ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 15, Issue 10, 2022

Online - 2455-3891
Print - 0974-2441

Research Article

A CLINICAL STUDY OF RETINAL GANGLION CELL LAYER AND RETINAL NERVE FIBER LAYER CHANGES IN COGNITIVE DYSFUNCTION IN ELDERLY PATIENTS ATTENDING PSYCHIATRY OPD IN A TERTIARY HOSPITAL IN NORTHEAST BIHAR

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Received: 25 May 2022, Revised and Accepted: 14 July 2022

ABSTRACT

Objective: The objective of this study was to study and compare retinal nerve fiber layer (RNFL) changes and retinal ganglion cell layer (GCL) changes in different quadrants of the eye in elderly patients (60 years or more) with cognitive impairment.

Methods: Study conducted in the Department of Ophthalmology and Psychiatry in M.G.M. Medical College and L.S.K. Hospital Kishanganj, Bihar. It was a cross-sectional study. Random sampling among elderly patients with cognitive impairment attending Psychiatry OPD. A total 50 patients (32 cases+18 control). Thirty-two cases with mild cognitive impairment (MCI) having mini-mental state examination (MMSE) score <24 and 12 controls with normal cognition (NC) having MMSE score >30 were enrolled in this study. Mini-mental status examination and montreal cognitive assessment-for selection of cognitive impairment patients. Optical coherence tomography (OCT) to compare changes in the retinal GCL and RNFL in different eye quadrants.

Results: The observation of the present study reveals mean thickness of the GCL and the inner plexiform layer (IPL) was significantly higher among healthy controls in both right and left eyes compared to the case group (p=0.05 and 0.008, respectively). The comparison of GCL and IPL thickness in the inferior temporal quadrant between case and control group. The observation of the present study reveals that the mean thickness of the GCL and IPL in the inferior temporal quadrant was comparable between healthy controls and the case group in the right eyes (p=0.606), and it was significantly higher among healthy controls compared to case group in the left eyes (p=0.05).

Conclusion: As a result, it is recommended that all patients over the age of 60 have a routine retinal evaluation with OCT to detect early neurodegenerative alterations for the early diagnosis and management. According to our study, the sensitivity of GCL+IPL to distinguish MCI from controls was often higher than that of RNFL.

Keywords: Retinal nerve fiber layer, Ganglion cell layer, Inner plexiform layer, Mild cognitive impairment, Optical coherence tomography.

 DOI: http://dx.doi.org/10.22159/ajpcr.2022v15i10.45342. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Cognitive disorders (CDs) are a subset of mental illnesses. Its capability refers to an individual's ability to do higher mental functions including reasoning, remembering, understanding, fast-thinking, and problem-solving [1]. Complex cognitive tasks require unbroken connections between distant brain regions, which constitute neural networks, to function efficiently [2]. One of the most feared elements of aging is cognitive decline in the senior population, which can have a considerable influence on an individual's quality of life as well as society's ability to care for those affected.

Mild cognitive impairment (MCI) is a prodromal stage of Alzheimer's disease (AD) that occurs in the period between expected aging-related cognitive decline and the more serious decline of dementia [3].

Hinton *et al.* [4] have the first to demonstrate retinal ganglion cell (RGC) loss and optic nerve degeneration in patients with AD, implying a clear link between retinal degeneration and AD pathogenesis [5].

As people get older, they experience cognitive loss in several cognitive domains on average, but the rate of decline differs between individuals [6].

The eye and brain areas involved in cognitive function have similar embryonic origins, and it's possible that they share age-related characteristics. Studies revealing amyloid-beta accumulation in retinal drusen in eyes with age-related macular degeneration and senile plaques in the brains of the elderly or people with AD have indicated common pathogenic pathways such as inflammation and complement activation (AD) [7]. While AD is at the extreme end of the cognitive loss range, senile plaques are common in older persons who do not have dementia.

Optical coherence tomography (OCT) is a non-invasive imaging equipment used to assess a number of ophthalmic disorders, such as glaucoma and retinal degeneration. With high-resolution pictures, it may also assess the normality of macular architecture by measuring cross-sectional retinal nerve fiber layer (RNFL) thickness and the volume and thickness of the macula [8]. Multiple neurodegenerative disorders, such as multiple sclerosis, Parkinson's disease, and schizophrenia, can now be detected using OCT measurements of the retina, which can now provide new biomarkers [9].

The RNFL consists primarily of RGC axons, which progressively degenerate in glaucoma, resulting in thinning and disappearance of axon bundles from the RNFL. RNFL defects may represent one of the earliest glaucomatous structural abnormalities that manifest in clinical examination of the ocular fundus [10], yet such defects can elude detection and are difficult to quantify by clinical examination or flash photography [11].

As age advances, mainly in elderly patients (60 years or more), it is suggested [12] to make a routine evaluation of the thickness of the RNFL and thickness of the retinal ganglion cell layer (GCL) with the help of OCT to detect early neurodegenerative changes. This helps in the early diagnosis of cognitive dysfunction and management of the disease [13].

