Article ▸ # Optical Coherence Tomography (OCT) Parameters in Nepalese Children with Anisometropic Amblyopia and their Relationship with Refractive Error

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ABSTRACT

Background: To date, there are several studies which compare RNFL and macular thickness amongamblyopic and normal eyes and the literature have shown varied results. We aimed to compare the Optical Coherence Tomography (OCT) Parameters in Nepalese Children with Anisometropic Amblyopia, compare our findings with that of other studies andestablish its Relationship with Refractive Error.

Case Report: A total of 115 children (69 males and 46 females) diagnosed with anisometropic amblyopia (either unilateral or bilateral) were enrolled in the study. All children were evaluated for RNFL thickness, macular thickness and macular volume by SD-OCT in amblyopic and fellow eyes for comparison. The amblyopic group was then separated into two groups: Unilateral Amblyopia and Bilateral Amblyopia groups. The mean RNFL and macular parameters were then compared within these groups and with the Normal Control group using ANOVA. The OCT parameters of the amblyopic eyes were furthercorrelated with the Spherical equivalent refractive error using Pearson correlation coefficient.

Results: The mean age of the amblyopic children was 11.4±3.15 years and control group was12.33± 3.24 years. The mean RNFL thickness, macular thickness and macular volume of the amblyopic eyes were slightly thicker in comparison with normal control eyesexcept for the RNFL thickness in the temporal quadrant where it was slightly thinner. The global RNFL thickness, mean macular thickness and the mean macular volume were 104.20 ± 23.12 µm, 266.39±42.12µm and 8.54±0.80 mm3 respectively inamblyopic eyes and 101.61±18.22 µm, 260.30±29.41 µm and 8.51±.87 mm3 in control eyes. The results were however statistically not significant. The RNFL parameters, the macular thickness and volume all were positively correlated with the spherical equivalent refractive error in the amblyopic eyes with statistically significant values.

Conclusions: Amblyopia is not associated with a change in RNFL thickness, macular thickness or macular volume in Unilateral or Bilateral amblyopia. These OCT parameters were seen to positively correlate with the mean spherical equivalent refractive error in amblyopic eyes.

Keywords: amblyopia, anisometropia, macular thickness, optical coherence tomography, refractive error, retinal nerve fiber layer thickness

Introduction

Amblyopia literally means "dullness of vision" (from the Greek am-blyos—dull; opia, from the stem ops—vision) and is defined as a decrease of best-corrected visual acuity in one or both eyes without any organic abnormality of the globe secondary to visual deprivation or abnormal binocular interaction.[1,2] The incidence of amblyopia varies between 0.5% and 3.5%.[3] In the context of Nepal, the prevalence of amblyopia examined over a five-year period in a tertiary eye care center was found to be 0.7%.[4] The three major subtypes of amblyopia are strabismic, refractive, and form-vision deprivation. The amblyopic eye is suppressed functionally, resulting in a loss of binocular function at the level of the binocular neurons in the visual cortex.[5,6]

Although the eye is believed to be structurally normal in amblyopia, several studies on humans and animals have revealed that, during the neonatal period, visual deprivation has an effect on the growth of cells in the lateral geniculate body and the visual cortex.[7]

Histologic examinations of the lateral geniculate nucleus (LGN) in animal models have revealed cell shrinkage in the layers of the LGN that receive stimuli from the amblyopic eye, with corresponding changes in the visual cortex.[8-10] Wiesel and Hubel, in their study with infant cats and monkeys, revealed that deprivation of visual stimulation via unilateral lid suture induced anatomical and electrophysiological changes of the lateral geniculate body and the visual cortex.[11] Histologic study of the LGNs from a human amblyopic brain have also shown similar findings.[10,12]

The involvement of the retina in amblyopia is, however, not clear. Some studies (Ikeda et al. and Chino et al.), in animal models with artificially induced amblyopia, report retinal ganglion involvement,[13,14] while another study by Cleland et al.[15] did not find any abnormality in the spatial resolution of ganglion cells. In humans, some researchers reported amblyopes to have a reduced electroretinogram to pattern stimuli,[16] while others observed no pattern ERG deficit in them.[17] Baddini-Caramelli et al.[7] and Wiesel and Hubel[11] reported that in humans, the ipsilateral lateral geniculate body that developed for the amblyopic eye showed severe atrophy; however, alteration of the anatomical structure of the retina was not found.

