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Retinal Findings in Alzheimer's Patients- Case Study

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Introduction: Alzheimer's disease is a neurodegenerative disorder that can cause degeneration of the retina and optic nerve and result in amyloid beta depositions. Tracking down ophthalmic changes in the retina can hence be used to assess the neurodegenerative changes that occur in AD.
Aim: To demonstrate early changes in the retina in patients with Alzheimer's disease.
Methodology: 50 patients with Alzheimer's disease were included in this study. All the patients underwent Fundus auto fluorescence (FAF) and optical scanning tomography (OCT). Drusen-like deposits of various sizes were seen in the retina.
Results: On analysing the macular layers with the help of OCT, it showed that there was a significant thinning of the retinal nerve fibre layer, ganglion cell layer and outer plexiform layer in patients with Alzheimer's disease. Significant superonasal and inferotemporal peripapillary thinning was also observed in certain patients.
Conclusion: This study was done to emphasize the early detection of Alzheimer's disease so that the progression of the disease can be slowed down. Middle-aged patients who have a family history of Alzheimer's disease and other cognitive impairments can undergo retinal examination, which is an easy, cheap, and non invasive procedure for early diagnosis and prevention.

Keywords: Retina; alzheimer; neurodegenerative disorder.

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1. INTRODUCTION

Alzheimer's disease (AD) is a chronic neurodegenerative disease associated with memory loss and cognitive decline. Neuropathologically, there is an increase in β–amyloid plaque deposition, neurofibrillary tangle formation, neuronal loss, and inflammation [1].

The primary culprit of Alzheimer's disease remains unknown though Ab protein5 has been identified as the hallmark of senile plaques.

During the aging process, the death of the neurons occurs, releasing lipofuscin. The lipofuscin cannot be rapidly degraded and starts slowly migrating to the extracellular space leading to a focal impairment in the tissue, representing the starting point of a senile plaque [2].

Alzheimer's disease begins many years before the symptoms become evident. Early AD diagnosis represents a window to intervene with potential therapies that help slow the disease progression [3].

AD had been detected before developing clinical symptoms through amyloid positron emission tomography (PET) imaging and cerebrospinal fluid assays (CSF) in clinical trials with satisfactory sensitivity and specificity [4]. However, they were limited in their availability and were invasive, time-consuming, and expensive. However one emerging technology that is not expensive, non invasive is the retinal imaging technique [5].

AIM: The aim of this study is to demonstrate retinal changes in patients with Alzheimer's disease.

2. METHODOLOGY

A cross-sectional study was conducted in a private hospital in Bangalore, India. A total of 50 patients were taken up for the study, ranging from 60 to 80 years. The patients were diagnosed with AD by the Department of Neurology in Bangalore according to the Mini Mental State Examination (MMSE). The MMSE involves five areas mainly orientation, registration, attention, calculation, memory and language [6]. The clinical evaluation of AD included a thorough evaluation of the medical records, physical and neurological examinations, a psychometric test, neuroimaging techniques and routine laboratory tests. 50 healthy individuals were taken as control in order to compare and analyse.

2.1 Inclusion Criteria

Patients having a MMSE score of more than 17, free of ocular disease and systemic disorders that can affect vision were taken into consideration. Patients having a best corrected visual acuity of 0.5dec, less than ±5 spherocylindrical refractive error and an intraocular pressure of less than 20 mmHg.

2.2 Exclusion Criteria

Patients diagnosed with an ophthalmological pathology such as glaucoma, or suspected glaucoma, media opacity and retinal diseaseswere excluded from the study. Patients having posterior pole pathologysuch as macular degeneration, diabetic retinopathy, retinal hole, retinal tear, drusen, epiretinal membrane or any vascular disorders of the retina which prevented ocular examination were also excluded from the study.

Patients were selected after ethical clearance.

All the participants underwent a complete ophthalmologic evaluation including visual acuity, refraction, anterior segment examination by slit lamp biomicroscopy, measurement of the intraocular pressure by applanation tonometry, colour vision test and a dilated fundus examination

All the patients were subjected to FAF and OCT using the Heidelberg Spectralis.

FAF test is crucial for evaluating patients with cognitive impairment or for those who have a family history of AD. The regions with hypo or hyper fluorescent lesions on FAF were noted, and OCT was performed through these abnormal areas of FAF.

While performing OCT, the macular thickness and the peripapillary retinal nerve fibre layer (RNFL) thickness were measured. The macular thickness was evaluated by the concentric circular rings pattern and then by the rectangular gridwidth 6 *6 sector pattern. The peripapillary RNFL thickness was studied by evaluating the average thickness around 360º, thickness of the four peripapillary quadrants and thickness at 3' o clock, 6'o clock , 9 'o clock and at 12' o clock positions.

