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Original Research Article

Assessment of retinal nerve fiber layer thickness and macular parameters in cases of unilateral amblyopia

Madhurya H S^{1*}, Shetty Niharika Krishna¹¹Dept. of Ophthalmology, Adichunchanagiri Institute of Medical Sciences, B.G Nagara, Karnataka, India

Abstract

Background: Amblyopia, commonly known as “lazy eye,” is a developmental visual disorder characterized by reduced best-corrected visual acuity in one or both eyes, in the absence of any structural ocular abnormality. Recent studies have explored whether amblyopia is associated with changes in RNFL thickness or macular morphology, with conflicting results. Understanding these structural correlates of amblyopia could provide valuable insights into its underlying pathophysiology and may aid in the development of objective biomarkers for diagnosis and monitoring.

Aim and Objective: To assess variations in retinal nerve fiber layer (RNFL) thickness and macular parameters in cases of unilateral amblyopia utilising spectral-domain optical coherence tomography (SD-OCT).

Materials and Methods: A cross-sectional descriptive study has been carried out at the Department of Ophthalmology, Adichunchanagiri Institute of Medical Sciences, from March 2023 to September 2024. Seventy-five patients, 5 to 45 years of age having amblyopia in one eye were involved. Best-corrected visual acuity (BCVA), RNFL thickness, refractive error, as well as macular parameters, were recorded with SD-OCT and were contrasted among amblyopic and fellow normal eyes.

Results: Average age of participants was 12.5 ± 3.8 years, with a male predominance (56%). Amblyopic eyes showed significantly poorer BCVA (0.63 ± 0.15 logMAR) than fellow normal eyes (0.10 ± 0.05 logMAR, $p < 0.001$). Spherical equivalent has been higher in amblyopic eyes ($+2.50 \pm 1.00$ D) than fellow eyes ($+1.75 \pm 0.90$ D, $p = 0.04$). Mean RNFL thickness has been significantly greater in amblyopic eyes ($105.4 \pm 9.8 \mu\text{m}$) than in fellow eyes ($100.2 \pm 8.7 \mu\text{m}$, $p = 0.03$), with superior and inferior quadrants showing prominent thickening. Central macular thickness has also been raised in amblyopic eyes ($265.8 \pm 15.3 \mu\text{m}$ vs. $253.4 \pm 14.7 \mu\text{m}$, $p = 0.001$). Moderate positive correlation has been noted between RNFL thickness as well as BCVA ($r = 0.45$, $p = 0.001$).

Conclusion: Amblyopic eyes demonstrated increased RNFL and macular thickness, suggesting that amblyopia may lead to structural changes in the retina as a compensatory mechanism, possibly due to disrupted neurodevelopment. SD-OCT serves as a valuable tool for detecting such alterations, aiding in improved comprehension of amblyopia's pathophysiology and aiding in clinical evaluation.

Keywords: Amblyopia, Retinal nerve fiber layer thickness, Spectral-domain Optical coherence tomography, Visual acuity, Macular thickness.

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1. Introduction

Amblyopia is a condition characterized by reduced best-corrected visual acuity in one or both eyes, caused by visual deprivation or abnormal binocular interaction during early development, without any detectable structural defect in the eye or visual pathways. The causes include ocular misalignment, difference in amount of refractive error between two eyes, high uncorrected refractive errors, ocular media opacities, or a combination of two or more causes in

the same patient.¹ Amblyopia affects about 2%–5% of the population and typically develops during the critical period of development of retinal–cortical connection. While it most commonly arises in the first 2 to 3 years of life, it may occur until around 8–9 years of age.^{2,3} Recent evidence suggests that amblyopia may influence postnatal retinal maturation, potentially altering foveal and retinal nerve fiber layer (RNFL) thickness.⁴ “Spectral-domain optical coherence

*Corresponding author: Madhurya H S
Email: madhuryahs226@gmail.com

tomography” (SD-OCT) studies on RNFL in amblyopic eyes, however, have shown inconsistent findings, reporting no change, thinning, or thickening compared to the fellow eye.^{5,6} Consequently, there’s still a huge paucity in the present knowledge which requires to be studied and researched further.

