

Evaluation of Retinal Nerve Fibre Layer and Macular Thickness in Amblyopia

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ABSTRACT

Introduction: Amblyopia is reduced visual acuity in one or both eyes due to abnormal visual development in early part of life. Purpose of this study was to evaluate and compare the retinal nerve fibre layer (RNFL) and central macular thickness (CMT) between amblyopic and fellow (normal) eyes using spectral-domain optical coherence tomography (SD-OCT).

Methods: This was a hospital based, cross-sectional comparative study conducted in the department of Ophthalmology, B.P. Koirala Lions Centre for Ophthalmic Studies (BPKLCOS), Institute of Medicine (IOM), Tribhuvan University Teaching Hospital (TUTH). All consecutive cases of age ≥ 5 years and ≤ 15 years diagnosed with unilateral amblyopia from January 2013 to June 2014 were included in this study. RNFL and macular thicknesses were measured using SD-OCT and compared between fellow eyes.

Results: A total of 32 cases with unilateral amblyopia, 19 with hypermetropic anisometropic, 4 with myopic anisometropic and 9 with strabismic amblyopia were enrolled in the study. The mean age of presentation was 9.75 ± 2.77 years. The mean CMT in amblyopic eyes ($241 \pm 45.27 \mu\text{m}$) was significantly greater than the normal fellow eyes ($233.22 \pm 44.24 \mu\text{m}$), $p = 0.042$. The difference remained significant in hypermetropic anisometropic group but not in myopic anisometropic and strabismic group. The mean RNFL thickness was similar in amblyopic ($104.16 \pm 13.64 \mu\text{m}$) and fellow eyes ($104.03 \pm 13.06 \mu\text{m}$).

Conclusions: The CMT was significantly greater in the amblyopic eyes than the normal fellow eyes. There was no significant difference in the RNFL thickness between the amblyopic and normal eyes.

INTRODUCTION

Amblyopia is decrease in best-corrected visual acuity in one or both eyes due to abnormal binocular interaction or visual deprivation during visual immaturity in early life in the absence of structural abnormality of the eye or the posterior visual pathways.^{1,2} Prevalence is approximately 3% and may vary depending on the population studied and the definition used.³

The causes of amblyopia include strabismus, anisometropia, high refractive errors, opacities in ocular media, high astigmatism or a combination of two or more etiologies in the same patient.

In a retrospective review of children diagnosed with amblyopia in the Nepal Eye Hospital (NEH) amblyopia was found in 0.7 % and anisometropia was the most common cause followed by ametropia in 29%, strabismus in 14%, mixed (strabismus and anisometropia) in 3% and stimulus deprivation in 1% of subjects.⁴

OCT is a noninvasive, non-contact technique of visualizing the retinal structure in vivo with an axial resolution of up to 5 μ m utilizing near-infrared interferometry. RNFL thickness measured by OCT is almost equivalent to that measured histologically.⁵ OCT has been utilized to study RNFL and macular thickness in amblyopic eyes. Till the date, the literatures have shown conflicting results. Yoon et al⁶ and Yen et al⁷ found thicker RNFL in eyes with anisometropic amblyopia. Kee et al⁸ and Altintas et al⁹ found no difference in the macular and RNFL thickness in amblyopic children. More recently, Huynh et al¹⁰ and Al Haddad et al¹¹ showed a thicker fovea in amblyopic children, while Quoc EB et al¹² found a thicker RNFL in adults with anisometropic amblyopia. To the best of my knowledge no such study has been done till now in Nepal, hence this study has been carried out to evaluate the difference in RNFL and CMT between amblyopic and normal fellow eyes using SD-OCT.

METHODS

This study was hospital based, cross-sectional comparative study conducted in the department of Ophthalmology, BP Koirala Lions Centre for Ophthalmic Studies (BPKLCOS), Institute of Medicine (IOM), Kathmandu, Nepal from January 2013 to June 2014.