Optical coherence tomography (OCT) is a noninvasive, noncontact optical imaging technique for high-resolution cross-sectional tomographic imaging of the retina and the optic nerve head.[18] There are several studies that compare retinal nerve fiber layer (RNFL) and macular thickness among amblyopic and normal eyes, with varied results. Some studies have reported a thicker RNFL and thicker macula in amblyopic eyes, whereas some have reported no change in macular or RNFL thickness compared to normal eyes.

We aimed to determine and to compare RNFL thickness, macular thickness, and macular volume among Nepalese children with unilateral or bilateral amblyopia and normal fellow eyes from children with unilateral amblyopia.

Methods

This was a hospital-based cross-sectional study conducted among children visiting the pediatric eye outpatient department (OPD) of B.P. Koirala Lions Centre for Ophthalmic Studies, a tertiary eye care Centre in Nepal, from January 2014 to December 2015. A total of 115 children (69 males and 46 females) diagnosed with anisometropic amblyopia (either unilateral or bilateral) were enrolled. Informed verbal consent from the parents was obtained. The experiment followed the tenets of Declaration of Helsinki and was approved by the Ethics committee at the Department of Ophthalmology, Institute of Medicine, Maharajgunj, Kathmandu.

A comprehensive eye exam was performed, including best-corrected visual acuity, slit-lamp examination, intraocular pressure assessment, extra ocular motility assessment, cycloplegic refraction, and dilated fundus examination. Visual acuity testing was performed with the Snellen chart. Children with organic eye disease were excluded from the study (including history of intraocular surgery, laser treatment, cataract, glaucoma, optic neuritis, or retinal disorders). The patients who were too young to cooperate for examination were also excluded.

Amblyopia was defined as an inter-ocular best-corrected visual acuity difference of two or more lines using the Snellen chart at six meters. Anisometropia was defined as a spherical equivalent difference between the two eyes of 2 diopters (D) or more, with no heterotropia on the alternate cover test. The anisometropic group included myopic and hyperopic anisometropic amblyopic participants. Patients with an inter-ocular astigmatism difference of more than 2 D were excluded from the study since the presence of a large amount of astigmatism may enhance magnification effects and subsequently differences in RNFL thickness measurements.

OCT-Spectralis (SD-OCT; Heidelberg Engineering, Germany with software version 6.0.14) was used to obtain two sets of structural measurements, the RNFL thickness and the macular parameters in each eye. All of the OCT measurements were performed by the first author after full dilation of the pupil on the first visit.

For RNFL thickness, we employed a fast RNFL scan (three consecutive 360 degree circular scans) around the optic disc centered at the optic nerve head. Each circular scan was composed of 128 A-scans, for a total of 768 A-scans. The entire circular area scanned was divided into four equal pie sections: superior, inferior, nasal, and temporal. The central circular area provided the global NFL for each eye.

To obtain a map of retinal thickness at the macula, fast scan protocol was used with a resolution of 30 x 25 mm. The fast scan protocol consisted of 768 total A-scans. The results were reported as average thickness and volume within four quadrants in each of two concentric circles outside the foveal central circle of 1 mm diameter. The outer circle diameters were 3 mm and 6 mm, respectively.

Statistical analyses were done with the SPSS software version 20.0. Paired sample t-test or independent sample t-test was used to determine whether differences between values of the amblyopic eyes and fellow eyes were significant. The amblyopic group was further separated into two groups: unilateral and bilateral. The mean RNFL and macular parameters were then compared within these groups and with the normal control group of eyes using Tukey test, analysis of variance (ANOVA), and a post-hoc procedure.

