MACULAR AND PERIPAPILLARY RETINAL NERVE FIBER THICKNESS IN UNILATERAL AMBLYOPIC EYE

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ABSTRACT

Amblyopia is the most common cause of monocular visual impairment in both children, and young to middle-aged adults, affecting 2%–5% of the general population. The objective of this study was to compare the peripapillary nerve fiber thickness and macular thickness in amblyopic eyes, fellow eyes and normal control eyes using spectral domain optical coherence tomography. This was a cross-sectional observational study conducted at R M Kedia Eye Hospital, Birgunj, Nepal from February 2020 to July 2020. Pediatric patients with unilateral amblyopia (anisometropic amblyopia, strabismic amblyopia or both) among the age group of 6-18 years attending pediatric department of RM Kedia Eye Hospital were enrolled for the study. All patients underwent a full ophthalmological assessment, including visual-acuity testing, anterior segment evaluation with Topcon slit lamp and fundus examination with Volk +90D lenses. All statistical analysis was done in SPSS V. 20. The average peripapillary retinal nerve fiber layer thickness was 120.6 µm (SD=14.6 µm) in the amblyopic eye, 118.1 µm (SD=15.6 µm) in the fellow eye and 113.2 µm (SD=9.4 µm) in the normal eye (p=0.104) respectively. The average macular thickness was 298.6 µm (SD=19.1 µm) in the amblyopic eye, 296.9 µm (SD=11.2 µm) in the fellow eye and 303 µm (SD=12.4 µm) in the normal eye (p=0.260) respectively. In conclusion, our study did not find any significant difference in the peripapillary retinal nerve fiber thickness or macular thickness when compared between amblyopic eyes, fellow eyes, gender and age matched normal eyes.

KEYWORDS

Amblyopia, spectral domain OCT, Retinal nerve fiber thickness, macular thickness

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INTRODUCTION

Amblyopia is a deficiency of form sense resulting in the reduction in visual acuity of greater than two lines between the eyes or an absolute reduction in acuity below 6/9 in either eye, associated with decrements in visual processing, accommodation, motility, spatial perception or spatial projection.[2] It is the most common cause of monocular visual impairment in both children, and young to middle-aged adults, affecting 2–5% of the general population.[1]

The types of amblyopia in frequency is strabismus (about 50%), usually esotropia in infancy or early childhood. The second type is anisometropia (approx. 17%), followed by a combination of strabismus and anisometropia (about 30%), and finally the least frequent cause is visual deprivation (≤3%) although this one may result in severe amblyopia.[3]

Yen *et al*[4] has hypothesized that there is a measurable increase in retinal nerve fiber layer thickness in amblyopic eyes as amblyopia may affect the postnatal maturation of the retina, including the postnatal reduction of ganglion cells.

Although most of the deficit is believed to be the result of impairment of cortical development, changes have been seen in the lateral geniculate nucleus of nonhuman primates and humans after visual deprivation amblyopia during the neonatal period.[5,6]

Some eyes diagnosed with amblyopia may also have abnormalities in the afferent visual system anterior to the striate cortex, including the retina, retinal ganglion cell, retinal nerve fiber layer (RNFL), optic nerve, and lateral geniculate body of the thalamus.[7]

Optical coherence tomography (OCT) of the peripapillary optic nerve is a non-invasive test in which the thickness of the RNFL is measured. RNFL thickness correlates with disc area in children.[8]

OCT has been used to compare the RNFL of amblyopic and fellow eyes of patients of varied ages.[4, 9] One study found a small statistically significant difference between eyes for anisometropic amblyopia and no difference for strabismic amblyopia.[4] Another study found no difference but had insufficient numbers to evaluate subgroups by cause.[9]

Spectral-domain OCT (SD-OCT) (also called Fourier-domain OCT) is a new-generation OCT technology that can provide ultrahigh image resolution at an ultrahigh rate. As distinct from the first-generation TD-OCT, SD-OCT uses a spectrometer instead of a photodetector. The depth data are obtained by analyzing the interference pattern, which is formed in the spectrum of the rays reflected from the ocular tissues. Then, the data from the spectrometer are exposed to the Fourier transformation to generate a 3-dimensional image.[10-14]

SD-OCT measurements of macular thickness and volume as well as peripapillary RNFL thickness in children was first reported by Turk *et al*.[15]

In Nepal, comparison between the OCT findings and amblyopia has not been reported till date. Hence this study will provide a baseline report of peripapillary retinal nerve fiber layer thickness and macular thickness in amblyopic patients.