All consecutive patients diagnosed with unilateral amblyopia (whether strabismic or anisometropic) were included in this study. Exclusion criteria were patients above 15 years of age, younger subjects not cooperative enough for OCT examination, patients with organic eye disease (corneal opacity, cataract, glaucoma or retinal disorders including history of intraocular surgery and laser treatment) and diagnosed cases of isoametropic and combined amblyopia (strabismic and anisometropic).

Informed consent was taken from the parents or caretaker of every patient before evaluation and inclusion in the study. Detailed eye examination was performed, including best corrected visual acuity (BCVA), cycloplegic retinoscopy, orthoptic evaluation, slit-lamp biomicroscopy, dilated fundus examination and intraocular pressure measurement.

Diagnosis of amblyopia was made when: 1) The difference in BCVA between the two eyes was two or more Snellen lines in the absence of any

organic lesion that could result in a decrease in vision or 2) The BCVA was less than 6/12 bilaterally on the Snellen's chart in the absence of any organic lesion that could result in a decrease in vision. For refractive amblyopia, diagnosis was made with above criteria along with the presence of amblyogenic refractive error as mentioned earlier.

OCT examination was done using Spectralis SD-OCT (Heidelberg Engineering). A single user performed the retinal scans in all the cases and all sectoral and global RNFL thickness and central macular thickness were measured.

Data Analysis was done by using statistical package for social service (SPSS) version 20.0. The parameters compared were central macular thickness (CMT) and RNFL thickness, global as well as quadrant thickness consisting of superior, nasal, inferior and temporal. The RNFL and CMT of amblyopic eyes were compared with the normal fellow eyes using Paired t-test. For the comparison in different types of amblyopia Wilcoxon test was used.

RESULTS

Amblyopia was diagnosed in 53 patients. Ten patients with isoametropic amblyopia, 3 with combined amblyopia (anisometropic and strabismic) and 8 with decentered OCT scans and missing data were excluded. An analysis was then performed on 32 patients. There were 17 male and 15 female patients with mean age of 9.75 ± 2.77 years. Demographic data are summarized in Table 1.

Table 1. Demographic and baseline data

Age (mean)	9.75 $\pm$ 2.77 years
Gender (frequency/%)	
Male	17 (53.1%)
Female	15 (46.9%)
Laterality	
RE	18 (56%)
LE	14 (44%)
Mean BCVA (decimal)	0.31 $\pm$ 0.14
Types of amblyopia	
Hypermetropic anisometropic	19 (59.4%)
Myopic anisometropic	4 (12.4%)
Strabismic	9 (28.1%)

Mean BCVA in decimal notation was 0.31 ± 0.14 in the amblyopic eyes and 0.92 ± 0.16 in the control eyes. The difference was statistically significant ($P < 0.001$) using paired t test. Out of 32 cases, BCVA of 6/12 with Snellen acuity was present in highest number (9 eyes, 28.1%) in affected

eyes while BCVA of 6/6 with Snellen acuity was present highest number (25, 78.1%) in control eyes. The mean refractive error of the amblyopic eyes was $+3.30 \pm 1.89$ D spherical equivalent in hypermetropic anisometropic amblyopes and -6.06 ± 1.25 D spherical equivalent in myopic anisometropic amblyopes. Similarly, the mean refractive error of the control eyes was $+0.51 \pm 0.86$ D spherical equivalent in hypermetropic and -1.69 ± 1.56 D spherical equivalent in myopic anisometropic amblyopes. The difference was statistically significant in hypermetropic group.

Out of 9 patients with strabismic amblyopia, 5 (55.6%) cases had esotropia and 4 (44.4%) had exotropia. The mean amount of deviation of eyes with esotropia was $23.6 \pm 11.61^\circ$ for near and $22.4 \pm 12.6^\circ$ for distance. The mean amount of deviation of eyes with exotropia was $-25 \pm 17.32^\circ$ for near and $-25 \pm 10^\circ$ for distance.

