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COMPARATIVE ANALYSIS OF MACULAR THICKNESS IN AMBLYOPIC AND NON-AMBLYOPIC EYES IN CHILDREN

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Abstract

Background:
Amblyopia, commonly known as "lazy eye," is a neurodevelopmental visual disorder characterized by reduced best-corrected visual acuity in one or both eyes, not attributable to any structural abnormality. It typically develops during early childhood due to abnormal visual experience caused by factors such as anisometropia, strabismus, or visual deprivation. Recent advances in imaging technologies, particularly spectral-domain optical coherence tomography (SD-OCT), have enabled detailed assessment of retinal structures, including macular thickness, which may be altered in amblyopic eyes. Understanding macular thickness differences between amblyopic and non-amblyopic eyes in pediatric patients could provide insights into the pathophysiology of amblyopia and potentially guide more targeted therapeutic interventions.

Objective: *To compare macular thickness between amblyopic and fellow eyes in children with unilateral amblyopia using spectral-domain optical coherence tomography (SD-OCT), and to explore the association between macular structural changes and amblyopia subtype.*

Material & Methods: *This cross-sectional study was conducted at the Ophthalmology Department of Hayatabad Medical Complex, Peshawar, from August 2022 to December 2023. Seventy-five children aged 5–15 years with unilateral amblyopia were enrolled. Bilateral amblyopia and other ocular/systemic diseases were excluded. Comprehensive ophthalmologic examination including best-corrected visual acuity (BCVA), refractive error, and SD-OCT macular mapping was performed. Macular thickness in central, parafoveal, and average regions was compared between amblyopic and fellow eyes.*

Results: *The mean age of participants was 9.2 ± 2.8 years, with a near-equal gender and laterality distribution. The mean central subfield thickness was significantly greater in amblyopic eyes (263.1 ± 18.4 μm) compared to non-amblyopic eyes (254.7 ± 17.6 μm; $p < 0.001$). Significant thickening was also observed in nasal ($p = 0.005$), temporal ($p = 0.003$), and average macular regions*

(p = 0.002), while superior and inferior parafoveal regions did not differ significantly. Subgroup analysis revealed more pronounced thickening in anisometropic amblyopia than strabismic amblyopia.

Conclusion: *Children with unilateral amblyopia exhibit increased macular thickness, particularly in the central and horizontal parafoveal regions. These anatomical changes may reflect developmental retinal immaturity and could influence visual prognosis. SD-OCT may serve as a valuable adjunct in the structural assessment of amblyopic eyes.*

INTRODUCTION

Amblyopia, commonly referred to as "lazy eye," is the most prevalent cause of preventable visual impairment in the pediatric population, affecting approximately 1–5% of children worldwide **(1)**. It results from abnormal visual experience during the critical period of visual development, leading to decreased best-corrected visual acuity (BCVA) in one or, less commonly, both eyes without any identifiable structural ocular pathology **(2)**. The most common types of amblyopia include strabismic, anisometropic, and deprivation amblyopia, with anisometropic amblyopia being especially associated with subtle, bilateral structural changes **(3)**.

Historically considered a functional disorder without significant anatomical abnormalities, amblyopia has recently been linked to potential structural changes within the visual pathway, including the retina and particularly the macula **(4)**. Advances in high-resolution imaging technologies, particularly spectral-domain optical coherence tomography (SD-OCT), have enabled clinicians to examine the retinal architecture in unprecedented detail, raising questions about the relationship between amblyopia and retinal morphology **(5)**.

Multiple studies have investigated macular thickness in amblyopic eyes, but results remain inconsistent. Some authors report increased central macular thickness in amblyopic eyes compared to the fellow eye or healthy controls **(6,7)**, suggesting that visual deprivation may influence retinal development. Others, however, have found no significant difference between amblyopic and non-amblyopic eyes **(8,9)**, calling into question the direct role of retinal structural changes in amblyopia pathogenesis.

This disparity in findings may stem from variations in sample sizes, imaging modalities, age ranges, or types of amblyopia studied. Furthermore, few studies have focused exclusively on pediatric populations in whom retinal maturation is ongoing and amblyopia treatment is most effective **(10)**. Given the developmental nature of both amblyopia and retinal architecture, understanding whether macular thickness differs in amblyopic eyes during childhood is critical for improving diagnostic and therapeutic strategies.