Allthetests were performed by the same optometrist and under the same conditions.

3. RESULTS

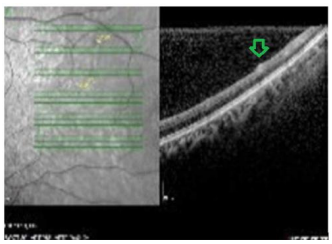


Fig. 1. Shows an OCT image –lesion in the nerve fibre and ganglion layer

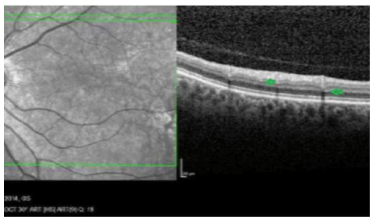


Fig. 2. Shows an OCT image – lesion in the outer plexiform and ganglion layer

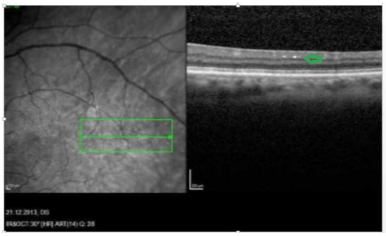


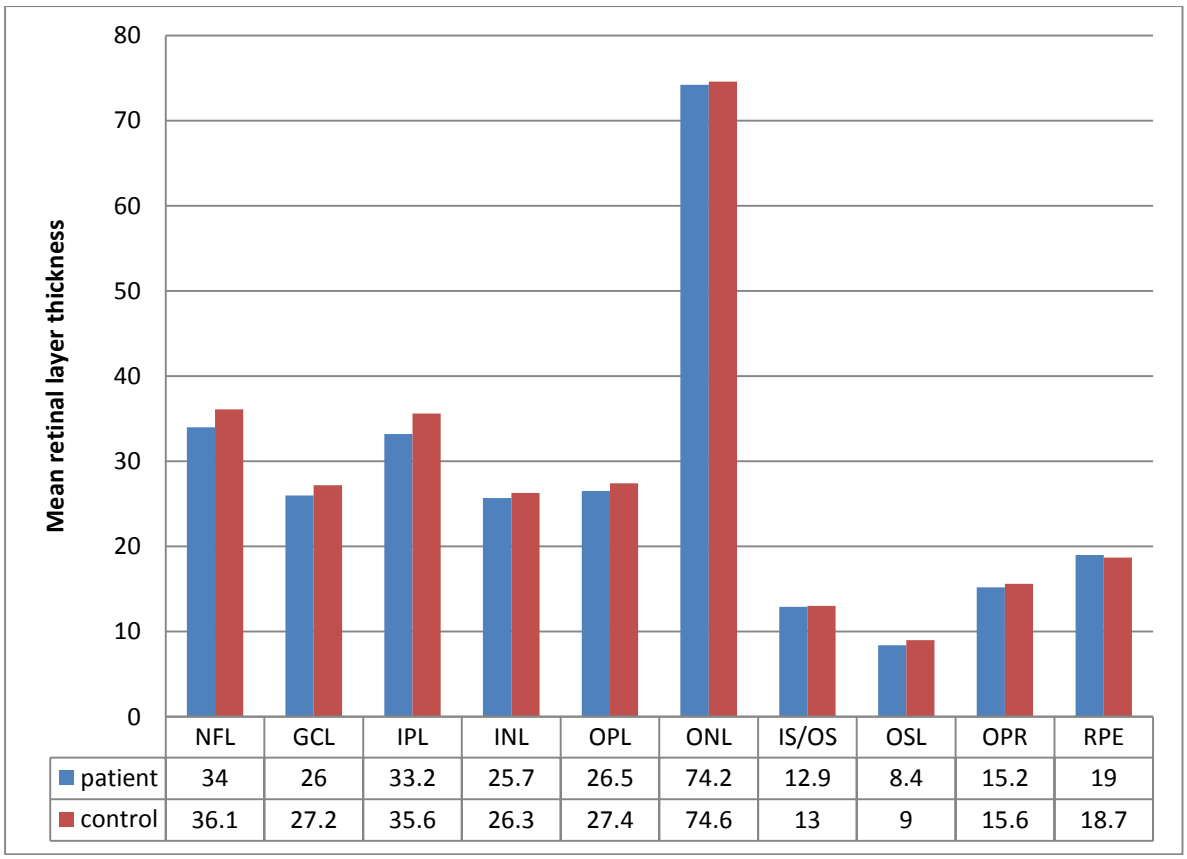
Fig. 3. Shows an OCT image of a bright plaque in the ganglion layer

Thethickness of the retinal nerve fibre layer:

There was significant thinning of the RNFL in the inner macular ring along the nasal and inferior sectors and also along the outer macular ring in the nasal zone with a p value of<0.05.

