



MACULAR THICKNESS AND VOLUME AMONG CHILDREN WITH STRABISMIC AMBLYOPIA ATTENDING OPHTHALMOLOGY OUT-PATIENT-DEPARTMENT OF BANKURA SAMMILANI MEDICAL COLLEGE AND HOSPITAL, WEST BENGAL

Ophthalmology

Rakhi

Bandyopadhyay

Assoc. Prof, Deptt. of Ophthalmology, Bankura Sammilani Medical College, Bankura

Dibakar Haldar*

Assoc Prof, Dept. of Community Medicine, Bankura Sammilani Medical College, Bankura *Corresponding Author

ABSTRACT

Background- Strabismic amblyopia is one of the leading causes of decreased vision in children.

Materials and Methods- A cross-sectional survey was conducted from August 2018 to January 2019 in out-patient-department of Ophthalmology, Bankura Sammilani Medical College and Hospital aiming to estimate and compare macular thickness and volume by SD-OCT between normal and amblyopic eyes of children suffering from strabismic amblyopia. Data were collected from consecutive eligible patient via interview and ophthalmological examination using predesigned questionnaire and necessary equipments.

Results- overall age was 10.65 ± 2.58 (mean $\pm$ SD) years with slight female preponderance (51.92%). In Binary logistic regression 67.3% to 89.7% of change in outcome variable was explained by variation in independent variables. Retinal thickness within 1mm inner circle, superior quadrant within 3mm of inner ring and female gender had positive association whereas that in superior quadrant of 6mm outer ring was found to have negative association with amblyopia.

Conclusion: Average macular thickness is greater in amblyopic eyes as compared to normal fellow eyes.

KEYWORDS

strabismic amblyopia, macular thickness, central

INTRODUCTION:

Amblyopia is defined as unilateral or bilateral reduction in the best corrected visual acuity due to abnormal visual experience during the critical period of vision development, for which no organic cause can be found on examination of the eye and which in selected cases can be reversed by appropriate therapeutic measures^[1]

The prevalence of amblyopia in the general population is 1.6 to 3.5%. It is the commonest cause of decreased vision in childhood.^[2]

Strabismus develops in about 5 to 8 % of the general population.^[3] Strabismic amblyopia is one of the commonest types of amblyopia and is almost always unilateral.^[1,4]

The pathological changes in the morphology and function of the neurones in the lateral geniculate body and striate cortex are well established, in experimentally induced amblyopia in animals. Similar neural anatomical changes have been observed in pathological studies in humans^[5,6]

Though an amblyopic eye is, by definition, is thought to be structurally normal with no detectable organic changes on examination of the fundus, researchers have undertaken studies to determine if the retina is affected in amblyopes and could have a role to play in the decreased visual acuity, that accompanies amblyopia.^[7-10] The studies conducted have been often contradictory in their observations with some observing thickening or thinning of the retina and some observing no changes.^[10-13]

Ocular coherence tomography (OCT), a noncontact ophthalmic diagnostic imaging device for cross sectional imaging of the retina has enabled study of the retinal structure in great detail. Spectral domain OCT (SD-OCT) offers better image quality than Time domain OCT, with good reproducibility in measuring retinal thickness.^[14] Several large sample sized studies have demonstrated effective use of OCT in young children.^[9]

Around a 450 patients predominantly from poor socio-economic strata attend Ophthalmology Out-Patient-Department (OPD) of Bankura Sammilani Medical College and Hospital (BSMCH) daily a substantial proportion of which suffers from strabismic amblyopia. The present study was aimed to measure the macular thickness and volume by SD-OCT, and compare between the normal and amblyopic eyes of children suffering from strabismic amblyopia. The study also was planned to find out the correlation between age and gender with the changes in retinal thickness and volume, if any in the best corrected visual acuity.

MATERIALS AND METHODS

A cross sectional survey that was conducted from August 2018 to January 2019 in the OPD, Department of Ophthalmology, BSMCH, a tertiary care peripheral government hospital in West Bengal.