MATERIALS AND METHODS

This was a comparative cross-sectional observational study conducted at R M Kedia Eye Hospital, Birgunj, Nepal from February 2020 to July 2020. All cases of pediatric amblyopia were included in the study. Fellow eyes and normal eyes were taken for comparison with affected eyes. Ethical clearance letter was taken from Nepal Health Research Council. Written informed consent was obtained from parents/guardians of each participating minors. Amblyopia was defined as a deficiency of form sense resulting in the reduction in visual acuity of greater than two lines between the eyes or an absolute reduction in acuity below 6/9 either eye, associated with decrements in visual processing, accommodation, motility, spatial perception or spatial projection. Unilateral amblyopia was defined as BCVA of 6/9 in either eye or as an interocular difference of two lines or more. Severe amblyopia was defined as BCVA of <6/36, moderate amblyopia as BCVA of < 6/12 to 6/36 and mild amblyopia as BCVA of 6/9 to 6/12. Anisometropia was defined as refractive difference of >1.50 D between the eyes.

Pediatric patients with unilateral amblyopia (anisometropic amblyopia, strabismic amblyopia or both) among the age group of 6-18 years attending pediatric department of RM Kedia Eye Hospital were enrolled for the study.

Inclusion criteria included children born at term (≥37 weeks gestational age), with normal birth weight (≥2500 g) with best-corrected visual acuity over 0.8 (on the Snellen scale) for both eyes with refractive error (in spherical

equivalent) within ±5.00 diopters, intraocular pressure ≤21 mm Hg in eyes, cup-to-disc (C/D) ratio ≤0.4 and C/D ratio asymmetry ≤0.2 between the 2 eyes without any retinal or optic disc anomaly. Patients with neurological diseases, ocular conditions such as glaucoma, retinal disorders and nystagmus, patients not cooperating for SD-OCT examination and patients not providing consent were excluded.

All patients underwent a full ophthalmological assessment, including visual-acuity testing with tumbling E chart, evaluation of ocular alignment, anterior segment examination with Topcon slit lamp and fundus examination with Volk +90D lens after dilatation of pupil. The Best corrected visual acuity was transformed to a logarithmic scale (logMAR) for statistical analysis. Cycloplegic refraction was performed using retinoscopy 60 min after the instillation of 1% cyclopentolate and 0.5% tropicamide. The best corrected visual acuity was converted to logarithmic scale (LogMAR) for statistical analysis. Cycloplegic refraction was performed using retinoscopy 60 minutes after the instillation of 1% cyclopentolate and 0.5% tropicamide. Axial length measurement (Nidek ECHO SCAN US 800) and intraocular pressure measurement (using Applanation tonometer in cooperative patients) were conducted.

The Spectralis OCT device (Heidelberg Engineering, Dossenheim, Germany were used for the SD-OCT assessment and were performed by the same experienced technician in the dilated pupil. The macula and peripapillary RNFL thickness was analyzed and automatically calculated by SD-OCT device. A fast macular map scan protocol was used to scan the macular thickness. It consisted of 6 consecutive 6-mm radial scans centered on the fovea with each scan 30 degree apart around the fovea. Data for macular retinal thickness were displayed in 3 concentric circles, with radii of 1 mm (foveal central), 3 mm (inner circle), and 6 mm (outer circle). Retinal thickness was defined as the distance between the reflection at the vitreoretinal interface and the anterior boundary of the reflective layer corresponding to the retinal pigment epithelium and choriocapillaris. The macular thickness parameters were divided into central (1 mm), inner circle (3 mm), outer circle (6 mm), and average thickness. The peripapillary RNFL thickness parameters were divided into temporal quadrant thickness (90 degrees), temporal superior quadrant thickness (45 degrees), temporal inferior quadrant thickness (45 degrees), nasal quadrant thickness (90 degrees), nasal superior quadrant thickness (45 degrees), nasal inferior quadrant thickness (45 degrees), and average thickness (360 degrees). After the exposures, the non-centered scans and the scans with signal strength <15 dB were excluded from the study.

The results obtained from the SD-OCT were expressed as mean +/- standard deviation. Visual acuity data were converted to logarithms of the minimal angle of resolution (logMAR) for statistical calculation and analysis.