The correlation between RNFL parameters and macular parameters with mean spherical equivalent refractive error was evaluated using Pearson's correlation coefficient. A P value of less than 0.05 was considered statistically significant.

Results

A total of 115 amblyopic eyes (69 male and 46 female) were included in the study. The fellow eyes of unilateral amblyopic children were taken as controls (N=63; 39 males and 24 females). The mean age was 11.4 ± 3.15 years; that of the control group was 12.33 ± 3.24 years. There were seven children on whom the OCT could not be performed due to unstable eye movements and lack of proper fixation and who were excluded from the study.

The VA of the amblyopic eyes ranged from 20/40 to 20/200. The mean spherical equivalent refractive error in the amblyopic group was +0.71 +/- 4.22 D and in the control

Table 1: RNFL Thickness and Macular Parameters in Amblyopic and Fellow Eyes

Parameter	Amblyopic Eyes	Fellow Eyes	P Value
RNFL Thickness (μm)			
Global	104.20 ± 23.12	101.61 ± 18.22	0.44
Nasal	78.46 ± 36.61	71.76 ± 20.73	0.18
Temporal	76.67 ± 19.86	78.11 ± 19.90	0.64
Superior	127.40 ± 39.69	127.21 ± 25.58	0.97
Inferior	133.18 ± 26.58	132.27 ± 24.84	0.82
Macular Parameters			
Macular Thickness (μm)	266.39 ± 42.12	260.30 ± 29.41	0.31
Macular Volume (mm³)	8.54 ± 0.80	8.51 ± 0.87	.085

group was +0.11 +/- 2.34 D. The range of refractive error in the amblyopic group was -11.00 D to +6.75 D and in the control group was -11.00 D to +5.00 D.

The mean RNFL thickness of the amblyopic eyes was slightly thicker in comparison to normal control eyes except for the temporal quadrant, where it was slightly thinner. The results were, however, not statistically significant (P> 0.05). Similarly, the mean macular thickness and macular volume were also found to be slightly thicker in the amblyopic eyes than the control eyes, but these results were also not statistically significant (P> 0.05). The mean RNFL thickness in all quadrants, the mean macular thickness, and the mean macular volume in the amblyopic and normal eyes are shown in Table 1.

The amblyopic group was separated into two groups: unilateral amblyopia and bilateral amblyopia. The mean RNFL and macular parameters were then compared within these groups and with the control group using ANOVA. The mean age of the amblyopic children in the unilateral amblyopia group was 12.18 ± 3.17 years (N = 61), in the bilateral amblyopia group was 10.56 ± 2.82 years (N = 54), and in the control group was 12.33 ± 3.24 years (N = 61). There was no statistically significant difference between mean RNFL thicknesses in all quadrants and macular parameters (thickness and volume) between the two amblyopic groups, as well as in comparison to the normal control eyes (P>0.05). The mean RNFL and macular parameters among the unilateral amblyopia, bilateral amblyopia, and the control groups are shown in Table 2.

We analyzed our OCT parameters of the amblyopic eyes in order to check the correlation with the spherical equivalent refractive error using Pearson correlation coefficient. The results are shown in Table 3. The RNFL parameters were positively correlated with the spherical equivalent refractive error (Table 3, Figure 1). The correlation was statistically significant for all quadrants except for the temporal quadrant, where it was not significant. The macular thickness and volume were also positively correlated with the spherical equivalent refractive error in the amblyopic eyes with statistically significant values (P<0.05) (Table 3, Figure 2).

