Original Article

Impact of Unilateral Amblyopia on Macular and Retinal Nerve Fiber Layer Thickness

Syed Amir Hamza, Maria Sultan, Maleeha Safdar Ali, Muhammad Tariq

ABSTRACT

Objective: To compare “retinal nerve fiber layer” (RNFL) and “macular thickness” in unilateral anisometropic and strabismic amblyopia using “optical coherence tomography” (OCT).

Study Design & Setting: Descriptive cross sectional study with purposive sampling technique. Department of Ophthalmology, Mardan Medical Complex, Mardan, July–December 2023.

Methodology: A total of 54 patients with anisometropic (n=27) or monocular strabismic (n=27) amblyopia with best-corrected visual acuity of 20/40 to 20/400 were included. Patients with refractive errors =5 diopters or axial length differences =1 mm were excluded. OCT was used to measure peripapillary RNFL and macular thickness in amblyopic and fellow eyes.

Results: The mean age of the patients was 10 ± 3.1 years 8.9 ± 3.7 years in the anisometropic group and in the strabismic group respevtively. Anisometropic amblyopic eyes had significantly increased macular thickness (224.5 ± 48.7ìm) compared to fellow eyes (207.5 ± 34.2ìm) (P=.002), with no significant RNFL difference (P=.55). Macular and RNFL thickness differences between amblyopic and the other eyes in the strabismic group were not statistically significant (P=.07 and .52). No significant differences were observed between anisometropic and strabismic amblyopic eyes.

Conclusion: Anisometropic amblyopia is associated with increased macular thickness, whereas strabismic amblyopia shows no significant change. Amblyopia does not appear to affect peripapillary RNFL thickness in either group.

Keywords: Amblyopia, anisometropia, strabismus, macular thickness, RNFL, optical coherence tomography.

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INTRODUCTION

“Reduced visual acuity” (VA) and contrast sensitivity in either one or both eyes are the hallmarks of amblyopia. It is a visual disorder brought on by either deprivation of vision or binocular interactions abnormally.

According to Malcol et al, reduced vision in one eye as a result of aberrant visual development during childhood is known colloquially as "lazy eye," or amblyopia.[1]

Amblyopia affects two or three out of every hundred children, making it the most prevalent cause of monocular visual acuity impairment in children. Normal visual development requires appropriate visual stimulation, such as clear retinal pictures in each eye and appropriate ocular alignment. Children under the age of seven are at risk for amblyopia due to frequent childhood eye problems such strabismus and anisometropia, which can disrupt visual stimulation throughout development. It is well known that the effectiveness of treating amblyopia decreases with age, and that if the condition is not identified and treated early, one eye's visual acuity may be permanently reduced.[2]

Many studies looking into the pathophysiology of amblyopia, like Hubel and Wiesel's animal experiments in the 1960s, have found anatomical and functional abnormalities in the lateral geniculate nucleus and visual cortex. Latest studies have identified abnormalities in the “visual cortex” (VC) and “lateral geniculate nucleus” (LGN) in human amblyopes[3,4,5]

According to Malcol et al, a disorder known as amblyopia occurs when an eye's visual pathways develop abnormally during childhood, resulting in impaired vision. The brain stops communicating with one eye when it receives inadequate information from that eye. This indicates that the brain depends on data from the "stronger" eye. A person

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may develop amblyopia in both eyes.[1]

Visual acuity testing is the gold standard for amblyopia screening, and visual acuity charts continue to be the main screening tool used by the majority of vision screening programs. Instead of directly identifying amblyopia, automated technologies offer a simpler and more effective screening method that looks for refractive error and strabismus risk factors. However, the prevalence of amblyopia is 2.5%, whereas the prevalence of risk factors is 21%. This means that 8 or 9 out of 10 children who fail automated screening due to a risk factor are false positives and do not actually have amblyopia. [2]