Mean RNFL thickness was $104.16 \pm 13.64 \mu\text{m}$ in amblyopic eyes and $104.03 \pm 13.06 \mu\text{m}$ in control eyes. Using paired t-test there was no significant difference in RNFL thickness between amblyopic and normal eyes. Wilcoxon test was used to compare the RNFL thickness in different groups of amblyopia, as the sample size was less than 30 in each group and normal distribution of data were not found. Mean retinal nerve fibre layer thickness in hypermetropic group was greater in amblyopic eyes, $105.42 \pm 13.61 \mu\text{m}$ compared to $104.79 \pm 12.86 \mu\text{m}$ in control eyes but the difference was not significant. Table 2 shows mean RNFL thickness of overall amblyopic and control eyes as well as in different subgroups.

Table 2. RNFL thickness overall and in different subgroups

RNFL thickness	Amblyopic eyes		Control eyes		P value
	Mean (μm)	SD	Mean (μm)	SD	
Overall (n=32)	104.16	13.64	104.03	13.06	0.923
Hypermetropic anisometropic (n=19)	105.42	13.61	104.79	12.86	0.913
Myopic anisometropic (n=4)	96.50	11.96	100.25	2.99	1.000
Strabismic (n=9)	104.89	14.74	104.11	16.64	0.552

Note: Paired t-test was used for overall cases (n=32) and Wilcoxon test was used for different subgroups, P value significant when < 0.05 .

The mean CMT in amblyopic eyes of all 32 cases was $241 \pm 45.27 \mu\text{m}$ while in normal fellow eyes was

$233.22 \pm 44.24 \mu\text{m}$. It was thicker in amblyopic eyes and the difference was statistically significant (mean interocular difference = $7.78 \mu\text{m}$, $p=0.042$) using paired t-test.

When compared in different types of amblyopia mean central macular thickness of amblyopic eyes was greater than the control in all types. However, the difference was statistically significant only in the hypermetropic anisometropic amblyopes (mean interocular difference = $11.58 \mu\text{m}$, $P=0.026$). Table 3 shows CMT in overall cases as well as in different subgroups.

Table 3. Central Macular Thickness in different groups

Types of amblyopia	Amblyopic eyes		Control eyes		P value
	Mean (μm)	SD	Mean (μm)	SD	
Overall (n=32)	241	45.27	233.22	44.24	0.04
Hypermetropic Anisometropic Amblyopia	235.05	43.82	223.47	40.37	0.026
Myopic Anisometropic Amblyopia	214.50	5.07	208.25	6.70	0.109
Strabismic Amblyopia	265.33	50.12	264.89	47.26	0.859

Note: Paired t-test was used for overall cases (n=32) and Wilcoxon test was used for different subgroups, P value significant when < 0.05 .

DISCUSSION

Amblyopia is the most common cause of unilateral visual impairment in children.¹³⁻¹⁵ It develops in children up to the age of 6–8 years and may persist life-long. Amblyopia may have various effects at different levels of the visual pathway. In case of eye misalignment, a blurred image in one eye or occlusion of the eye, the animal's binocular neurons are found to disappear from the visual cortex and only monocular neurons are identified.¹⁶ Receiving input from the amblyopic eye causing atrophy for the cells in the lateral geniculate nucleus has been reported.¹⁷⁻¹⁹ Several experiments have demonstrated that light deprivation can cause modifications of retinal ganglion cells, such as cell loss,²⁰ mean nuclear volume diminution in ganglion cell cytoplasm, internal plexiform layer thinning in rats and cats,²¹ and reduction in optic nerve size area in mice.²² In many studies, retinal changes were investigated using imaging devices. OCT studies of RNFL and macular thickness in amblyopia reported different findings.