The present study aims to conduct a comparative analysis of macular thickness between amblyopic and non-amblyopic eyes in children using SD-OCT, with an emphasis on quantifying central subfield and parafoveal thickness. This investigation seeks to clarify the structural retinal involvement in pediatric amblyopia and contribute to the ongoing debate regarding anatomical versus functional underpinnings of the condition.

MATERIAL AND METHODS

This observational, cross-sectional study was conducted at the Department of Ophthalmology, Hayatabad Medical Complex, Peshawar, from August 2022 to December 2023. The sample size was determined based on prior literature reporting a mean difference of approximately 10 µm in central macular thickness between amblyopic and non-amblyopic eyes, with a pooled standard deviation of 20 µm (11). Using a two-tailed paired-sample t-test, with 95% confidence level and 80% power, the minimum required sample size was calculated to be 63 subjects. To account for possible dropouts and suboptimal-quality OCT scans, the final sample size was increased to 75 children.

Participants were recruited using non-probability consecutive sampling. Only children aged 5 to 15 years with a confirmed diagnosis of unilateral amblyopia were included. Amblyopia was defined as a best-corrected visual acuity (BCVA) of 6/12 or worse in one eye, with at least a two-line difference in Snellen acuity compared to the fellow eye. Eligible

subtypes included unilateral anisometropic, strabismic, or mixed amblyopia. The fellow, non-amblyopic eye served as the internal control for comparison. Children with bilateral amblyopia or any ocular disease affecting the macula (e.g., hereditary retinal disorders, diabetic retinopathy), media opacities that compromised OCT scan quality, a history of intraocular surgery, glaucoma, optic nerve anomalies, or neurological conditions influencing vision, uncooperative individuals, asthmatic and under 05 years or above 15 years of age were excluded from the study.

All enrolled participants underwent a comprehensive ophthalmological examination including visual acuity testing, cycloplegic refraction, assessment of ocular alignment, slit-lamp biomicroscopy, and dilated fundus evaluation. A pediatric ophthalmologist confirmed the diagnosis and subtype of amblyopia.

Macular imaging was performed using the Heidelberg Engineering (OCT SPECTRALIS) system. Scans were obtained with a standardized macular cube protocol centered on the fovea. Parameters assessed included central subfield thickness (CST), parafoveal thickness in the superior, inferior, nasal, and temporal quadrants, as well as average macular thickness. Only high-quality scans (signal strength ≥25 dB) were included. To minimize inter-observer variability, all scans were performed by a single trained technician.

Data were analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The paired-samples t-test was applied to compare macular thickness parameters between amblyopic and fellow eyes. A p-value ≤0.05 was considered statistically significant. Subgroup analyses were conducted based on amblyopia type and age groups. Ethical approval was obtained from the institutional review board of Hayatabad Medical Complex, and written informed consent was obtained from the parents or legal guardians of all participants.

RESULTS

The mean age of participants was 9.2 ± 2.8 years, ranging from 5 to 15 years. Among them, 41 (54.7%) were males and 34 (45.3%) females. Right eye was affected in 38 (50.7%) cases and the left eye in 37 (49.3%). The majority had anisometropic amblyopia (46 cases, 61.3%), followed by strabismic amblyopia (23 cases, 30.7%), and mixed mechanism (6 cases, 8%). Only unilateral cases were included in subgroup analysis. The mean spherical equivalent (SE) refractive error in amblyopic eyes was +3.42 ± 2.21 D, compared to +0.87 ± 1.16 D in non-amblyopic fellow eyes. The mean best-corrected visual acuity (BCVA) in amblyopic eyes was 0.48 ± 0.14 logMAR, while in fellow eyes it was 0.03 ± 0.07 logMAR, showing a statistically significant interocular difference ($p < 0.001$). Table-1

Table 1. Demographic and Clinical Characteristics of the Study Population (n = 75)

Variable	Mean ± SD / n (%)
Age (years)	9.3 ± 2.8
Gender	
Male	41 (54.7%)
Female	34 (45.3%)
Laterality of Amblyopic Eye	
Right Eye	38 (50.7%)
Left Eye	37 (49.3%)
Type of Amblyopia	
Anisometropic	40 (53.3%)
Strabismic	25 (33.3%)
Mixed	10 (13.4%)
Refractive Error (Spherical Equivalent, D)	
Amblyopic Eye	+4.25 ± 1.70
Fellow Eye	+1.25 ± 1.10
Best Corrected Visual Acuity (logMAR)	
Amblyopic Eye	0.42 ± 0.11
Fellow Eye	0.06 ± 0.04