Since amblyopia is common in youngsters and can cause severe visual impairment that lasts a lifetime if left untreated, it is a significant public health issue. The quality of life can be significantly impacted by amblyopia and its treatment. Prevalence estimates vary depending on the age, race, and ethnicity of the population studied; study methodology; and the definition of amblyopia used. For children aged 30 to 71 months, prevalence estimates from population-based studies range from 0.7% to 2.6%, while school-based studies of older children usually report higher rates (range, 1.0% to 5.5%).[6]

Ikeda, on the other hand, studied the neurophysiology of cats and found that amblyopia was associated with retinal ganglion cell defects. A functional impairment of the retina in human amblyopes was discovered through an electrical experiment. However, after a second evaluation, Hess was unable to confirm these retinal abnormalities. It hasn't been established, nevertheless, that amblyopes' retinas are completely normal.[5,7].

Human retinal anatomy can now be quickly and non-invasively assessed due to to the innovative use of "Optical Coherence Tomography" (OCT). Spectral-domain OCT (SD-OCT) has greatly improved scanning speed and spatial resolution, allowing for more thorough retinal research. According to a study by Yen et al, in eyes with refractive amblyopia, the circumpapillary retinal nerve fiber layer (cpRNFL) was found to be thicker than in their normal fellow eyes using time-domain OCT. Amblyopic eyes have thicker foveas than visually normal control eyes, according to OCT results reported by Li et al. However, it is still unclear why amblyopic eyes have thicker cpRNFL or foveal tissue than healthy eyes.[4,7] Amblyopia is characterized by a decrease in best corrected visual acuity (BCVA) in one or both eyes, without any associated anatomical abnormality of the globe. This unusual visual perception takes place as the visual system develops. Despite the fact that amblyopia is thought to have a structurally normal eye, it is well known that the VC (visual cortex) and LGN (lateral geniculate nucleus) are altered by deprivation of vision. [3,4] According according to certain authors, amblyopia is caused by abnormal variations in the RNFL, cells of ganglion and the optic nerve.[5]"Optical coherence tomography" (OCT) is an imaging technique which is simultaneously a noninvasive procedure that provides cross-sectional scans of the head of the optic nerve and the retina in a highly resolution form. OCT has been utilised to assess the RNFL and the thickness of macula in anisometropic and strabismic amblyopia; however, the results of the majority of earlier studies have been inconsistent and variable. [7,8,9] Therefore, in the current investigation, we utilized OCT to evaluate the thickness of peripapillary RNFL and macula in amblyopic eyes (both anisometropic and strabismic) and their normal contralateral eyes to identify any differences. Additionally, we aimed to explore the variations in the morphology or anatomy between these two amblyopia subgroups."

Since amblyopia's visual results are best when treated as soon as possible, risk factors for the condition must be detected in the pediatric population as early in life as possible and controlled appropriately. Newer ideas for binocular vision therapy are continually developing, despite the fact that monocular therapies like occlusion or penalization have proven to be quite helpful over time.

Amblyopia can be caused by strabismus, refractive error, or stimulus deprivation, all of which can be promptly detected with early and regular visual screening of newborns and toddlers. The prognosis is known to improve with early detection and treatment of these issues.[6]

METHODOLOGY

The research project was conducted for a total span of 6 months from July 2023 to December 2023 at Ophthalmology Department, Mardan Medical Complex, Mardan. This was a descriptive cross sectional study with a purposive sampling technique. Patients with presence of amblyopia unilaterally (BCVA ranging from 20/40 to 20/400) between the ages of 6 and 16 years were included in this study. Ethical approval was obtained from MTI BKMC Mardan ethical committee bearing NO.328 BKMC dated 02/06/2023.

Sample Size Calculation

G*Power software was used to calculate the appropriate sample size, assuming an appropriate size to authenticate the results. It is also based on past researches, a power of 80% , confidence interval 95% and an alpha level of 0.05.