In our study, comparative evaluation of RNFL and macular thickness in amblyopic and normal fellow eyes was done in 32 children where the mean central macular thickness in the amblyopic eyes ($241 \pm 45.27 \mu\text{m}$) was greater than that of the fellow eyes ($233.22 \pm 44.24 \mu\text{m}$). The difference was statistically significant with mean interocular difference = $7.78 \mu\text{m}$ and $p = 0.042$. Among subgroup, the difference was significant only for the hypermetropic anisometropic amblyopes (mean interocular difference = $11.58 \mu\text{m}$, $p = 0.026$) but not the myopic anisometropic (mean interocular difference = $6.25 \mu\text{m}$, $p = 0.109$) and strabismic group (mean interocular difference = $0.44 \mu\text{m}$, $p = 0.859$). Similarly, Al Haddad et al¹¹ also measured RNFL and macular thickness in 45 patients with unilateral amblyopia and compared with the fellow eyes. He found significantly greater mean central macular thickness in the amblyopic eyes ($273.8 \pm 30.8 \mu\text{m}$) compared to the fellow eyes ($257.9 \pm 21.5 \mu\text{m}$), $p = 0.001$. The difference was significant only for the anisometropic amblyopes (mean interocular difference = $19.5 \mu\text{m}$) but not the strabismic group (mean interocular difference = $8 \mu\text{m}$). Huynh et al¹⁰ also measured slightly thicker foveal thickness in amblyopic eyes with SD-OCT, although the difference was not statistically significant.

Likewise, S. Agrawal et al²³ compared the mean macular thickness between normal and amblyopic eyes in 51 patients with unilateral strabismic ($n = 29$) and anisometropic ($n = 22$) amblyopia. Mean macular thickness in the amblyopic eyes was $277.5 \mu \pm 15.3$ and in the fellow normal eyes was $272.4 \mu \pm 13.1$ ($P < 0.05$). However, on subgroup analysis, the difference was statistically significant in strabismic ($P = 0.01$) and not significant in anisometropic amblyopia ($P = 0.08$). This variation in result is probably due to different study population. In our study, mean RNFL thickness was $104.16 \pm 13.64 \mu\text{m}$ in amblyopic eyes and $104.03 \pm 13.06 \mu\text{m}$ in control eyes. There was no significant difference between the fellow eyes. In the similar study done by Al Haddad et al¹¹ the mean RNFL thickness in the amblyopic eyes ($95.4 \pm 39.2 \mu\text{m}$) was also not significantly different from that of the fellow eyes ($94.0 \pm 19.2 \mu\text{m}$), $p = 0.8$.

Similarly, Elvan Yalcin et al²⁴ evaluated whether there was a difference in peripapillary RNFL and foveal thickness between hyperopic anisometropic amblyopic and normal individuals with optical coherence tomography. His results are comparable to this study. The mean RNFL thickness in amblyopic eyes was 101 ± 10.77 microns; in fellow eyes was 104.4 ± 10.95 microns, and 105.08 ± 10.10 microns in normal controls but the difference was not statistically significant. The mean foveal thickness in amblyopic eyes was 220 ± 38.25 microns, in fellow eyes was 202.87 ± 31.01

microns, in normal control eyes was 198.91 ± 22.50 microns and this difference was statistically significant.

However, Yoon et al²⁵ showed conflicting results in his study done in 31 patients with hypermetropic anisometropic amblyopia. The mean macular thickness was $252.5 \mu\text{m}$ and $249.7 \mu\text{m}$, and the mean RNFL thickness was $115.2 \mu\text{m}$ and $109.6 \mu\text{m}$, in the amblyopic eye and the normal eye, respectively. The difference in RNFL thickness was statistically significant ($P = 0.019$), but no significant difference was found in macular thickness ($P > 0.05$). They concluded that RNFL in patients with amblyopia was significantly thicker and the amblyopic process may involve the peripapillary RNFL, but not the macula. In contrast to the result of our study, Kee et al⁸ in his study found that the average thickness of the fovea was $157.4 \mu\text{m}$ in normal eyes and $158.8 \mu\text{m}$ in amblyopic eyes. There was no significant difference between the two groups ($p = 0.551$).