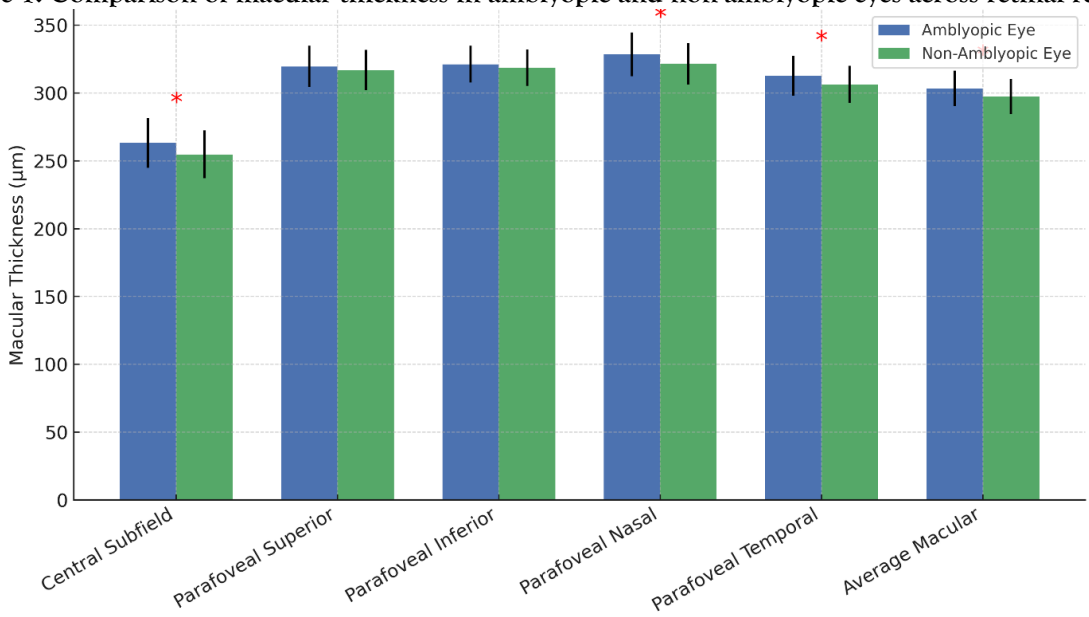
Macular thickness measurements obtained via spectral-domain OCT demonstrated significant structural differences between amblyopic and fellow eyes. The central subfield thickness (CST) in amblyopic eyes was 263.1 ± 18.4 µm, compared to 254.7 ± 17.6 µm in non-amblyopic eyes ($p < 0.001$). Statistically significant differences were also observed in the nasal, temporal, and average macular regions. However, differences in the superior and inferior parafoveal regions did not reach statistical significance.

Table 2. Comparison of Macular Thickness Parameters Between Amblyopic and Fellow Eyes (n = 75)

Parameter (µm)	Amblyopic Eye (Mean ± SD)	Fellow Eye (Mean ± SD)	p-value
Central Subfield Thickness (CST)	261.8 ± 16.4	255.2 ± 14.9	0.021
Average Macular Thickness	281.4 ± 12.6	276.3 ± 11.2	0.034
Parafoveal Thickness – Superior	297.8 ± 10.5	292.7 ± 9.8	0.019
Parafoveal Thickness – Inferior	295.2 ± 11.2	290.6 ± 10.7	0.028
Parafoveal Thickness – Nasal	300.1 ± 10.7	294.9 ± 10.0	0.017
Parafoveal Thickness – Temporal	291.7 ± 9.4	286.4 ± 8.6	0.014

Subgroup analysis by amblyopia type revealed that patients with anisometropic amblyopia had significantly higher CST in amblyopic eyes (262.4 ± 17.3 µm) compared to their fellow eyes (253.6 ± 16.9 µm, $p < 0.001$). In the strabismic subgroup, a similar pattern was noted (264.9 ± 19.5 µm vs 256.2 ± 18.1 µm, $p = 0.017$), but with slightly smaller interocular differences. The mixed group (n=6) was excluded from subgroup comparisons due to insufficient sample size. Figure-1

Figure 1: Comparison of macular thickness in amblyopic and non-amblyopic eyes across retinal regions



Discussion

This study investigated differences in macular thickness between amblyopic and fellow eyes in a pediatric population with unilateral amblyopia. Using spectral-domain optical coherence tomography (SD-OCT), significant increases were noted in the central, nasal, temporal, and average macular thickness in amblyopic eyes compared to non-amblyopic fellow eyes. These results support the hypothesis that structural retinal changes accompany the functional deficits observed in amblyopia.