Fifty two consecutive patients fulfilling the predetermined eligibility criteria were selected for the study.

The inclusion criteria were:

- Children aged 6 to 16 years having unilateral amblyopia with manifest strabismus
- Best corrected visual acuity (BCVA) in the amblyopic eye (AE) between 20/40 to 20/120
- Best corrected visual acuity in the Normal eye (NE) 20/30 or better
- Spherical equivalent (spherical power + half of the cylindrical power) between the eyes within 1 Dioptre
- For patients having astigmatism only, cylindrical power within 1.5 Dioptre
- Children able to cooperative for OCT examination

The exclusion criteria were:

- Mixed etiology of strabismic and anisometric amblyopia
- Severe amblyopia with BCVA less than 20/200
- Gross unsteady fixation or nystagmus
- Ocular trauma
- Congenital abnormalities
- Intraocular surgery
- Unwilling to participate in the study

All selected patients underwent a thorough ophthalmological examination that included visual acuity examination, slit lamp examination of the anterior segment, cover tests, measurement of the angle of squint in prism diopters and fundus examination after pupillary dilatation. Cycloplegic retinoscopy was done and refractive error, if any, converted into spherical equivalent (spherical power + half of the astigmatic power).

Snellen visual acuity was converted into logMAR visual acuity for ease of result analysis. Amblyopia was diagnosed if the difference in Snellen acuity between the two eyes was two lines or more.

SD OCT scanning was performed using the Spectralis tracking laser tomography (Heidelberg Engineering). All OCT tests were done in the morning, in a child friendly room, by a single trained optometrist who was unaware of the diagnosis. Scans with poor signal strength were repeated.

Retinal thickness maps of 6mm size, with centre on the fovea were

obtained with superimposed 1, 3, 6 mm Early Treatment Diabetic Retinopathy Study (ETDRS) grid superimposed on the map. The macula was divided into 9 standard ETDRS regions with three concentric rings centred on the fovea. These were 1mm (innermost ring), 3mm (inner ring) and 6 mm (outermost ring) with the inner 3mm and outer 6 mm rings divided further into 4 quadrants each, namely superior, inferior, temporal and nasal. [Pic.1]

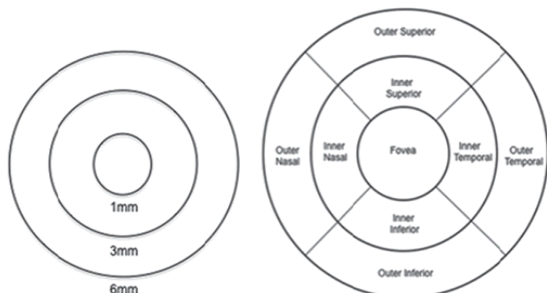


Fig.1: Figure 1: Map diameters centered on fovea (left) and nine standard early treatment diabetic retinopathy study regions (right). The macula is divided into nine regions with three concentric rings measuring 1 mm (innermost ring), 3 mm (inner ring) and 6 mm in diameter (outer ring) centered on the fovea with inner and outer ring being divided into four quadrants each (Courtesy: Agrawal S et al.)

The parameters were to be studied:

- Central minimum macular thickness
- Retinal thickness in the 1mm innermost ring
- Retinal thickness in the superior, inferior, nasal and temporal quadrants of the 3mm inner ring
- Retinal thickness in the superior, inferior, nasal and temporal quadrants of the 6 mm outer ring
- Macular volume

These parameters were estimated in the amblyopic eyes and the fellow normal eyes of each patient. The fellow eye in each patient served as the control in this study.

The study protocol and the informed consent forms were both approved by the Institutional Ethical Committee After collection all the data were entered in Microsoft Excel sheet and analysed by estimating mean and Standard Deviation (SD) for continuous variables and proportion for categorical variables. Data were displayed with the help of Tables and charts. Shapiro-Wilk Normality test revealed that the data set followed normal distribution. For drawing inference statistical tests like Independent t test, Pearson correlation test were done. For the sake data analysis Statistical Package for Social Sciences (SPSS)-22nd version was used. P value of 0.05 at 95% CI and 5% precision was considered to be significant.