Both our findings and those of Al Haddad support Yen's hypothesis of a thicker retina in amblyopia. Yen attributed that to an arrest of the normal postnatal reduction of ganglion cells which requires sharply focused objects as appropriate stimuli; in their study, however, significant differences were obtained in RNFL thickness.⁷ Other possible hypothesis is that ageing affects the normal and amblyopic eyes differentially, with the former being affected more, producing a thinner macula on OCT. Thinning of retinal nerve fibre layers with increasing age has been reported in the study of Kanamori et al.²⁶

The changes in macular thickness in the amblyopic eyes have opened a new horizon for the future researches in the field of amblyopia. The interpretation and clinical significance of our results should be considered in the future studies. The increased central macular thickness may have a role in pathogenesis of amblyopia. It may also serve as a tool in monitoring the treatment outcome if future studies show changes in OCT with amblyopia therapy.

CONCLUSIONS

In this study, the retinal nerve fibre layer and the central macular thicknesses were measured using spectral domain optical coherence tomography.

The central macular thickness was significantly greater in the amblyopic eyes compared to the fellow (normal) eyes. There was no significant difference in the retinal nerve fibre layer thickness between amblyopic and normal eyes. Further studies including adequate sample size, considering the duration and types of amblyopia are required to confirm the difference between

amblyopic and normal eyes.