METHODS

The study was conducted in the Department of Ophthalmology and Psychiatry in M.G.M. Medical College and L.S.K. Hospital Kishanganj, Bihar. It was a cross-sectional study. Random sampling among elderly patients with cognitive impairment attending Psychiatry OPD. A total 50 patients (32 cases+18 control). 32 Cases with MCI having mini- mental state examination (MMSE) score <24

Exclusion criteria

The following criteria were excluded from the study:

1. Elderly patient where OCT cannot be done.
2. Neuropathies:
   - Optic neuritis.
   - Glaucoma.
   - Congenital anomalies of the optic disc.
   - Severe proven AD.
   - Uncooperative/bed-ridden patients.
   - Opacified eye media.

Statistical analysis – statistical tests used for the study are

- Independent two-sample t-test – for a parametric variable.
- Chi-square test – for the association of study variables with a group.

RESULTS

Age distribution among case and control group

Age in year	Case (n=32)		Control (n=18)	
	Number of cases	Percentage	Number of cases	Percentage
60–70	23	71.9	16	88.8
71–80	04	12.5	01	5.6
>80	05	15.6	01	5.6
Total	32	100.0	18	100.0
Mean and SD	68.43±9.56		64.16±5.18	
p-Value	0.012			

The age distribution of the study subjects. The present study's most common age group was 60–70 years in both cases (71.9%) and the control group (88.8%). The mean age was 68.43±9.56 years and 64.16±5.18 years, respectively, in the case and control groups. Mean age was significantly high among cases compared to the control group (p=0.012).

Sex distribution among case and control group

Sex	Case (n=32)		Control (n=18)	
	Number of cases	Percentage	Number of cases	Percentage
Male	09	28.1	08	44.5
Female	23	71.9	10	55.6
Total	32	100.0	18	100.0
Statistical Interferences	Chi-square=1.36722 p-value=0.242			

The distribution of both case and control groups according to sex. There was a female preponderance observed in both cases (71.9%) and the control group (55.6%) with no significant difference between groups (p = 0.242).

MMSE

	Case (n=32)	
	Mean	SD
Mini-mental state examination	18.87	±2.07

The mean level of mini-mental state examination score among study subjects. The mean level of the MMSE score was 18.87±2.07, which was lower than the normal level indicating cognitive impairment.

RNFL (comparison between case and control group)

The RNFL	Case (n=32)		Control (n=18)	
	Mean	SD	Mean	SD
U	74.65 t-test p=0.001**	±21.34	104.27	±7.09

The thickness of the RNFL was evaluated between the case and control groups. In the case group, the mean RNFL thickness was 74.65 21.34 microns, while in the control group, it was 104.27±7.09 microns. The case group's RNFL thickness was significantly lower than the control group's (p=0.0001).

Comparison of the RNFL in patients and controls (group with MCI); (superior quadrant)

Quadrant superior	Case (n=32)		Control (n=18)	
	Mean	SD	Mean	SD
U	95.03 t-test p=0.008*	±33.67	132.27	±12.00

Between the case and control groups, the thickness of the RNFL in the superior quadrant was compared. In the case group, the mean RNFL thickness in a superior quadrant was 95.03±33.67 microns, while in the control group, it was 132.27±12.00 microns. In the superior quadrant, the thickness of the RNFL was significantly lower in the case group than in the control group (p=0.008).

Comparison of RNFL among control and cases (MCI); (inferior quadrant)

Inferior quadrant	Case (n = 32)		Control (n = 18)	
	Mean	SD	Mean	SD
U	88.78 t-test p=0.006*	±31.41	133.94	±12.34

The thickness of the RNFL in the inferior quadrant was compared between the case and control groups. The mean RNFL thickness in a superior quadrant in the case group was 88.78±31.41 microns, while it was 133.94±12.34 microns in the control group. Patients in the case group had a substantially lower mean RNFL thickness in the inferior quadrant than normal controls (p=0.006).

Comparison of RNFL among control and cases (MCI); (nasal quadrant)

Nasal quadrant	Case (n=32)		Control (n=18)	
	Mean	SD	Mean	SD
U	66.06 t-test p=0.004*	±24.75	81.27	±11.75

Between the case and control groups, the thickness of the RNFL in the nasal area was compared. In the case group, the mean RNFL thickness in

Control and patients (MCI) RNFL comparison (temporal quadrant)

Quadrant of time	Case (n=32)		Control (n=18)	
	Mean	SD	Mean	SD
U	51.28 t-test p-value- 0.072	±15.17	72.00	±10.36

a nasal quadrant was 66.06 24.75 microns, while in the control group, it was 81.27±11.75 microns. The case group's mean RNFL thickness in the nasal region was substantially lower than normal controls (p=0.004).