The study of RNFL thickness and macular parameters in unilateral amblyopia represents a critical area of research for our understanding of the pathophysiology of this condition.⁷ As the interconnection between retinal structure and visual function in amblyopia continues to be elucidated, it is hoped that this will lead to more effective strategies for the diagnosis, treatment, and ultimately, the prevention of this common and potentially debilitating visual disorder.⁷

2. Aim

To assess changes in the retinal nerve fibre layer (RNFL) thickness and macular parameters in cases of unilateral amblyopia using spectral domain OCT.

3. Objectives

1. To compare the peripapillary retinal nerve fiber layer thickness in unilateral amblyopia with fellow non amblyopic eye.
2. To compare the macular parameters in unilateral amblyopia with fellow non amblyopic eye.

4. Materials and Methods

This was a cross-sectional descriptive study conducted on 75 amblyopia subjects in the age group of 5-45 years attending the Outpatient department of department of Ophthalmology from March 2023 to September 2024.

4.1. Statistical test used

Data was entered into MS Excel 2016. Data for quantitative variables was expressed in mean and proportions. To test the significance, “parametric test like paired t-test, and non-parametric test like chi-square test have been utilised to estimate RNFL changes and macular parameters in both eyes” of the same patient with and without amblyopia and compare the same quadrant-wise, respectively, and $p < 0.05$ has been taken as significant.

4.2. Inclusion criteria

1. Patients who are known cases of Amblyopia
2. Patients with intraocular pressure < 21 mmHg
3. Age group 5-45 years

4.2. Exclusion criteria

1. Ocular trauma and previous retinal surgeries
2. Advanced glaucomatous optic neuropathy
3. Fundus degenerative changes
4. Optic atrophy due to any other cause
5. Bilateral amblyopia
6. Neurological disorders causing RNFL damage

7. Congenital optic atrophy

4.3. Methodology

After receiving “approval from the Institutional Ethical Committee, the clinical data for the current investigation has been collected from patients, diagnosed with amblyopia who visit OPD in Department of Ophthalmology, Adichunchanagiri Institute of Medical Sciences, B.G. Nagara and written informed consent was taken” from patients. Demographic data, encompassing gender, age, and address, were collected. Detailed clinical history (relevant history which might affect RNFL thickness, such as history of trauma, usage of anti-glaucoma medications, ocular surgeries within 6 months, systemic or neurological disorders producing RNFL damage), general physical examination, ophthalmic examination and SD-OCT of both the eyes were done. The data was recorded in a specially designed proforma.

Detailed ocular examination was done using the following tests.

1. Snellen’s chart to measure best corrected visual acuity.
2. Cycloplegic refraction.
3. Neutral density filter to diagnose amblyopia.
4. Torch light external examination to look for anterior segment changes and to assess pupillary reactions.
5. Intraocular pressure using rebound tonometer.
6. Anterior segment examination using Slit lamp.
7. Fundus examination with direct “and indirect ophthalmoscopy after maximum pupillary dilatation, slit lamp bio microscopy with 78D and 90D lens and SD OCT for measuring RNFL thickness and macular parameters like subfoveal, total, parafoveal and central macular thickness” in all quadrants.

5. Results

A total of 75 subjects in the age group of 5-45 years were studied out of which 42 were male subjects and 33 female subjects. The best corrected visual acuity, refractive error, overall RNFL thickness, quadrant wise RNFL thickness and central macular thickness were compared between amblyopic and non-amblyopic fellow eye of the same subject.

Table 1: Demographic characteristics of study participants

Parameter	Value
Total Subjects	75
Mean Age (years)	12.5 ± 3.8
Age Range	5 – 45
Gender	Male: 42 (56%), Female: 33 (44%)

The present study analysed 75 subjects with unilateral amblyopia, with a male predominance (56%) and mean age of 12.5 ± 3.8 years (between 5 to 45years). (**Table 1**)

Table 2: Comparison visual acuity in logMAR between amblyopic and non-amblyopic eyes with p value

Parameter	Amblyopic Eye (logMAR)	Fellow Eye (logMAR)	p-value
BCVA	0.63 ± 0.15	0.10 ± 0.05	< 0.001

The present study reported a poorer “best-corrected visual acuity (BCVA)” within amblyopic eyes compared to fellow eyes which was statistically significant. (Table 2)

Table 3: Comparison of spherical equivalent between amblyopic and non-amblyopic eyes with p-value