Table 2: RNFL Thickness and Macular Parameters in the Three Groups

Parameter	Bilateral Amblyopia (N=54)	Unilateral Amblyopia (N=61)	Control Eyes (N=63)	P Value
RNFL Thickness (μm)				
Global	104.33 ± 24.98	104.10 ± 21.56	104.10 ± 21.56	0.74
Nasal	74.55 ± 30.91	81.91 ± 40.95	81.91 ± 40.95	0.19
Temporal	77.70 ± 22.44	75.75 ± 17.40	75.75 ± 17.40	0.78
Superior	128.54 ± 48.79	126.40 ± 29.79	126.40 ± 29.79	0.94
Inferior	135.06 ± 25.67	131.52 ± 27.46	132.27 ± 24.84	0.75
Macular Parameters				
Macular Thickness (μm)	266.98 ± 48.69	265.86 ± 35.71	260.30 ± 29.41	0.59
Macular Volume (mm³)	8.46±0.91	8.59±0.68	8.51±.87	0.67

Table 3: Relationship between OCT Parameters and Spherical Equivalent of Amblyopic Eyes

Parameter	Pearson Correlation	P Value
RNFL Thickness		
Global	0.28	<0.05
Nasal	0.28	<0.05
Temporal	0.03	0.69
Superior	0.15	<0.05
Inferior	0.34	<0.05
Macular Parameters		
Macular Thickness	0.30	<0.05
Macular Volume	0.18	<0.05

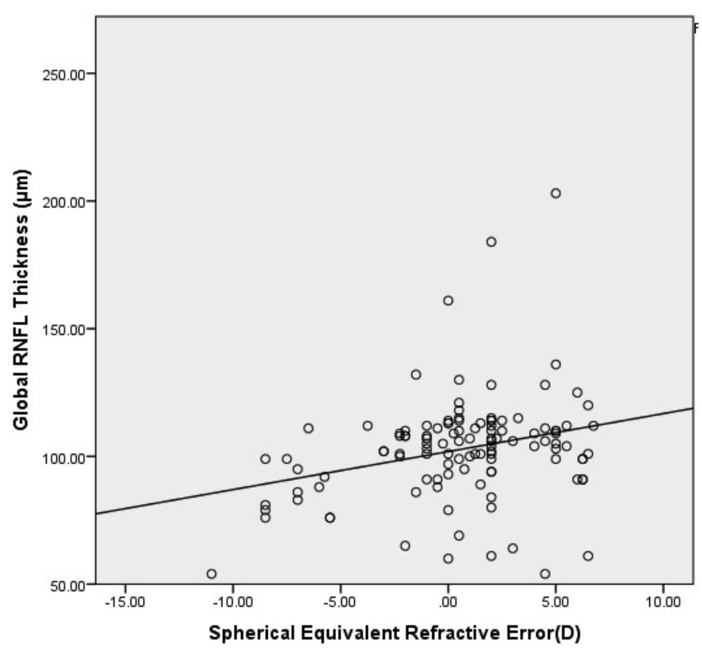

Figure 1. *Relationship between global RNFL thickness and mean spherical equivalent refractive error*

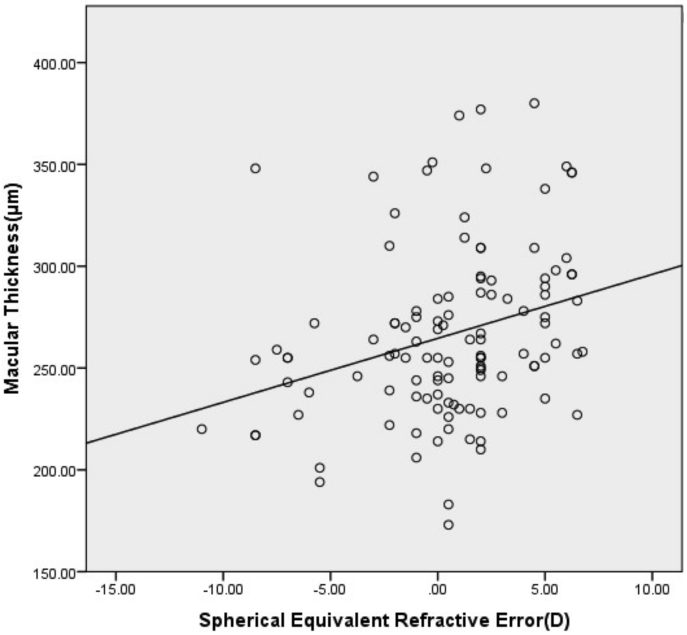

Figure 2. *Relationship between mean macular thickness and mean spherical equivalent refractive error*

Discussion

There are several studies that incorporate the use of SD-OCT in examining RNFLs and the macula in amblyopic eyes; however, this has been the first study of its kind done in Nepal to analyze the RNFL thickness and macular parameters in comparison to fellow normal eyes of amblyopic children.