Two groups of patients were identified:

One for strabismic amblyopia and the other for anisometropic amblyopia. There was no deviation on cover test when performed on patients in anisometropic group. Anisotropia was measured as difference of 1, 1.5, and 3 diopters in hyperopia, astigmatism, and myopia, respectively. According to the study's criteria, none of the patients in the strabismic group exhibited anisometropia. In the cover test, the smallest deviation angle that was visible was 10 prism diopters.

A thorough ophthalmic examination including slit-lamp including and fundus examination, visual acuity assessment and cycloplegic refraction was performed. The subjects who were unable to keep a constant fixation behind the OCT camera, or who had any kind of neurologic or ocular disorder were removed from the study. To minimize the impact of refractive error on measurements, patients were excluded from the anisometropic group if the axial length difference between their eyes exceeded 1 mm or if either eye had myopia or hyperopia greater than 5 diopters.

Following complete pupil dilation, a single technician conducted all OCT measurements. Three consecutive 360-degree circular scans with a 3.4 mm diameter around the optic disc were employed as part of a rapid RNFL scan. Three samples were used to determine the average thickness using the OCT programmed. We performed a macular scan that comprised six radial scans in order to determine the macular thickness. The measurement was then carried out using a 6-mm diameter map.

Data Analysis

By applying software (SPSS) the statistical analysis was carried out. The paired sample t-test was used to compare the macular and RNFL thicknesses, and the Kolmogorov-Smirnov test was used to assess the distribution pattern. P-values less than or equal to 0.05 were taken as statistically significant.

RESULTS

Our study included 27 individuals with monocular strabismic amblyopia and 27 individuals with monocular anisometropic amblyopia**.** The average patient age in the strabismic group was 8.9 ± 3.7 years (range: 6 to 16 years), whereas the mean age in the anisometropic group was 10 ± 3.1 years (range: 6 to 16 years). There were 24 patients with esotropia and 3 patients with exotropia (16 males and 10 females) in the strabismic group. There were five anisomyopic patients and twenty-two anisohyperopic patients (9 females and 17males)in the anisometropic group.

The thickness of the macula in amblyopic eyes in the anisometropic group was significantly greater than the other contralateral normal eyes. But in this group, there was no significant change in thickness of the RNFL between amblyopic and fellow normal eyes as shown in Table 1. On the other hand, there was no statistically significant difference in thickness of peripapillary RNFL and macula between amblyopic and opposite normal eyes in the strabismic group as shown in Table 1. Also there was no significant difference between thickness of RNFL and macula between strabismic and anisometropic eyes with amblyopia as indicated in Table 2.

The possible reason of which could be that in anisometropic amblyopia, the increased macular thickness but unaltered RNFL thickness is probably due to selective alterations in the inner retinal layer, incomplete apoptosis, and aberrant retinal development rather than direct damage to the pathways of the optic nerve pathways.

The comparison of anisometropic and strabismic amblyopia reveals no statistically significant variations in macular or thickness of RNFL. The macular thickness in anisometropic amblyopia (224.5 ± 48.7 µm) is marginally lower than in strabismic amblyopia (232 ± 30.6 µm), although the difference is not statistically significant (p = 0.51). The thickness of RNFL in anisometropic amblyopia (89 ± 30.1 µm) is somewhat greater than that in strabismic amblyopia (85.7 ± 23.3 µm), although there is no noticeable significant difference statistically (p = 0.66). The findings indicate that both forms of amblyopia display comparable anatomical traits regarding macular and RNFL thickness, suggesting that abnormalities in the retina and nerve fiber layer may not be exclusive to a certain amblyopia subtype. The data reveal that in

Table-1: Average Thickness of Macula and RNFL (µm)

Parameter	Amblyopic Eyes	Fellow Eyes	p-value
Anisometropic Amblyopia			
Macular Thickness	224.5 ± 48.7	207.5 ± 34.2	.002
RNFL Thickness	89 ± 30.1	92 ± 28.7	.55
Strabismic Amblyopia			
Macular Thickness	232 ± 30.6	219.2 ± 33.4	.07
RNFL Thickness	85.7 ± 23.3	88.2 ± 31.1	.52
RNFL = Retinal Nerve Fiber Layer			