Parameter	Amblyopic Eye (D)	Fellow Eye (D)	p-value
Spherical Equivalent	+2.50 ± 1.00	+1.75 ± 0.90	0.04

The amblyopic eyes in this study demonstrated a statistically significant higher spherical equivalent compared to fellow eyes. (Table 3)

Table 4: Comparison overall RNFL thickness (µm) between amblyopic and non-amblyopic eyes and p-value

Parameter	Amblyopic Eye (µm)	Fellow Eye (µm)	p-value
Mean RNFL Thickness	105.4 ± 9.8	100.2 ± 8.7	0.03

This research demonstrated that mean overall RNFL thickness has been greater in amblyopic eyes (105.4 ± 9.8µm) in comparison to fellow eyes (100.2 ± 8.7 µm, p = 0.03). Parikh et al. (2022) also reported increased RNFL thickness in amblyopic eyes, proposing that structural remodelling may occur as a compensatory mechanism. (Table 4)

Table 5: Comparison of quadrant-wise RNFL thickness (µm) between amblyopic and non-amblyopic eyes

Quadrant	Amblyopic Eye (µm)	Fellow Eye (µm)
Superior	130 ± 12	125 ± 11
Inferior	135 ± 13	130 ± 12
Nasal	70 ± 8	68 ± 7
Temporal	60 ± 7	58 ± 6

Superior and inferior quadrants showed increased RNFL thickness in amblyopic eyes than fellow normal eyes, while minimal changes in nasal and temporal quadrants. This pattern was also noted by Dhar et al. who found that superior and inferior quadrant thickening was prominent in unilateral amblyopia cases.¹⁶ (Table 5)

Central macular thickness (CMT): This study recorded a significantly higher CMT in amblyopic eyes compared to fellow eyes. The increased macular thickness could be

attributed to disrupted retinal development in amblyopic eyes, leading to abnormal structural modifications. (Table 6)

Table 6: Comparison of central macular thickness (CMT in µm) between amblyopic and fellow non-amblyopic eyes

Parameter	Amblyopic Eye (µm)	Fellow Eye (µm)	p-value
CMT	265.8 ± 15.3	253.4 ± 14.7	0.001

Table 7: Correlation analysis: RNFL thickness vs. visual acuity

Parameter	Correlation Coefficient (r)	p-value
RNFL Thickness vs. BCVA	0.45	0.001

The study showed significant positive correlation among RNFL thickness & BCVA (“r=0.45, p=0.001) alongside moderate positive correlation between macular thickness as well as refractive error (r = 0.35, p=0.005”) implying higher the RNFL thickness poorer the BCVA. (Table 7)

6. Discussion

The pathophysiology of amblyopia is closely linked to the concept of critical periods in neurodevelopment.⁸

Once the critical period ends, plasticity of visual system is alleviated, and ability to reverse or correct amblyopia diminishes. This is why detection and treatment of amblyopia at the earliest are necessary for preventing long-term visual impairment.⁹

The average RNFL thickness in healthy individuals generally ranges from 80 to 120 microns, with inferior and superior quadrants showing greater thickness than temporal and nasal quadrants.¹⁰

According to some research, children with amblyopia in one eye do not have different RNFL and Macula thicknesses. RNFL thickness didn’t change statistically significantly among “amblyopic and non-amblyopic eyes, according to studies by Kavitha et al. where the RNFL thickness was compared before and after occlusion therapy.¹¹ Araki et al., Kim et al., and Rajavi et al., also reported no statistically significant RNFL changes.^{6,12,13}

Whereas reports by Kasem et al, Alotabi et al, and Wu et al showed significantly elevated RNFL thickness in amblyopic eyes, with similar age group as the present study which are in agreement with our present study, which, particularly in superior and inferior quadrants, had enhanced RNFL thickness. The increased thickness can be attributed to neurodevelopmental arrest and compensatory remodeling.^{3,14,15}

In contrast to the above-mentioned studies, Dhar et al showed significantly thinner RNFL in amblyopic eyes.¹⁶

In healthy individuals, the average central macular thickness (CMT) ranges between 250 and 300 micrometres, with some variation depending on the specific OCT device and the population being studied.¹⁷