In this study, we observed no statistically significant difference between the RNFL thicknesses of the amblyopic eyes in comparison to normal eyes in all quadrants. We further separated the amblyopic group in two categories, unilateral and bilateral, to see any changes in our previous results. While comparing the mean RNFL parameters within these groups and with the control eyes, our results were consistent with no statistical difference. We compared our findings with similar studies done in different parts of the world. Andalib et al.[19] reported that there was no significant difference between amblyopic and fellow eyes in peripapillary nerve fiber layer thickness in either strabismic or anisometropic amblyopia. Yakar et al.,[20] who studied 30 eyes of anisometropic adults, yielded results that were consistent with those of our study with no statistically significant changes in RNFL thickness at all quadrants. Al-Haddad et al.[21] also reported the mean RNFL thickness to be similar in amblyopic (95.4 mm) and fellow eyes (94.0 mm) of 45 patients. Similarly, Irkeç et al.,5 in their assessment of RNFL thickness by means of scanning laser polarimetry (GDx), found no difference between the two eyes in patients with unilateral amblyopia.

However, there were a few studies with different findings compared to ours. Yoon et al.[3] reported that OCT assessment yielded a significantly greater RNFL thickness in patients with hyperopic anisometropic amblyopia. Kee et al.[22] demonstrated a significantly thicker RNFL in anisometropic amblyopia compared to strabismic amblyopia.

Yen et al.[23] studied 18 patients with refractive amblyopia, 20 patients with strabismic amblyopia, and 17 patients with anisometropia without amblyopia using OCT and found that mean RNFL thickness of the amblyopic eyes (142.2 ± 18.6 μm) was thicker than the fellow eyes (129.7 ± 18.5 μm) in patients with refractive amblyopia ($p<0.001$). They suggested that the process of postnatal reduction of ganglion cells requires sharply focused objects as appropriate stimuli, and refractive amblyopia affects the process of post-natal reduction of ganglion cells, so the RNFL thickness measured in the amblyopic eyes was greater than the normal eyes. Similarly, Yoon et al.3 reported that RNFL thickness in amblyopic eyes was significantly thicker than in normal eyes in subjects with hyperopic anisometropic amblyopia.

Our results showed slightly greater RNFL thickness in the amblyopic eyes, but the findings were not statistically significant in comparison to normal fellow eyes. The results from the literature are confusing, which may be due to variation in the study designs; differences in OCT devices used; number of subjects studied; and the subjects' age, race, and type of amblyopia included. We believe that amblyopia is a functional loss of vision and cannot be attributed to an organic cause. The RNFL involvement in the amblyopic process is thus controversial.

The macular thickness and macular volume were found to be slightly thicker in amblyopic eyes than in control eyes, the results being statistically insignificant. While comparing the macular parameters in the separate groups of unilateral and bilateral amblyopia, we found that the mean macular thickness was in the order bilateral > unilateral > controls, and macular volume in the order unilateral > controls > bilateral); the results were however neither statistically nor clinically significant.

Yoon et al.[3] evaluated 31 patients with hyperopic anisometropic amblyopia and found no significant difference in macular thickness among amblyopic and fellow eyes. Similarly, Kee et al.,[22] in their study of 26 children with unilateral amblyopia due to anisometropia or strabismus, reported the average thickness of the fovea being 157.4 μm in normal eyes and 158.8 μm in amblyopic eyes. The difference between the two groups was not statistically significant ($p=0.551$).