Table-2: Average Macular and RNFL Thicknesses (µm) in Strabismic and Anisometropic and Eyes

Parameter	Strabismic Amblyopia	Anisometropic Amblyopia	p-value
Anisometric Amblyopia			
Macular Thickness	232 ± 30.6	24.5 ± 48.7	0.51
RNFL Thickness	85.7 ± 23.3	89 ± 30.1	0.66
RNFL = Retinal Nerve Fiber Layer			

anisometropic amblyopia, macular thickness is markedly higher in amblyopic eyes (224.5 ± 48.7 μm) than in companion eyes (207.5 ± 34.2 μm, p = 0.002), indicating structural alterations in the macula. Nonetheless, RNFL thickness showed no noticeable difference between eyes with amblyopia (89 ± 30.1 μm) and fellow eyes (92 ± 28.7 μm, p = 0.55). In strabismic amblyopia, macular thickness is greater in amblyopic eyes (232 ± 30.6 μm) compared to companion eyes (219.2 ± 33.4 μm), although this difference lacks statistical significance (p = 0.07). Likewise, RNFL thickness showed no noticeable difference between eyes with amblyopia (85.7 ± 23.3 μm) and fellow eyes (88.2 ± 31.1 μm, p = 0.52). The data indicate that macular thickness may be influenced in anisometropic amblyopia, but RNFL thickness remains similar across amblyopic and fellow eyes throughout both forms of amblyopia.

DISCUSSION

In our study, we found that in anisometropic amblyopia, the difference in the thickness of macula between normal healthy eyes and contralateral with amblyopia is considered statistically significant.

Our results are consistent with a research by AlHaddad et al. In their study they reported significant increase in central macular thickness in anisometropic amblyopia patients by using OCT.[10]

We measured the anisometropic amblyopia in 27 eyes (four had myopic anisometropia and 22 had hyperopic anisometropia). According to research by Pang et al., children who are unilaterally high myopic and amblyopic typically have thicker foveas in their eyes with amblyopia than in their healthy eyes.[11] According to Huynh et al., individuals with hyperopic anisometropia amblyopia had thicker foveas.[12] On the other hand, some other previous studies show variable results. There was no difference in the thickness of macula between normal healthy eyes and eyes with amblyopia when Dickmann et al. assessed 20 eyes with mixed anisometropic amblyopia (10 with myopic and 10 with hyperopic anisometropia) [13]. Yoon et al. came to the same conclusion after examining 31 patients with hyperopic anisometropic amblyopia.[14]

Although it is reported by some authors that myopia—particularly more than 5 diopters—was linked to a shift in the thickness of macula [15], we were unable to find any evidence in the literature between hyperopia and macular thickness. In order to decrease the effect of refractive errors on macular thickness in our study, Patients having myopia or hyperopia of more than 5 diopters in either eye or with a difference in the axial length between two eyes of more than 1 mm were not included.In our study most of patients in anisometropic group had hyperopic anisometropia(22 patients).

According to Leone et al the increase in macular thickness in amblyopia may result from inadvertent measurement of parafoveal eccentric point.[16]In our study, the patients with unsteady fixation were excluded and to examine off-center scans in patients with steady fixations, the scan placement was adjusted. So in our study difference in macular thickness is not result of off-centered scans.

According to Al-Haddad et al., in nonamblyopic anisometropia control group, the interocular difference is not significance.[10] Therefore, the change in macular thickness may be primarily because of amblyopia and not because of anisometropia and refractive error alone.The increase in the thickness of macula in amblyopic eyes was not statistically significant in amblyopia with strabismus, according to our findings as well. This result is in line with previous research.[7,14] Patients with strabismic amblyopia did not exhibit any change in macular thickness, according to Altintas et al. [7] Quoc et al. found the similar results in patients with amblyopia having strabismus.[14] In contrast, one research conducted by Dickmann et al. found that the only significant difference in thickness between their normal contralateral healthy eyes and eyes with strabismic amblyopia in the macular region only[13] According to a research by Huynh et al. also stated increase in foveal thickness in strabismic amblyopia patients.[12]

Our results confirm the theory of Huynh et al. that increase in macular thickness is seen only in amblyopic patients having inisometropicamblyopia. The reason of which suggested that disruption in the typical postnatal development of amblyopic eyes may hinder the maturation of normal macula. This could cause Henle’s fibers to migrate away from the foveola, potentially resulting in increased thickness of fovea as observed on OCT.[12] Nevertheless, future research has to decide how to interpret our findings.