RESULTS AND ANALYSIS

Univariate analysis revealed that the overall average age was estimated to be 10.65 ± 2.58 (mean $\pm$ SD) years with a median of 10 and range of 6-16 years. There was slight female preponderance as well as exotropia type of amblyopia (51.92% each).

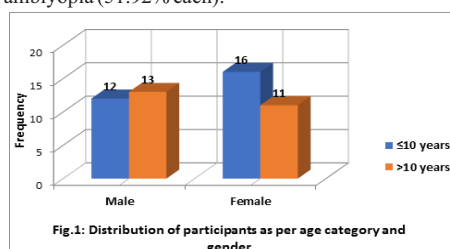


Fig.1: Distribution of participants as per age category and gender

The angle of squint (D) was found to be 33.56 ± 7.23 (mean $\pm$ SD) dioptre with median value of 30 D. Overall estimates for others parameters were given in table-1.

Table-1: Estimated overall values for different parameters of study. [n=52]

Parameters	Attributes	Minimum	Maximum	Mean $\pm$ SD
Retinal thickness (central)	Normal Eye	198.00	224.00	208.62 $\pm$ 8.44
	Amblyopic Eye	204.00	230.00	215.31 $\pm$ 7.96
One mm sub-field thickness	Normal Eye	220.00	247.00	227.81 $\pm$ 5.71
	Amblyopic Eye	223.00	258.00	234.52 $\pm$ 7.40
Superior quadrant of 3 mm inner ring	Normal Eye	249.00	310.00	280.19 $\pm$ 20.51
	Amblyopic Eye	286.00	318.00	298.73 $\pm$ 10.79
Inferior quadrant of 3 mm inner ring	Normal Eye	210.00	296.00	281.40 $\pm$ 18.61
	Amblyopic Eye	262.00	301.00	279.63 $\pm$ 10.13
Inferior quadrant of 3 mm inner ring	Normal Eye	276.00	314.00	294.23 $\pm$ 10.21
	Amblyopic Eye	274.00	304.00	287.12 $\pm$ 9.38
Temporal quadrant of 3 mm inner ring	Normal Eye	250.00	287.00	277.25 $\pm$ 9.84
	Amblyopic Eye	262.00	284.00	273.85 $\pm$ 6.14
Superior quadrant of 6 mm outer ring	Normal Eye	260.00	291.00	273.46 $\pm$ 9.29
	Amblyopic Eye	224.00	270.00	253.42 $\pm$ 11.88
Inferior quadrant of 6 mm outer ring	Normal Eye	254.00	288.00	272.19 $\pm$ 8.81
	Amblyopic Eye	262.00	290.00	274.54 $\pm$ 7.10
Inferior quadrant of 6 mm outer ring	Normal Eye	257.00	310.00	279.21 $\pm$ 13.09
	Amblyopic Eye	258.00	303.00	276.73 $\pm$ 13.56
Temporal quadrant of 6 mm outer ring	Normal Eye	246.00	294.00	270.04 $\pm$ 11.43
	Amblyopic Eye	256.00	292.00	270.31 $\pm$ 10.24
Macular Volume	Normal Eye	7.08	8.55	7.98 $\pm$ 0.28
	Amblyopic Eye	7.24	8.81	8.16 $\pm$ 0.30

Bivariate analysis revealed that the best corrected visual acuity was higher in normal eyes in terms of logMAR values compared to that of the amblyopic eyes and the difference was found to be statistically significant. In central, 1mm sub-central, superior and nasal quadrant under 3 mm inner ring the retinal thickness was revealed to be

significantly higher in amblyopic eyes compared to their counterpart. However, the retinal thickness in temporal quadrant of 3mm inner ring and superior quadrant of six mm outer ring was found to be significantly lower in amblyopic eyes. [Table-2]