By contrast, Andalib et al.[19] studied 25 monocular strabismic and 25 anisometropic amblyopic eyes and found a thicker macula in anisometropic amblyopic eyes, but the increase of macular thickness in strabismic amblyopic eyes was not significant. ($p=0.07$). Similarly, Al-Haddad et al.21 reported that the mean macular thickness was significantly increased in amblyopic (273.8 μm) vs. fellow eyes (257.9 μm). This difference remained significant in the anisometropic group but not the strabismic group.

In our study, the mean macular thickness and macular volume in amblyopic eyes were 266.39 ± 42.12 μm and 8.54±0.80 mm3, respectively, whereas in normal eyes they were 260.30 ± 29.41 μm and (8.51 ± 0.87) mm3, respectively.

Though the amblyopic eyes had slightly greater macular thickness and volume, the results were not statistically significant, indicating that the amblyopic process does not have significant effect on the macula.

Refractive error has been shown to affect the RNFL thickness with OCT.[24] In our study, the RNFL thickness in all quadrants and the macular parameters (thickness and volume) were positively correlated with the mean spherical equivalent refractive error (Table 3). The Pearson correlation coefficients for the global RNFL and macular thickness were 0.42 and 0.31, respectively, with $P<0.05$ for both. The findings were statistically significant in all quadrants. This indicates that with the increase in refractive error (from minus to plus), the RNFL thickness (in all quadrants), macular thickness, and macular volume increases.

Our findings were consistent with the study by Salchow et al.[25] They showed that the RNFL thickness is positively correlated with refractive error (RNFL being thicker in more hyperopic eyes). The mean RNFL thickness was seen to increase by approximately 1.7 µm for each diopter of hyperopia.

In the study performed by Kremser et al.,[26] of 129 eyes of 79 healthy persons, a reduction of retinal thickness at the fovea and posterior pole, with increase of myopia, was found. They reported that the axial elongation that causes stretching of the ocular tissues with the progression of myopia causes significant thinning of the retina.

Budenz et al.[27] found that the retinal nerve fiber layer thickness also was associated significantly with axial length: the longer the eye, the thinner the mean RNFL. For every 1 mm increase in axial length, RNFL thickness was thinner by approximately 2.2 µm. Similarly, when refractive error was used in the linear regression model instead of axial length, the regression coefficient for refractive error was significant as well, with mean RNFL thickness decreasing by approximately 0.9 µm for every 1 D change in SE power toward greater myopia.

Lam et al.,[28] using Stratus OCT fast macular thickness map protocol, showed a negative correlation between outer and overall macular thickness and axial length. Refractive error and axial length had opposing effects on macular thickness and volume in their study.

Our study corroborates the trend of these studies, and thus we conclude that myopic eyes result in thinner RNFL and macular parameters, which can be explained by the axial elongation causing stretching of the ocular tissues, consequently resulting in thinner retina. However, the thickening of retinal layers with increase in hyperopia still needs to be studied in detail, collaborating with histological studies to determine the underlying cause. Since OCT is an optical method, it is logical that refractive error could affect its measurements. Thus, a through systematic study needs to be done to define the limits of reliability of OCT measurement with refractive errors.

There are some limitations to our study. We did not include a control group of normal children to compare OCT parameters with unilateral and bilateral amblyopic children; the retinal thickness of the sound eyes may not accurately reflect normal retinal thickness. Similarly, we did not include strabismic children with amblyopia. Comparison of OCT parameters among strabismic, anisometropic, and normal children could provide further insight to our findings. We have correlated mean spherical refractive error of amblyopic children with OCT parameters and compared our results to those of studies done in normal children (non-amblyopes). Although the trend appears similar in both cases, the correlation established in a larger group of normal children compared to that of studies of normal children across other countries would be beneficial.

Conclusion

Our results indicate that amblyopia is not associated with a change in RNFL thickness, macular thickness, or macular volume in unilateral or bilateral amblyopia. The OCT parameters (RNFL thickness, macular thickness, and macular volume) were seen to correlate positively with the mean spherical equivalent refractive error in amblyopic eyes. The variable results from the literature indicate the involvement of RNFL and macula to be controversial in the amblyopic process. Further studies, including a larger study group along with histological sections, might be helpful to confirm these findings.

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