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Evaluation of macular and retinal nerve fibre layer thickness in unilateral amblyopic patients by using optical coherence tomography

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Abstract
Aim: To evaluate the macular and the retinal nerve fiber layer thickness in patients with unilateral amblyopia.
Design: Prospective observational study.
Material and Methods: 188 eyes of 94 patients with unilateral amblyopia diagnosed by difference of at least two lines between the normal and amblyopic eye on Snellen visual acuity charts was included.
Statistical analysis: Unpaired sample t-test.
Results: Majority of the cases was seen in age group 21-30 years with male preponderance. The average macular thickness was 271.4µm for normal eye versus 278.0µm for amblyopic eye, values by unpaired t-test was t-value=3.169, p=0.002<0.01 which shows highly statistical significant difference of macular thickness. But no statistical significance seen in retinal nerve fibre layer thickness.
Conclusion: Average macular thickness varies in amblyopic eyes is an important concept for future studies. However Retinal Nerve Fibre Layer thickness does not show corresponding outcomes with amblyopia and actually being thinner in amblyopes.

Keywords: Amblyopia, macular thickness, retinal nerve fibre layer thickness, optical coherence tomography

Introduction
Amblyopia also called as "Lazy eye" is defined as unilateral or bilateral dimension of best corrected central visual acuity which is due to form vision deprivation and/or abnormal binocular communication, without any seen organic cause to correspond with visual loss [1]. Amblyopia transpires during the duration when the neuronal complexes among retina and of cerebral cortex is developing and maturing. Therefore amblyopia often develops during postnatal time in initial span of 2-3 years; however, it can also develops until the span of 8-9 years [2]. Amblyopia occurs due to insufficient excitement of visual system in early critical time of visual formation. In monocular amblyopia, uneven input coming through two eyes to the primary cortex causes shortfall in visual processing. Because of this inequality in image quality among the two eyes stereovision (3D vision) can be highly affected or even absent altogether, especially in strabismus [3, 4]. This disparity in image quality is also analogous with a frequent repression of central visual field of the amblyopic eye [5]. Probably amblyopia is most ordinary cause of preventable monocular vision loss in children and young adults [6] and affects approximately 2%-5% of general population [7]. In India the incidence is around 1.1% [8] although its occurrence could be higher in medical underserved populations.
Unilateral amblyopia has 2 major causes:
1. Anisometropic amblyopia: It is difference in state of refraction of minimum 1 D or more between 2 eyes [9].
2. Strabismic amblyopia: It is the one in which due to constantly unaligned optical axis there is abnormality in binocular communication. The amount of divergence is not related to development and severity of stabismic amblyopia.

Deprivational amblyopia
It is a rare form of amblyopia existing in only about 0.1% of population and is associated with vision obstructing disorders like congenital cataract, lid ptosis, vitreous haemorrhage, corneal opacities corneal opacities [10].

These block the visual axis and deprive retina to get clear image. And hence there is loss of sight in early age. It is relatively difficult to cure.

Combined amblyopia

In this patients are with both anisometropic and strabismic type of amblyopia. Clinically there are different levels of severity in unilateral amblyopia, and they are explained as difference in best corrected visual acuity (BCVA) among 2 eyes of 0.2logMAR (2 lines on acuity chart) [11]. Mild amblyopia: visual acuity (VA) 6/9-6/12(or 0.2-0.3logMAR); Moderate: the VA poor than 6/12 to 6/36 (0.3-0.8logMAR); Severe: the VA poor than 6/36 (0.8logMAR) [11].

Optical Coherence Tomography (OCT) is a noninvasive, non-contact method for measuring Retinal Nerve Fibre Layer Thickness (RNFLT) [12, 13]. It gives a highly qualitative, objective, and reproducible structural evaluation of retinal morphology. The RNFLT done by OCT is similar to the RNFLT done histologically [12] due to basic principle used in OCT which is established on infrared interferometry, hence the thickness calculated does not get influenced by refractive status or axial length of eye, or by change in light in nuclear sclerotic cataract density [13]. Hence this study was planned to understand the anatomical changes in amblyopia. Therefore we have done the study to compare between the macular and retinal nerve fibre layer thickness of amblyopic eyes to the normal corresponding eyes.