Table-2: Comparison of different macular parameters of two groups of eyes

Parameters	Normal eye mean $\pm$ sd	Amblyopic eye mean $\pm$ sd	Unpaired t, P at 102 df
Visual Acuity(logMAR)	0.6327 $\pm$ 0.038	0.008 $\pm$ 0.133	32.326, 0.000
Central macular thickness(μ)	208.62 $\pm$ 8.44	215.31 $\pm$ 7.96	4.160, 0.000
1mm central sub-field(μ)	227.81 $\pm$ 5.7	234.52 $\pm$ 7.4	5.178, 0.000
3mm inner ring (superior quadrant) [μ]	280.19 $\pm$ 20.51	298.73 $\pm$ 10.79	5.769, 0.000
3mm inner ring (inferior quadrant) [μ]	281.40 $\pm$ 18.61	279.63 $\pm$ 10.13	0.602, 0.548
3mm inner ring (Nasal quadrant) [μ]	294.23 $\pm$ 10.21	287.11 $\pm$ 9.38	3.701, 0.000
3mm inner ring (temporal quadrant) [μ]	277.25 $\pm$ 9.84	273.85 $\pm$ 6.14	2.117, 0.037
6mm outer ring (superior quadrant) [μ]	273.46 $\pm$ 9.29	253.42 $\pm$ 11.88	9.577, 0.000

6mm outer ring (inferior quadrant) [μ]	272.19 $\pm$ 8.81	274.54 $\pm$ 7.10	1.495, 0.138
6mm outer ring (nasal quadrant) [μ]	279.21 $\pm$ 13.09	276.73 $\pm$ 13.56	0.949, 0.345
6mm outer ring (temporal quadrant) [μ]	270.04 $\pm$ 11.43	270.31 $\pm$ 10.24	0.127, 0.900

Retinal thickness in the central part and inferior quadrant within 3mm ring of normal eyes as well as nasal quadrant within 3mm inner ring of

Amblyopic eyes was found to have significant correlation with age, negative for the earlier two and positive for the later one. [Table-3]

Table-3: Correlation between age and other retinal parameters having significant association with amblyopia. (n=52)

Correlations						
Variables		r/P(2-tailed)	Age (yr)	Retinal thickness		
				Central (AE)	Inferior quadrant within 3 mm inner ring (NE)	Nasal quadrant within 3 mm inner ring (AE)
Age		r	1	-0.316*	-0.281*	0.287*
		P	-	0.022	0.043	0.039
Retinal thickness	Central in AE	r	-0.316*	1	-0.193	-0.078
		P	0.022	0.170	0.580	
	Inferior quadrant within 3 mm inner ring (NE)	r	-0.281*	-0.193	1	0.251
		P	0.043	0.170	-	0.073
	Nasal quadrant within 3 mm inner ring (AE)	r	0.287*	-0.078	0.251	1
		P	0.039	0.580	0.073	-
	*. Correlation is significant at the 0.05 level (2-tailed).					

Bivariate analysis with stratification showed that gender was having its association with visual acuity of normal eyes; retinal thickness at superior quadrant of normal eye, inferior and nasal quadrant within 3mm ring of amblyopic eyes; nasal quadrant in the 6mm outer ring of amblyopic eyes and macular volume of amblyopic eyes. The best corrected visual acuity in male and retinal thickness on the nasal quadrant of 3mm inner ring among female was found to be

significantly greater. However, retinal thickness on the superior, inferior quadrant of 3 mm inner ring and nasal quadrant of 6mm outer ring along with macular volume were revealed to be positively affected by male gender. On the other hand, higher age and greater central retinal thickness were found to be associated with exotropia and esotropia, respectively. [Table-4]

Table-4: Relation between different macular parameters, type of squint and gender