The temporal quadrant was used to compare the thickness of the RNFL between the case and control groups. The mean RNFL thickness in a nasal quadrant in the case group was 51.17±15.17 microns, while it was 72.00±10.36 microns in the control group. Between the case and the healthy control, there was no significant difference in mean RNFL thickness in the temporal quadrant (p=0.072).

Comparison of GCL and inner plexiform layer thickness in both groups (mean thickness)

GCL+IPL thickness	Mean thickness			
	Right eye		Left eye	
	Mean	SD	Mean	SD
Case	22.15	±1.39	22.68	±1.61
Control	80.88	±2.51	78.55	±3.63
p-value	0.05		0.008	

The comparison of GCL and inner plexiform layer thickness between case and control group. The observation of the present study reveals the mean thickness of the GCL and the inner plexiform layer was significantly higher among healthy controls in both right and left eyes compared to the case group (p=0.05 and 0.008, respectively).

DISCUSSION

The goal of our study was to use spectral-domain OCT to assess the thickness of the RNFL and GCL in patients with MCI. We also looked at the relationship between RNFL and MMSE scores and observed that in MCI patients, RNFL was much thinner than in age-matched controls. The superior and inferior quadrants of the RNFL showed substantial thinning on OCT. The GCL+inner plexiform layer (IPL) layer thinning was most noticeable in the superotemporal and inferonasal quadrants.

Researchers from all over the world have conducted extensive research to better understand the relationship between the retina and the brain. London *et al.* explained the biological link between retinal and brain illnesses in their study. Both the retina and the optic nerve are extensions of the CNS's diencephalon during embryonic development [10].

As a result, the microvasculature system has similar physiology, and the blood-ocular barrier has a structure and features that are similar to the blood-brain barrier [5]. As a result, anatomical similarities exist between RGC and CNS neurons, as well as between the optic nerve fiber tract and other CNS fiber tracts.

The same neurodegenerative mechanisms that afflict directly wounded neurons affect RGCs, resulting in axon degeneration, glial scar development, and myelin loss [5,10].

According to Lee *et al.*, the frequency of dementia in adults over 60 is pretty consistent over the world, ranging between 5% and 7%.

Case (MCI) had a mean age of 68.43±9.56 years, while the control had a mean age of 64.16±5.18 years. The relationship between retinal structural degeneration (OCT parameters) and CI (MMSE scores) in MCI was investigated, and our findings revealed that MMSE scores and various OCT parameters have a significant relationship.

Cunha *et al.* investigations on the quantification of neuronal loss with CI support this conclusion [14].

In AD and MCI patients, Iseri *et al.* discovered a strong association between total macular volume and MMSE score [15].

In comparison to earlier investigations, the thickness of the RNFL was measured. In comparison to MCI, Liu *et al.* discovered a substantial decrease in RNFL thickness in the superior and inferior quadrants of AD [16].

The superior quadrant also showed significant thinning (p=0.05). When comparing patients with AD and MCI to controls, Kesler *et al.* and Shen *et al.* discovered a significant reduction in RNFL in the inferior quadrants [17]. Furthermore, researchers discovered that RNFL thickness in the inferior quadrant was inversely related to higher cognitive function [18]. The inferior quadrant of our investigation also showed significant thinning.

A total of 32 cases and 18 controls were included in the study, and MOCA was used to examine them. GCL thickness is linked positively with cognitive performance and adversely with age [19]. MOCA was also used in our study to assess the CI and investigate RNFL thinning.

In their investigation, Cheung *et al.* found that the sensitivity of GC-IPL was higher than that of RNFL in distinguishing AD and MCI from controls [20].

In a similar study, Shao *et al.* discovered that in both AD and MCI groups, the thickness differences were negative (thinning), primarily in the RNFL, macular ganglion cell, and inner plexiform layer, as compared to controls [21].

Our findings were comparable to those of the previous research, with considerable thinning in all quadrants and statistically significant thinning (p<0.05) in the superonasal and superotemporal areas.

In their study, Lad *et al.* and Choi *et al.* hypothesized that macular GCL+IPL thickness might be used as a non-invasive biomarker to diagnose and track the progression of MCI to AD. He also speculated that NFL and GCIPL might be changed dynamically as AD progresses [22].

CONCLUSION

- In MCI patients, the mean RNFL and mean GCL+IPL layer exhibited thinning.
- The superior and inferior quadrants of the RNFL-OCT showed significant thinning.
- In the superior and inferior quadrants, the GCL+IPL layer showed substantial thinning. There was a significant link between age and retinal thinning.
- It can be concluded that MCI patients develop retinal neurodegeneration despite the absence of microvascular alterations.
- As a result, it is recommended that all patients over the age of 60 have a routine retinal evaluation with OCT to detect early neurodegenerative alterations for the early diagnosis and management.
- According to our study, the sensitivity of GCL+IPL to distinguish MCI from controls was often higher than that of RNFL.

ACKNOWLEDGMENT

AUTHORS CONTRIBUTIONS

Equal contribution.

CONFLICTS OF INTEREST

Nil.

AUTHORS FUNDING

Nil.

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