Children with ametropic and anisometropic amblyopia who did not regain normal visual acuity after treatment had a thicker macula on OCT examination, according to Liu et al.[15] Thus, macular involvement in anisometropic amblyopia seems to be a potential source of treatment resistance. Our patient's medical history and records about the treatment of amblyopia were inadequate. More investigation is needed to confirm the impact of amblyopia treatment on macular thickness.

According to our research findings, neither strabismic nor anisometropic amblyopia was associated with a statistically significant difference in the thickness of the macular or peripapillary RNFL between normal healthy eyes and opposite eyes with amblyopia.

Also reported in earlier researches, majority of writers have presented findings that are comparable to our study.[16–18] Patients with hyperopic anisometropic amblyopia showed a considerably higher RNFL thickness according to Yoon et al.'s report on OCT examination.[14] Kee et al. found that in comparison to strabismic amblyopia, anisometropic amblyopia had a much thicker RNFL.[18] In our study we found that in anisometropic amblyopia group, the average thickness of the peripapillary RNFL was more as compared to strabismic amblyopia group but this difference in thickness was not statistically significant.

It has been noted that refractive error influences RNFL thickness measurement by OCT.[19] RNFL thickness has positive correlation with refractive error.[20] To lessen the influence of refractive errors on thickness of RNFL thickness, we excluded the individuals with myopia and hypermetropia of 5 diopters or more in each eye from our study.

In comparison to the control group, the Parkinsons disease (PD) group's mean for the average, superior, and inferior RNFL thickness was noticeably smaller. In comparison to the control group, the PD group's mean for the average, central, outer superior, outer inferior, and outer nasal macular thickness was noticeably smaller.[21] However we didn't evaluate parkinson's disease which may be a confounding factor in our research. Hence it is advisable to consider this factor to eradicate the maximum number of confounding factors which may hider your effective results.

According to a study[22], alcohol is a possible risk factor influencing RNFL and macular thickness, as evidenced by the substantial correlation between increased alcohol consumption and thinner RNFL and macular thickness.

In our study, we were unable to do subgroup analysis based on anisometropia type and deviationas there were less number of individuals involved, which is limitation of our study. The absence of a control group comprising patients with anisometropia or strabismus with absence of amblyopia was another limitation in our research.

Our findings indicate that the maculae of anisometropic amblyopic eyes were significantly thicker than those of the corresponding normal fellow eyes. On the other hand, there was no statistically significant increase in the macular thickness of eyes with amblyopia having strabismus. Moreover, it was discovered that amblyopia had no effect on the thickness of the peripapillary RNFL in both groups. A contentious and disputed issue is retinal involvement in amblyopia. Further research is required to identify changes in retina in amblyopia and determine whether involvement of retina influences the responsiveness to amblyopia therapy.

CONCLUSION

According to our research, compared to other normal eyes, the anisometropic amblyopic eyes were thicker in the macular region, and this difference in macular thickness was statistically significant. Eyes with amblyopia having strabismus did not exhibit a noticeable significant increase in macular thickness statistically. Furthermore, it was found that neither group's peripapillary RNFL thickness was impacted by amblyopia.

Authors Contribution:
Syed Amir Hamza: Concept & design of study, final approval of version
Maria Sultan: Drafting, critical review, final approval of version
Maleeha Safdar Ali: Data analysis, final approval of version
Muhammad Tariq: Data analysis final approval of version

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