Variable	Gender		Unpaired t, p at df 50	Type of squint		Unpaired t, p at df 50
	Male[n=25]	Female[n=27]		Esotropia [n=25]	Exotropia[n=27]	
	mean $\pm$ sd	mean $\pm$ sd		mean $\pm$ sd	mean $\pm$ sd	
Age (year)	-	-	-	9.8 $\pm$ 2.48	11.44 $\pm$ 2.45	2.40, 0.020
Visual acuity(logMAR) [NE]	0.004 $\pm$ 0.03	0.020 $\pm$ 0.04	2.289, 0.026	-	-	-
Central retinal thickness (AE)	-	-	-	217.60 $\pm$ 8.76	213.19 $\pm$ 6.52	2.06, 0.045
Superior quadrant of 3 mm ring (NE)	288.22 $\pm$ 17.72	271.52 $\pm$ 20.07	3.187, 0.002	-	-	-
Inferior quadrant of 3 mm ring (AE)	282.52 $\pm$ 10.92	276.52 $\pm$ 8.32	2.214, 0.031	-	-	-
Nasal quadrant of 3 mm ring (AE)	286.63 $\pm$ 7.85	287.64 $\pm$ 10.94	2.175, 0.030	-	-	-
Nasal quadrant of 6 mm ring (AE)	280.04 $\pm$ 13.81	273.16 $\pm$ 12.59	2.039, 0.047	-	-	-
Macular Volume (AE)	8.25 $\pm$ 0.25	8.07 $\pm$ 0.33	2.162, 0.035	-	-	-

Macular volume was significantly higher in amblyopic eyes (8.16 $\pm$ 0.30 vs 7.98 $\pm$ 0.28, unpaired t=3.146 & P=0.002 at df 102).

Considering amblyopia as outcome variable, the Binary logistic model was run after including other input variable found to be associated with amblyopia in bivariate analysis. It was revealed that the model worked significantly (2=116.176 with p=0.000 at df 7) and 67.3% to 89.7% of

variation in outcome variable revealed to be explained by the changes in independent variables. Model indicated that retinal thickness within 1mm inner most circle, superior quadrant within 3mm of inner ring and female gender had positive association whereas the retinal thickness in the superior quadrant of 6mm outer ring was found to have negative association with amblyopia. [Table-5]

Table-5: Multivariate analysis considering amblyopia as outcome variable.

Variables in the Equation								
Variables		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)
								Lower Upper
Step 1 ^a	Central	-0.019	0.075	0.064	1	0.800	0.981	0.848 1.136
	1mm inner circle	0.384	0.149	6.606	1	0.010	1.468	1.095 1.966
	Superior quadrant of 3 mm inner ring	0.102	0.046	4.783	1	0.029	1.107	1.011 1.213
	Nasal quadrant of 3 mm inner ring	-0.040	0.068	0.340	1	0.560	0.961	0.841 1.098
	Temporal quadrant of 3 mm inner ring	-0.079	0.055	2.041	1	0.153	0.924	0.829 1.030
	Superior quadrant of 6mm outer circle	-0.356	0.114	9.793	1	0.002	0.701	0.561 0.875
	Gender(1)	4.480	1.842	5.913	1	0.015	88.239	2.385 3264.916
	Constant	11.711	55.015	0.045	1	0.831	121917.00	-- --

a. Variable(s) entered on step 1: Central, OnemmmSubcentral, threeMmSup, ThreemmmNasal, threeMmTemp, sixMmSup, Gender.

DISCUSSION

In the present study, it was found that the central minimum retinal thickness at the fovea to be 215.31 $\pm$ 7.96 in amblyopic eyes and 208.62 $\pm$ 8.44 in fellow eyes. Average retinal thickness of the central 1 mm subfield was 234.52 $\pm$ 7.4 in amblyopic eyes and 227.81 $\pm$ 5.7 in control eyes.

In the present study thickness in central retina, 1mm central sub-field and superior quadrant of 3mm inner ring was reflected to be higher in amblyopes whereas nasal and temporal field of 3mm inner ring as well as superior quadrant of 6mm outer retinal thickness was found to be significantly less among the amblyopic eyes.