REFERENCES

1. Von Noorden GK. Physiology of the ocular movements. Binocular vision and ocular motility. 2002;52-84.
2. Noorden GK. Mechanisms of amblyopia. *Adv Ophthalmol*. 1977;34:93-115. [\[PubMed\]](#)
3. Williams C, Harrad RA, Harvey I, Sparrow JM; ALSPAC Study Team. Screening for amblyopia in preschool children: results of a population-based, randomised controlled trial. *ALSPAC Study Team. Avon Longitudinal Study of Pregnancy and Childhood. Ophthalmic Epidemiol*. 2001 Dec;8(5):279-95. [\[PubMed\]](#)
4. Sapkota K, Pirouzian A, Matta NS. Prevalence of amblyopia and patterns of refractive error in the amblyopic children of a tertiary eye care center of Nepal. *Nepal J Ophthalmol*. 2013 Jan-Jun;5(1):38-44. [\[PubMed\]](#)
5. Huang D, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W, Hee MR, Flotte T, Gregory K, Puliafito CA, et al. Optical coherence tomography. *Science*. 1991 Nov 22;254(5035):1178-81. [\[PubMed\]](#)
6. Yoon SW, Park WH, Baek SH, Kong SM. Thicknesses of macular retinal layer and peripapillary retinal nerve fiber layer in patients with hyperopic anisometropic amblyopia. *Korean J Ophthalmol*. 2005 Mar;19(1):62-7. [\[PubMed\]](#)
7. Yen MY, Cheng CY, Wang AG. Retinal nerve fiber layer thickness in unilateral amblyopia. *Invest Ophthalmol Vis Sci*. 2004 Jul;45(7):2224-30. [\[PubMed\]](#)
8. Kee SY, Lee SY, Lee YC. Thicknesses of the fovea and retinal nerve fiber layer in amblyopic and normal eyes in children. *Korean J Ophthalmol*. 2006 Sep;20(3):177-81. [\[PubMed\]](#)
9. Altintas O, Yüksel N, Ozkan B, Caglar Y. Thickness of the retinal nerve fiber layer, macular thickness, and macular volume in patients with strabismic amblyopia. *J Pediatr Ophthalmol Strabismus*. 2005 Jul-Aug;42(4):216-21. [\[PubMed\]](#)
10. Huynh SC, Samarawickrama C, Wang XY, Rochtchina E, Wong TY, Gole GA, Rose KA, Mitchell P. Macular and nerve fiber layer thickness in amblyopia: the Sydney Childhood Eye Study. *Ophthalmology*. 2009 Sep;116(9):1604-9. [\[PubMed\]](#)
11. Al-Haddad CE, Mollayess GM, Cherfan CG, Jaafar DF, Bashshur ZF. Retinal nerve fibre layer and macular thickness in amblyopia as measured by spectral-domain optical coherence tomography. *Br J Ophthalmol*. 2011 Dec;95(12):1696-9. [\[PubMed\]](#)
12. Quoc EB, Delepine B, Tran TH. Thickness of retinal nerve fiber layer and macular volume in children and adults with strabismic and anisometropic amblyopia. *J Fr Ophtalmol*. 2009 Sep;32(7):488-95. [\[PubMed\]](#)
13. Wright KW. Visual development and amblyopia. In: Wright KW, Spiegel PH, eds. *Pediatric Ophthalmology and Strabismus*. New York: Springer, 2003:157-71.
14. von Noorden GK. Amblyopia: a multidisciplinary approach. Proctor lecture. *Invest Ophthalmol Vis Sci*. 1985 Dec;26(12):1704-16. [\[PubMed\]](#)
15. Campos E. Amblyopia. *Survey of ophthalmology*. 1995 Jul 1;40(1):23-39. doi: 10.1016/s0039-6257(95)80044-1
16. Crawford ML, von Noorden GK. Concomitant strabismus and cortical eye dominance in young rhesus monkeys. *Trans Ophthalmol Soc U K* (1962). 1979;99(3):369-74. [\[PubMed\]](#)
17. Wiesel TN, Hubel DH. Effects of visual deprivation on morphology and physiology of cells in the cat's lateral geniculate body. *Journal of neurophysiology*. 1963 Nov 1;26(6):978-93. doi: 10.1152/jn.1963.26.6.978
18. von Noorden GK, Crawford ML, Levacy RA. The lateral geniculate nucleus in human anisometropic amblyopia. *Invest Ophthalmol Vis Sci*. 1983 Jun;24(6):788-90. [\[PubMed\]](#)
19. von Noorden GK, Crawford ML. The lateral geniculate nucleus in human strabismic amblyopia. *Invest Ophthalmol Vis Sci*. 1992 Aug;33(9):2729-32. [\[PubMed\]](#)
20. Wendell-Smith CP. Effect of light deprivation on the postnatal development of the optic nerve. *Nature*. 1964 Nov;204(4959):707. doi: https://doi.org/10.1038/204707a0
21. CHOW KL. Failure to demonstrate changes in the visual system of monkeys kept in darkness or in colored lights. *J Comp Neurol*. 1955 Jun;102(3):597-606. [\[PubMed\]](#)
22. Russell EL, Kada JM, Hufhines DM. Orange County vision screening project. *Ophthalmologic evaluation*. *Sight Saving Rev*. 1961;31:215-9.
23. Agrawal S, Singh V, Singhal V. Cross-sectional study of macular thickness variations in unilateral amblyopia. *Journal of Clinical Ophthalmology and Research*. 2014 Jan 1;2(1):15. doi: 10.4103/2320-3897.122630 [\[Full Text\]](#)
24. Yalcin E, Balci O. Peripapillary retinal nerve fiber layer and foveal thickness in hypermetropic anisometropic amblyopia. *Clin Ophthalmol*. 2014 Apr 12;8:749-53. [\[PubMed\]](#)
25. Yoon SW, Park WH, Baek SH, Kong SM. Thicknesses of macular retinal layer and peripapillary retinal nerve fiber layer in patients with hyperopic anisometropic amblyopia. *Korean J Ophthalmol*. 2005 Mar;19(1):62-7. [\[PubMed\]](#)
26. Kanamori A, Escano MF, Eno A, Nakamura M, Maeda H, Seya R, Ishibashi K, Negi A. Evaluation of the effect of aging on retinal nerve fiber layer thickness measured by optical coherence tomography. *Ophthalmologica*. 2003 Jul-Aug;217(4):273-8. [\[PubMed\]](#)