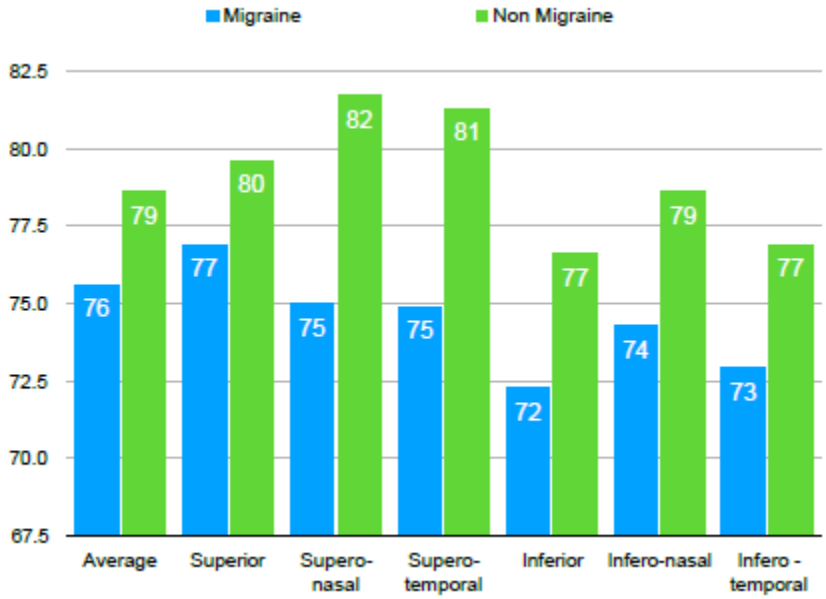
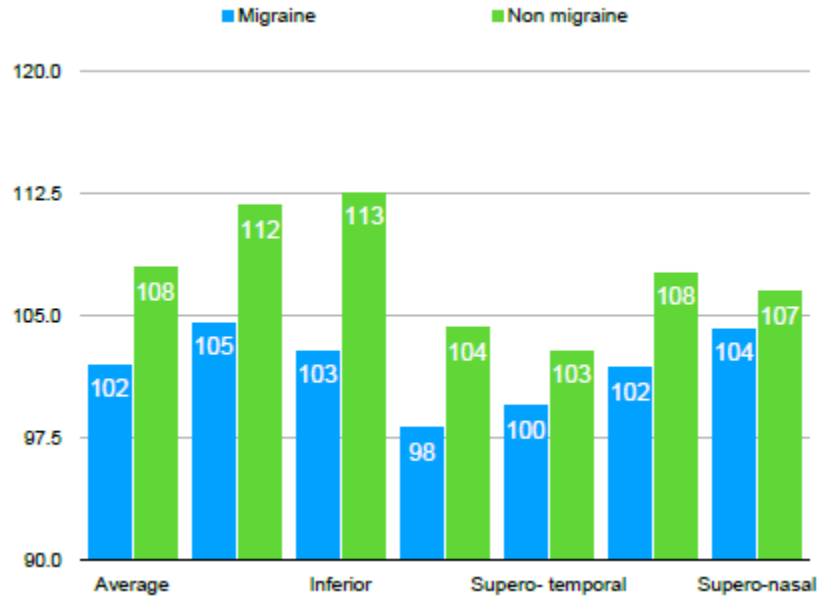


Figure 3: GCL++ thickness (µm) in migraine and Non migraine groups



Discussion: The findings of this cross-sectional study demonstrate a statistically significant



reduction in both peripapillary retinal nerve fiber layer (pRNFL) and macular ganglion cell complex (GCC and GCC++) thicknesses among migraine patients compared to healthy non-migraine controls. Specifically, the mean average pRNFL thickness was significantly lower in the migraine group (98.9 ±7.9 µm vs. 104.7±6.6 µm, p=0.004), with consistent sectoral thinning observed across all quadrants, particularly the superior and inferior regions. Similarly, evaluations of the macular ganglion cell complex demonstrated widespread and significant thinning across nearly all sectors. These objective measurements support the concept that migraine is not merely a transient episodic functional headache disorder, but one associated with measurable, subclinical structural changes in retinal micro-architecture.

These observations align closely with recent optical coherence tomography (OCT) investigations establishing a link between migraine pathophysiology and retinal neurodegeneration. For instance, a multi-center analysis by Patil et al. [10] also documented significantly reduced mean pRNFL and GCC thickness values in migraine cohorts compared to controls,highlighting robust regional vulnerability in superior and inferior sectors. Furthermore, studies by Kirbas et al. [11] and Gipponi et al. [12] corroborated that recurrent neurovascular dysregulation targets both peripapillary and macular layers. The structural concordance across these independent cohorts

reinforces the validity of utilizing high-resolution spectral-domain OCT to detect early ocular structural involvement.

The underlying mechanisms connecting migraine pathology to retinal thinning involve complex neurovascular alterations.Because the retina is embryologically and anatomically an extension of the central nervous system, it shares susceptibility to the ischemic and vasospastic events characteristic of migraine attacks. Recurrent cycles of cortical spreading depression, trigeminovascular system activation, and local neurogenic inflammation release vasoactive substances and metabolites that induce sustained regional vasoconstriction and retrobulbar hypoperfusion. [13,14] Over time, chronic subclinical ischemia and oxidative stress compromise axonal transport and metabolic stability, ultimately driving the gradual apoptosis of retinal ganglion cells and thinning of the nerve fiber layer. Consequently, quantitative assessment of pRNFL and GCC thickness via OCT holds substantial promise as a non-invasive, objective structural biomarker for tracking neurodegenerative changes and microvascular burden in migraine patients.

3. Conclusion

Specifically, optical coherence tomography (OCT) evaluation revealed that patients with migraine exhibit a statistically significant reduction in peripapillary retinal nerve fiber layer (pRNFL) thickness compared to non-migraine participants (mean average of 98.9 ±7.9 µm vs.

104.7 ±6.6 µm,p=0.004), alongside consistent and significant thinning across nearly all analyzed sectors of the macular ganglion cell complex (GCC and GCC++). These structural differences support the hypothesis that repeated neurovascular alterations, vasospasm, and chronic ischemic episodes associated with migraine may contribute to subclinical retinal neuronal injury and neurodegeneration. Consequently, spectral-domain OCT measurements of pRNFL and GCC thickness hold potential utility as objective structural biomarkers for monitoring ocular involvement and neurodegenerative changes in migraine patients.

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