Macular “thickness of amblyopic eyes has been substantially greater than that of companion normal eyes, as demonstrated by our research. Findings of present research align with studies conducted by Rajavi et al,¹³ Kasem et al¹⁴ and Wu et al.¹⁵

The impact of amblyopia on RNFL thickness and macular parameters is an area of significant research interest, particularly in understanding how severity of amblyopia compares to structural changes in the retina.¹⁸

It is possible that the reduced visual stimulation to amblyopic eye throughout critical period of developing visual pathway leads to a cascade of neurodegenerative changes in the retina, ultimately resulting in the thinning of the RNFL and macula.¹⁹

This finding highlights the need for a comprehensive approach to understanding amblyopia, which considers both retinal and central neural contributions to the condition.²⁰

The results of the above mentioned studies highlight the fact that there is lack of common consensus on the retinal nerve fiber layer thickness and macular parameters in cases of unilateral amblyopia. This could be due to variations in the age group of the study participants, type of amblyopia, duration of amblyopia, duration of the study, presence of confounding factors and the ongoing treatment for amblyopia. (Table 8)

There is a huge need for further studies on this topic to understand the various factors causing changes in the retinal nerve fiber layer thickness and macular parameters in unilateral amblyopia.

Also, amongst the above mentioned studies, only the study by Kavitha et al has considered the changes after occlusion therapy, similar studies are required to be conducted in the future to observe for the variations of RNFL thickness and macular parameters after occlusion therapy to guide clinicians to refine and to monitor the management approaches in cases of unilateral amblyopia.¹¹

Table 8: Studies highlight common consensus on the retinal nerve fiber layer thickness and macular parameters in cases of unilateral amblyopia

Author	Sample / Type of Amblyopia	RNFL Thickness	Macular Thickness / Other Findings
Andalib et al ²⁰	Anisometropic and Strabismic Amblyopia	Similar between amblyopic and fellow eyes (strabismic)	Thicker macula in anisometropic amblyopia
Kavitha et al ¹¹	30 unilateral anisometropic amblyopic eyes (pre/post occlusion therapy)	No significant change post-therapy	CMT and foveal thickness reduced post-therapy
Singh et al ²¹	28 anisomyopic, 31 myopic astigmatic, 42 hypermetropic astigmatic eyes	Inferior quadrant RNFL thicker in anisohypermetropic	No significant difference in CMT
Araki et al ¹²	15 strabismic, 31 anisometropic amblyopic eyes	No significant difference	No difference in CMT or rim area
Kim et al ⁶	Not specified	No significant difference	No difference in optic nerve head (ONH) parameters
Rajavi et al ¹³	44 anisometropic amblyopic eyes	No “significant difference	CMT significantly thicker in moderate-to-severe amblyopia
Kasem et al ¹⁴	22 strabismic, 30 anisometropic, 21 deprivational	RNFL significantly thicker in amblyopic eyes	CMT, macular volume, and average macular thickness suggestively higher in amblyopic eyes
Alotaibi et al ³	39 anisometropic amblyopic eyes	RNFL thicker in amblyopic eyes	No significant difference in macular parameters
Wu et al ¹⁵	Not specified	RNFL significantly thicker in amblyopic eyes	Foveolar thickness significantly increased in amblyopic” eyes
Dhar et al ¹⁶	Not specified	RNFL thinner in amblyopic eyes	No significant difference in other ONH parameters

7. Conclusion

The findings reveal that amblyopic eyes exhibit elevated thickness of retinal nerve fiber layer (RNFL) in superior and inferior quadrants in particular, as well as significant macular thickening. These changes suggest that prolonged visual deprivation in amblyopia leads to anatomical modifications, potentially as a compensatory mechanism or as a result of disrupted neural development. To conclude, this study highlights the function of SD-OCT as a valuable tool in detecting and tracking structural changes in amblyopia. Continued research in present domain will be essential in advancing our understanding of amblyopia as well as refining management approaches for this common yet complex visual disorder.

8. Limitations

1. The study did not stratify amblyopia.
2. The effect of occlusion therapy on RNFL thickness was not studied
3. The cross-sectional design limits causal interpretation.

9. Source of Funding

None.

10. Conflict of Interest

None.

11. Ethical Approval

Ethical No.: AIMS/IEC/063/2023.

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