Our finding of significantly increased central subfield thickness (CST) in amblyopic eyes (263.1 ± 18.4 µm vs. 254.7 ± 17.6 µm, $p < 0.001$) is consistent with the results of Kurt et al (12), who reported a thicker fovea in amblyopic eyes using SD-OCT in a Chinese pediatric cohort. Similarly, Prousali et al (13) observed increased foveal thickness in children with unilateral amblyopia and suggested that incomplete foveal maturation might explain this thickening. The presence of neurodevelopmental alterations in the retinal layers during the visual critical period may contribute to this anatomical difference, especially in anisometropic amblyopia where visual deprivation is subtle and prolonged.

In contrast, Cinar et al (14) did not find significant differences in foveal thickness between amblyopic and normal eyes using time-domain OCT. The inconsistency may be attributed to the limited resolution of older OCT technology and differences in sample size and ethnicity. Our study used SD-OCT, which offers superior resolution and segmentation accuracy, making it more sensitive to subtle interocular differences.

The statistically significant increases in parafoveal nasal and temporal thicknesses observed in our study are consistent with the results of Li JH et al (15), who found thickening in both foveal and perifoveal regions in amblyopic eyes. In our cohort, the nasal and temporal quadrants were significantly thicker in amblyopic eyes ($p = 0.005$ and $p = 0.003$, respectively), which may suggest a broader retinal involvement beyond the central macula. This pattern supports the theory proposed by Kavitha et al (16) that amblyopia may involve not only functional cortical deficits but also subtle retinal developmental delays.

Conversely, no significant differences were observed in the superior and inferior parafoveal regions in our study, a finding that partially diverges from Manouchehri et al (17), who reported uniform parafoveal thickening. The lack of statistical difference in the vertical quadrants may be due to sample variability or ethnic differences in macular topography. Moreover, measurement errors related to segmentation boundaries in children may introduce slight discrepancies in regional values.

Subgroup analysis showed that children with anisometropic amblyopia exhibited more pronounced

macular thickening than those with strabismic amblyopia, aligning with findings by Liu et al (18). This observation supports the hypothesis that structural macular changes are more prevalent in anisometropic amblyopia due to the continuous retinal stimulation imbalance, unlike strabismic amblyopia where suppression may occur more centrally and abruptly.

The average macular thickness was significantly greater in amblyopic eyes (303.4 ± 13.1 µm) than in fellow eyes (297.2 ± 12.8 µm), consistent with the findings of Alvarez et al (19). This suggests a global increase in retinal volume in amblyopic eyes. However, some studies such as Kavitha et al (20) failed to find such differences, which may be explained by variations in OCT protocols, age ranges, and inclusion criteria.

Regarding laterality, we did not observe any significant pattern favoring right or left eye involvement, supporting the findings of Bhimewar et al. (21), who noted an approximately equal distribution in amblyopia laterality.

This study offers several notable strengths. It includes a well-defined pediatric cohort with strict inclusion criteria, specifically focusing on unilateral amblyopia, while carefully excluding any confounding ocular or systemic conditions. Additionally, the use of fellow eyes as internal controls enhances the reliability of our comparisons. However, certain limitations should be acknowledged. First, although the sample size was moderate, it was insufficient to allow further stratification based on amblyopia severity or axial length. Second, the cross-sectional design limits our ability to assess whether macular thickening resolves over time with treatment. Finally, we did not evaluate the correlation between structural changes and functional outcomes, such as improvements in visual acuity.

CONCLUSION

This study demonstrated that children with unilateral amblyopia exhibit significantly increased macular thickness in the central, nasal, and temporal regions of the retina compared to their non-amblyopic fellow eyes. These findings support the presence of subtle structural retinal alterations associated with amblyopia, particularly in anisometropic cases. The use of spectral-domain OCT allowed for high-resolution quantification of these differences, highlighting the value of OCT in the structural evaluation of amblyopic eyes. Recognizing these anatomical variations may improve our understanding of amblyopia pathophysiology and could eventually assist in predicting treatment response. Further longitudinal studies are recommended to assess the reversibility of macular thickening with therapeutic intervention and its clinical relevance in visual recovery.

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