Materials and Method

The present study entitled "Evaluation of Retinal Nerve Fibre Layer thickness and Macular thickness in patients with Unilateral Amblyopia" was conducted after clearance from Clinical research committee and Ethical committee of the institute. After explaining the nature and possible consequences of the study an informed consent was obtained from the study subjects. Total 94 subjects diagnosed with monocular amblyopia were included during the study period between January 2019 to December 2019.

All patients of either gender between 18-45 years of age, with unilateral amblyopia whose difference in visual acuity was minimum two lines between the normal and amblyopic eye on Snellen visual acuity charts were included. Patients with any other significant ocular/systemic condition which may hinder examination on OCT, or any other systemic/ocular co-morbidities that could substantially affect the macular or RNFL thickness, with any history of ocular trauma, on OCT showing abnormal macular and RNFL thickness in normal eye, with history of previous intraocular or refractive surgery, whose pupillary dilation is insufficient to perform OCT, who is not able to maintain stable fixation behind the OCT camera and not singed the informed consent were excluded from the study.

After taking detailed ocular and systemic history. Each patient was assessed for best corrected visual acuity, Intraocular pressure (IOP) with goldmann applanation tonometer, Anterior segment examination using slit lamp was done, Fundus examination under mydriasis for characteristic optic disc changes was done and noted and RNFL thickness and macular thickness of both amblyopic and fellow normal eyes of the unilateral amblyopic patients were measured using OCT Cirrus HD. The peripapillary RNFL thickness was measured using Optic Disc Cube 200*200 protocol. Macular thickness was measured using macular cube scan 512*128 protocol.

The data was analysed and for (categorical variables)-descriptive statistics frequency analysis and percentage analysis were used and for (continuous variables) the mean and S.D were used. The unpaired sample t-test was used to find a significant difference among the bivariate samples in independent groups and probability value of 0.05 is taken as significant level.

Results

In present study age of patients enrolled ranged between 18-45 years with more frequency for age group 21-30 years i.e. 38.3% (table 1) with male preponderance 63.8% (table 2). BCVA distribution in 94 patients and 188 eyes, all patients had normal visual acuity in one eye and in amblyopic eye visual acuity was further divided as 11.17% from 6/12-6/18, 22.87% from 6/24-6/36 and 15.95% in 6/60 (table 3; figure 1). Average RNFL thickness was 90.2µm in normal contralateral eye versus 88.6µm in amblyopic eye; by unpaired t-test showed t-value=0.822, p=0.412>0.05 which shows no statistical significant difference between normal contralateral eye and amblyopic eye (table 4; figure 2). The mean average macular thickness was 271.4µm for normal corresponding eye versus 278.0µm for amblyopic eye, values by unpaired t-test were t-value=3.169, p=0.002<0.01 which shows highly statistical significant difference of macular thickness among normal corresponding eye and amblyopic eye (table 5; figure 3).

Table 1: Age distribution

Age in years	Frequency	Percent
18 - 20 years	25	26.6
21 - 30 years	36	38.3
31 - 40 years	17	18.1
41- 45 years	16	17.0
Total	94	100.0

Table 2: Gender distribution

Gender	Frequency	Percent
Female	34	36.2
Male	60	63.8
Total	94	100.0

Table 3: BCVA distribution in study population

BCVA	Frequency	Percent
Normal	94	50.0
6/12 to 6/18	21	11.17
6/24 to 6/36	43	22.87
6/60	30	15.95
Total	188	100.0