Data was entered in MS Excel. All statistical analysis was done in SPSS V. 20. Descriptive statistics such as frequencies, percentages Mean (SD) etc were determined. For the independent continuous variable, if the data followed normality assumption independent t test was used and if the data did not follow normality assumption Mann Whitney U test was used. P-value <0.05 was considered as statistically significant.

RESULTS

Thirty amblyopic patients (23, 76.7% males and 7, 23.3% females) were recruited in the study with average ± SD age of 14.0 ± 3.1 (range: 6-18) years. Twenty patients (66.7%) had anisometropic amblyopia, 4 (13.3%) had strabismic amblyopia and 6 (20%) had a mixed-type amblyopia. Out of twenty anisometropic amblyopia patients, 17 (85.0%) had hypermetropic anisometropia and 3 (15.0%) had myopic anisometropia. Fifteen patients (50%) had severe amblyopia, 13 (43.3%) had moderate amblyopia and 2 (6.7%) had mild amblyopia.

Fellow eyes and normal eyes were also taken for comparison with affected eyes. There were no statistically significant difference in between right and left eyes of normal participants in terms of visual acuity (p=0.841), axial length (p=0.981), macula average (p=0.916) and RNFL thickness (p=0.676). Thirty normal eyes (23 male eyes, 7 female eyes) were selected randomly

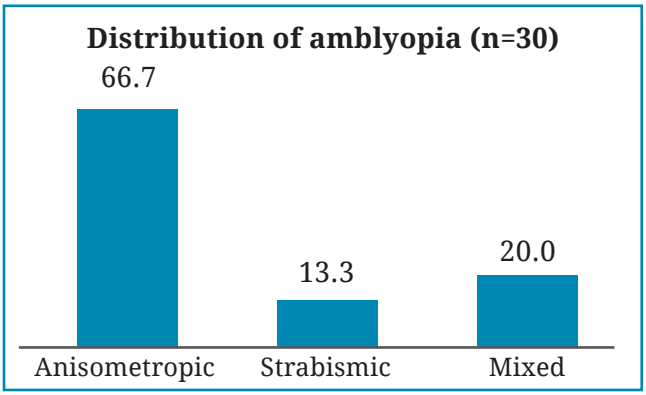

Fig. 1: Distribution of Amblyopia

Table 1: Topographical measurements of amblyopic eyes, fellow eyes and normal eyes.

		Affected Eye	Fellow Eye	Normal	Overall P value	Ae vs FE P value	N vs AE P value	N vs FE P value
LOGMAR AE	Median (Range)	1.3 (0.6 - 1.8)	0 (0 - 0.8)	0 (0 - 2)	<0.001	<0.001	<0.001	.299
SE	Median (Range)	4 (-4 - 4)	0 (-1 - 1.3)	0 (-2.8 - 0)	<0.001	<0.001	<0.001	.002
AXIAL LENGTH	Mean (SD)	21.6 (1.3)	22.7 (1.1)	23.5 (1)	<0.001	.002	<0.001	.021
M-Average	Mean (SD)	298.6 (19.1)	296.9 (11.2)	303 (12.4)	.260	1.000	.751	.338
SN	Mean (SD)	139.3 (25)	126.9 (36.6)	124 (27.6)	.121	.347	.161	1.000
ST	Mean (SD)	136.8 (20.4)	150.5 (23.5)	141.1 (22)	.052	.053	1.000	.300
IN	Mean (SD)	136.1 (23.3)	127.5 (31.7)	113.3 (17.9)	.003	.561	.002	.090
IT	Mean (SD)	152 (25.8)	148.1 (31.4)	153.2 (25)	.757	1.000	1.000	1.000
T	Mean (SD)	71.5 (11.4)	76.3 (12.5)	75.2 (14.8)	.324	.457	.816	1.000
N	Mean (SD)	87.7 (17.6)	79 (20.6)	72.4 (16.7)	.007	.206	.005	.496
M-RNFL-Average	Mean (SD)	120.6 (14.6)	118.1 (15.6)	113.2 (9.4)	.104	1.000	.111	.496

to match the distribution of gender and age of the affected eye for better comparison. The average ± SD age of normal group was 14.0 ± 3.1 (range: 6-18) years which was not statistically significant with mean age of participants of the affected eye (p=0.71).