The thickness of the ganglion cell layer:

There was a significant decrease in the thickness in the inner and outer macular ring along the superior, nasal and temporal sectors with a p value of <0.05. More over there was also a significant decrease in the total volume of the ganglion cell layer.



	NFL	GCL	IPL	INL	OPL	ONL	IS/OS	OSL	OPR	RPE
patient	34	26	33.2	25.7	26.5	74.2	12.9	8.4	15.2	19
control	36.1	27.2	35.6	26.3	27.4	74.6	13	9	15.6	18.7

Graph 1. Thickness changes in the retinal layers in Alzheimer's paients on OCT

Thickness of the inner plexiform layer:This layer showed a generalised thinning at the macula level.

Thickness of the inner nuclear layer: This layer showed a slight decrease in the thickness at the level of the fovea and along the superior sectors.

Thickness of the outer plexiform layer: This layer showed a significant thickness decrease in the inner macular ring in the superior sector and temporal sector and also along the outer macular ring in the superior sector.

The retinal pigment epithelium showed no significant difference in the thickness in any of the sectors.

4. DISCUSSION

In AD, visual disturbances are often the earliest complaints. They reveal abnormalities in contrast sensitivity, in-depth and motion perception. Histopathologically it has been attributed to the lesion being localized in the cerebral cortex. A study done by Rizzo et al. [7] confirmed that visual disturbances in patients with AD are associated with pathological changes in the visual cortex rather than changes in the retina or optic nerve. However, a report by Hinton et al. [8] showed that in patients with AD, there was retinal ganglion cell loss and optic nerve degeneration.

Clinical studies of the optic nerve head and retinal nerve fibre layer using photographic methods revealed optic neuropathy and RNFL abnormalities. Another study also showed a generalized reduction of the peripapillary RNFL thickness when evaluated by optical coherence tomography (OCT) in patients with AD compared to the age-matched control subjects.

Study done by Daniel et al. [9] reported a reduction in the macular volume in patients with AD and it was in correlation with the severity of the disease. Rizer et al. [10] showed a reduction in the optic nerve fibers in patients with AD when they were examined by confocal scanning laser ophthalmoscopy.

In our study it showed a reduction of thickness in the peripapillary RNFL in all quadrants when measured by OCT. However in a study done by Leon et al. [11], it showed that the RFNL thickness was restricted mainly to the superior quadrant or in some cases to both superior and inferior quadrants. However this could be attributed to the fact the patients were included at different stages of AD , or failure of usage of a single standard OCT device or even including patients with certain retinal pathologies like epiretinal membrane or drusen that can influence the thickness of the retina.

In our study the macular area also showed a significant decrease in the thickness. In a study conducted by Ravele et al. [12], it showed that when the foveal area was analysed, it showed a non-significant thickening in patients with AD.

For AD diagnosis, magnetic resonance imaging (MRI) and positron emission tomography (PET) have been limited due to their sensitivity and resolution. Since the optic nerve and the retina are an extension of the brain, imaging of the eye is an easy, non-invasive and accessible alternative [13].

With the help of retinal photography, scanning laser ophthalmoscopy (SLO) and optical coherence tomography (OCT), retinal nerve fiber loss, retinal blood flow changes, and optic disc changes can be easily identified in patients with AD.

5. CONCLUSION

Over the past 2 decades, retinal imaging as a potential biomarker for Alzheimer's disease and neurodegenerative disease has been of significant importance. The retinal biomarkers are capable of identifying biological changes that are linked with AD, and they also help to track the progression of the disease [14].

There have been many strategies to reduce the risk, slow down the progression of the disease, and identify the disease at an early stage through interventions that are sensitive, reliable, cost-effective, and acceptable by the patient.

This study aims to use retinal biomarkers capable of identifying biological changes related to AD and help track the disease and monitor its progression.

Evaluating the retina with FAF and OCT, can help us detect patients who have a risk factor for developing AD. It gives us an indication about the neurodegenerative changes and they can be used as biomarkers for AD.

The early detection of AD is extremely important. Studies have shown us that the plaques usually

start in the retina and if it can be detected early then this will give us sufficient time to stop the progression of the disease.

The usage of antioxidants, exercise, having a healthy lifestyle can also help to slow down the progression of the disease. Newer drugs have also been introduced that helps to stop the progression [15].

It is of paramount importance to detect the disease early. More emphasis is laid on people who have relatives with AD to undergo a thorough examination.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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