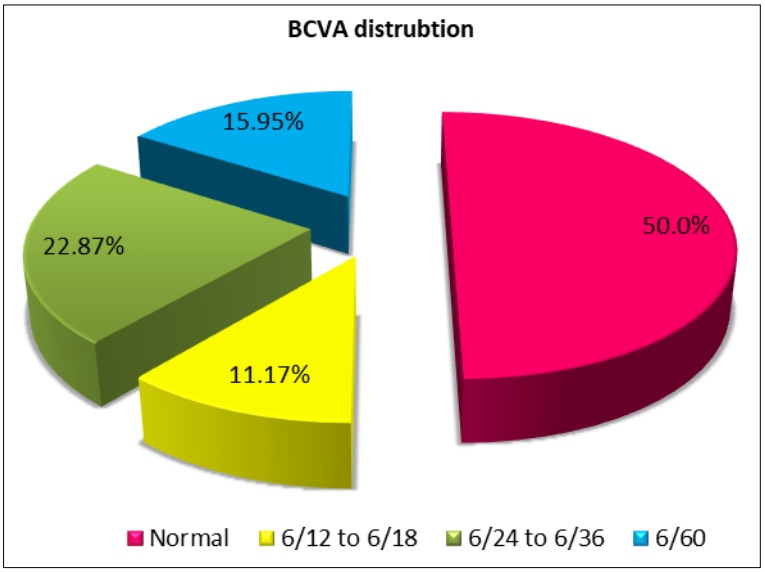

Fig 1: BCVA distribution in study population

Table 4: Comparison of average RNFL thickness

Variable	Groups	N	Mean	S.D	t-value	*p* - value
Average RNFL thickness	Normal eye	94	90.2	13.0	0.822	0.412 #
	Amblyopic eye	94	88.6	14.8		

No Statistical Significance at *p*> 0.05 level

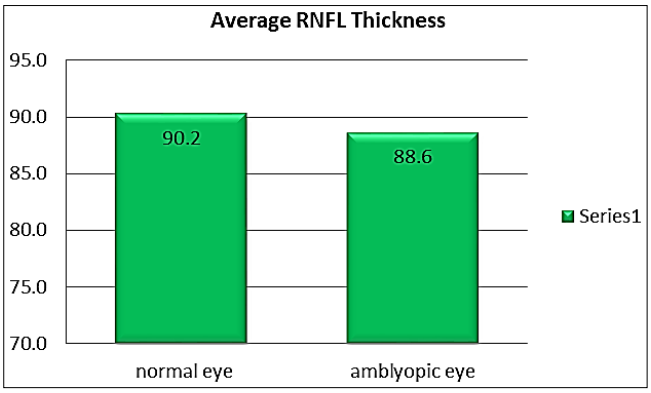

Fig 2: Comparison of average RNFL thickness

Table 5: Comparison of macular thickness

Variable	Groups	N	Mean	S.D.	t-value	*p*-value
Macular thickness	Normal eye	94	271.4	14.4	3.169	0.002 **
	Amblyopic eye	94	278.0	14.0		