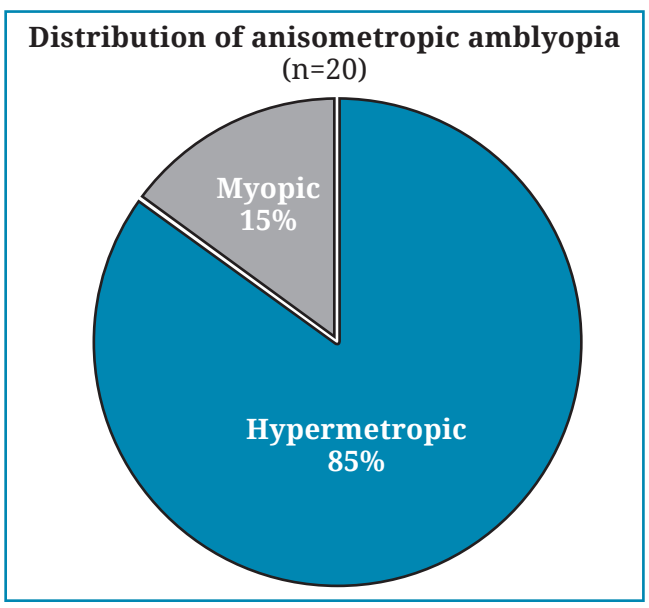

Fig. 2: Distribution of anisometropic amblyopia

Visual acuity in amblyopia ranged from LogMAR 0.6 to 1.8 (median= 1.3), in fellow eye ranged from LogMAR 0.0 to 0.8 (median=0.0) and in normal group ranged from LogMAR 0.0 to 2 (median=0.0) (p <0.001).

The median (range) spherical equivalent was 4D (-4 to 4) in amblyopic eyes, 0D (-1 to 1.3) in fellow eyes and 0D (-0.2 to 0) in normal eyes, p<0.001.

The average peripapillary RNFL thickness was 120.6 µm (SD=14.6 µm) in the amblyopic eye, 118.1 µm (SD=15.6 µm) in the fellow eye and 113.2 µm (SD=9.4 µm) in the normal eye (*p*=0.104).

In anisometropic amblyopia, the average peripapillary RNFL thickness was 120.9µm (SD=13.6µm) in the amblyopic eye and 115.8µm (SD=12.3µm) in the normal eye (*p* = 0.219). Superonasal (SN) and Inferonasal (IN) quadrant was thicker in anisometropic eye in comparison with normal eyes which was statistically significant (p value SN=0.22, IN=0.003)

The average macular thickness was 298.6 µm (SD=19.1 µm) in the amblyopic eye, 296.9 µm (SD=11.2 µm) in the fellow eye and 303 µm (SD=12.4 µm) in the normal eye (*p*=0.260).

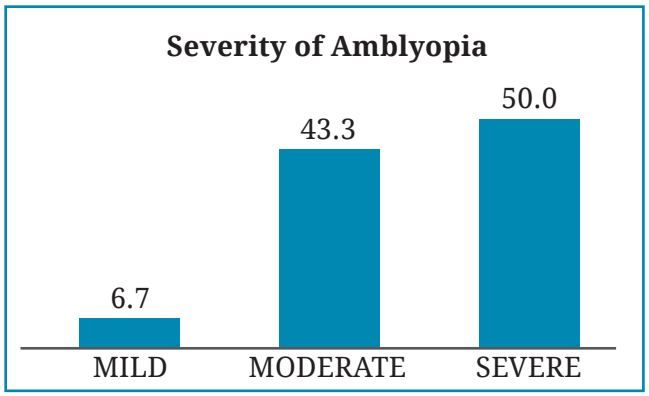

Fig. 3: Severity of amblyopia

Regarding anisometropic amblyopia, the values for the amblyopic and normal eyes were 301.7 µm (SD=17 µm) and 304.3µm (SD 12 µm) (p = 0.575) respectively. The average macular thickness was 298.6 µm (SD=19.1 µm) in the amblyopic eyes, 296.9 µm (SD=11.2 µm) in the fellow eyes and 303 µm (SD=12.4 µm) in the normal eyes (p=0.260).

DISCUSSION

Our study did not find any difference in either peripapillary RNFL thickness or macular thickness when compared between the amblyopic eye and fellow eyes; and also between amblyopic eyes and normal control eyes. The patients presented with anisometropic, strabismic and mixed type of amblyopia and no significant difference between macular thickness and peripapillary RNFL thickness was observed between all these types of amblyopia.

Repka *et al*[9] compared the peripapillary RNFL thickness of sound and amblyopic eyes in a prospective observational case series. Both eyes of seventeen patients (mean age 10.7 years) were imaged. The mean thickness of the sound eye was 109.2 µm (median 112.7) and of the amblyopic eye was 104.2 µm (median 105.0), and the average difference (sound eye less amblyopic eye) was 5.0 µm (median 3.0) (95% confidence interval -2.3, 12.2, P =.17). The difference in nerve fiber layer (NFL) thickness between amblyopic and sound eyes was clinically non-significant like in our study.

Huynh *et al*[16] examined macular and peripapillary retinal nerve fiber layer (RNFL) thickness in amblyopia of 4118 children in the Sydney Childhood Eye Study. Amblyopic eyes had slightly greater foveal minimum thickness than the normal fellow eye (by 5.0 µm; 95% confidence interval 0.1-9.9) with P<0.05. This was more pronounced in 6-year-old children (6.9 µm). Amblyopic eyes also had slightly thicker central macula (1 mm diameter region) but was not statistically significant. Peripapillary RNFL thickness was not significantly different between amblyopic and normal fellow eyes or normal eyes of non-amblyopic children similar to our study.

Altintas *et al*,[17] found no significant differences while comparing the thickness of the RNFL, the macular volume, and the macular thickness of the amblyopic eye with those of the non-amblyopic eye in patients with unilateral strabismic amblyopia using optical coherence tomography (OCT). The mean age was 10.43 years (+/- 4.09 years).

Dickmann et at.[18] examined 30 consecutive patients with spectral domain optical coherence tomography to determine the difference in the retinal nerve fiber layer thickness (RNFLT), macular thickness (MT), and foveal volume (FV) among the amblyopic and the fellow eyes in patients with unilateral amblyopia. There were no significant differences between the amblyopic and sound eyes in FV, MT, and RNFLT.

Repka *et al*[19] compared the peripapillary RNFL thickness of amblyopic and fellow eyes of 37 patients between the age of 7 to 12 years with unilateral strabismic, anisometropic, or combined-mechanism amblyopia in 2009. The mean global RNFL thickness of the amblyopic and fellow eyes was 111.4 µm and 109.6 µm respectively. No significant difference was found between the amblyopic and fellow eye which is similar to our study.

Kee *et al*[20] studied 52 eyes of 26 children with unilateral amblyopia (anisometropia or strabismus) and compared it with fellow eyes and normal eyes. No difference was seen in peripapillary and macular thickness between the amblyopic eye and fellow eye, nor between amblyopic eyes and normal control group.

Yoon *et al*[21] assessed OCT of 31 patients with hyperopic anisometropic amblyopia. It showed significantly thicker RNFL in amblyopic patients (P=0.019), but no statistically significant difference was found in macular retinal thickness (P>0.05).

In a study by Demircan *et al*[22] mean central macular thickness in the hyperopic anisometropic amblyopic eyes was found to be significantly thicker (P=.001) in the group aged 5 to 12 years; but not in case of group aged 13 to 42 years. There was no significant difference in average RNFL thickness in either group.

In our study no significant difference is seen in either macular thickness (P=0.22)

or peripapillary RNFL thickness (P=0.084) among patients with hyperopic anisometropic amblyopia when compared with normal eyes which is similar to many other studies.[23,24]

The peripapillary RNFL thickness in the fellow eye in the current study is 118.1 µm which is similar to the normative data reported by Salchow[25] and associates among similarly aged children, supporting our use of the fellow eye as an appropriate comparison.

Strength of the study is sample size, detailed ocular examination and equal distribution of age and gender of patient between amblyopic and normal group.

The limitation of this study is that the patients enrolled had different types of amblyopia including 66.7% anisometropic amblyopia, 13.3% strabismic amblyopia and 20% mixed-type of amblyopia, so the results cannot be generalized to those with deprivational amblyopia.

In conclusion, our study did not find any significant difference in the peripapillary retinal nerve fiber thickness or macular thickness when compared between amblyopic eyes, fellow eyes, gender and age matched normal eyes. This study also helps to determine the baseline peripapillary retinal nerve fiber thickness and macular thickness among amblyopic and normal pediatric patients in Nepal. Future studies involving pediatric patients with equal number of different types of amblyopic may help to generalize the result in deprivational amblyopia.

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