** Highly statistical significance at *p*<0.01 level

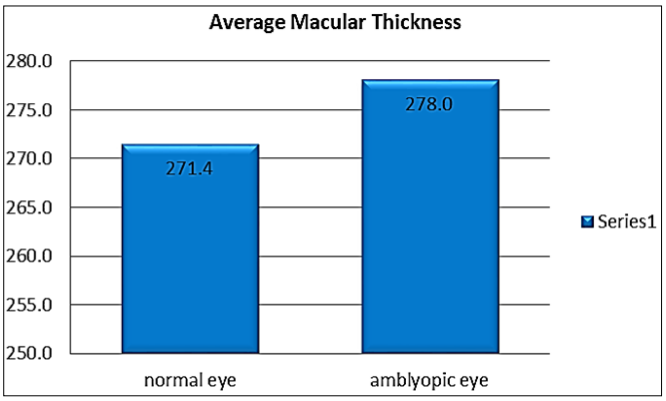

Fig 3: Comparison of macular thickness

Discussion

In our study we included total of 94 patients (188 eyes), among them 34 were females, 60 were males which is a bit similar to study conducted by Alotaibi AG *et al.* [2] where they studied on 93 patients (males-48, females-45). The age distribution of the study population was found to be 18-45 years, which was approximately similar to study done by Abdulghaffar TT *et al.* [14] where age of the study group ranged from 18-40 years which is an adult age range similar to our study. In our study total 188 eyes with unilateral amblyopia were included which coincides with study of Alotaibi AG *et al.* [2] who included subjects of unilateral amblyopia diagnosed by difference in visual acuity of at least 2 lines among normal and amblyopic eye on snellen VA charts. Therefore in current study among 188 eyes, 94 eyes were monocular amblyopic, whereas the other 94 eyes were not amblyopic, and they had a BCVA of 6/6 and were considered as normal fellow eyes and they were control group of our study. In current study, the mean average macular thickness was 271.4µm for normal corresponding eye versus 278.0µm for amblyopic eye (p=0.002<0.01) which shows highly statistical significant difference between 2 groups regarding average macular thickness. Our study results were similar to studies done by: Dickmann and colleagues[15] who showed higher thickness values of macula and foveola in strabismic amblyopic eyes than in normal corresponding eyes (Macular Thickness was 267±14 and 253±14µm in amblyopic and sound eyes, respectively), but no changes has been seen in anisometropic amblyopia group (Macular Thickness was 257±20 and 256±18µm in amblyopic and sound eyes, respectively). Chatterjee A, Bandyopadhyay SK (2019) [16] conducted similar study and there results showed that in anisometropic amblyopia children, macular thickness is more in amblyopic eye 247.8947+/-34.3926 as compared to normal eye 222.2386+/-31.1919 with *p* value=0.00106; which shows a statistical significance. Hence, concluded that macular thickness is more in anisometropic and strabismic but not the RNFL thickness. It is presumed that visual deprivation and binocular competition causes decreased diameter of cone of fovea and hence henle's fibre layer moves far from fovea. Hence more foveal thickness occurs as result of affected normal maturation of macula [17]. According to our

study, RNFLT was 90.2µm in normal eye versus 88.6µm in amblyopic eye; p=0.412>0.05.This study showed thinner RNFL in amblyopic eye versus normal corresponding eye, but difference was not statistically significant. Similar results in RNFL thickness were found by: Andalib D *et al.* (2013) [18] where in results no changes were seen in peripapillary nerve fibre layer (p=.55). In some studies contradictory results were also reported. As per study done by Repka MX *et al.* (2009) [19] to compare peripapillary RNFL thickness of amblyopic and corresponding eyes with a hypothesis that RNFL of amblyopic eye may be narrower. For study purpose unilateral strabismic, anisometropic or mixed amblyopia were included and OCT performed. Results shows RNFL thickness of amblyopic and corresponding eyes was (111.4 and 109.6µm, respectively; mean difference, 1.8µm broader in amblyopic eyes). Similar results were shown in study by Alotaibi AG *et al.* (2011) [2] through the study mean RNFL thickness came out to be 112.16µm and 106µm in amblyopic and corresponding eye respectively. Hence total RNFL thickness of amblyopic eyes can be due to declined ganglion cells in postnatal period which causes more RNFL thickness and less count and size of axons which causes thinning of RNFL [2, 20].

Conclusion

In conclusion, our findings of markedly thicker macula in unilateral amblyopic patients suggests that although amblyopia primarily affects the visual cortex, it is also a process that leads to secondary changes at retinal level which is an important concept for future studies. However RNFL thickness does not show corresponding outcomes with amblyopia and actually being thinner in amblyopes. The cause behind can be racial difference or some other yet unknown factors. Therefore studies involving autopsies can throw more light on histopathological changes in amblyopic eyes, both at retinal and higher centers of visual pathway. And further studies are warranted to establish retinal changes in amblyopia and to determine whether retinal involvement has any effect on response to amblyopia therapy.

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