Bandyopadhyay et al. found in their study a statistically increased macular thickness in amblyopes (229.59 $\pm$ 31.91 microns) as against fellow eyes (206.87 $\pm$ 28.49) with p=0.00141.^[15]

Agarwal et al. reported overall mean macular thickness to be increased in 51 patients of amblyopia (p<0.05) and this difference was more significant in the strabismic amblyopia group (p=0.01).^[14]

From their larger study, Huynh et al. also reported that foveal minimum thickness in amblyopic eyes was greater than normal fellow eyes by 5 microns. In addition, amblyopic eyes had increased retinal thickness in the 1mm central sub-field in concordance with the findings of the present study. However, their observation about decreased retinal

thickness in the inner macular ring and no change in the outer macular ring weren't found consistent with that of the increased thickness in the superior quadrant of 3mm inner ring and decreased thickness in superior quadrant of outer ring as revealed in the present study.^[13]

Silva et al. found increased foveal minimum thickness in amblyopic eyes, decreased thickness of nasal and inferior retina in the inner ring and decreased inferior retinal thickness in the outer ring.^[16]

In this study central macular thickness was revealed to be significantly greater in Esotropic type of amblyopic eyes in concurrence with Dickman et al. who observed statistically significant increased macular thickness in 20 esotropic amblyopes in one study and again in 25 patients of esotropic amblyopia in another study done 2 years later, to reach the same results.^[12]

A study carried out by Kasem et al. reported statistically significant increased central macular thickness and macular volume ($p=0.033$ and $p=0.047$) in strabismic amblyopia due to both esotropia and exotropia.^[17]

Rajavi et al. found significantly ($p<0.001$) increased retinal thickness (275 ± 39) at the fovea in amblyopes compared to the same that of their controls (220 ± 33) and in central 1mm (277 ± 27 in amblyopes versus 235 ± 26 in controls ($p<0.001$)).^[18]

Altindag et al. found increased central macular thickness in strabismic amblyopia compared to normal ($p<0.01$) but not in other macular regions.^[19]

On the contrary, several studies did not find changes in this regard.

Xu et al. in their study on strabismic amblyopia in esotropic children found slight but not significant increase in foveal minimum thickness and central 1mm thickness. No significant difference in any section of macular thickness was noted between amblyopic and fellow eyes.^[20]

Al Haddad et al. studied both strabismic and anisometropic amblyopia and found increased mean macular thickness in amblyopic eyes than fellow eyes (273.8 vs 257.9 microns with $p=0.001$). This was not significant in the strabismic group of 14 patients.^[9]

Altinas et al. found no significant difference in macular thickness and macular volume in 14 patients of unilateral strabismic amblyopia.^[8]

Araki et al. using swept source OCT did not find any significant change in macular retinal and choroidal thickness in their study.^[21]

Quoc et al. reported no difference in macular volume between normal and amblyopic eyes.^[7]

El Hifnawy found increased macular thickness in amblyopic eyes than the fellow eyes (288.65 ± 22.61 vs 281 ± 22.6 micron) without any statistical significance.^[11]

Kusbeci T et al. observed no significant difference between the average central macular thickness between Amblyopic eyes and their counterpart.^[10]

The conflicting results of these studies might be due partially to difference in study populations, sample size, defining criteria and type of amblyopia, instruments used to measure the macular thickness and other co-existing factors like refractive errors.

As it was cross-sectional survey being carried out in a single hospital setting with small sample size the present study has a handicap of restricted external validity. A community based or multicentric hospital based study with larger sample size and multivariate analysis of the data might have a better scope for exploring the changes in macular profile and its correlates.

CONCLUSION:

Mean macular thickness was greater in amblyopic eyes as compared to normal fellow eyes. Moreover, thickness within 1mm ring as well as superior quadrant of 3mm inner ring was significantly more than that of the control eyes. On the contrary, retina in superior quadrant of 6mm outer ring in amblyopic eyes was found to be thinner. Multicentric larger study is required to draw inference about variation in macular parameters among amblyopes which can earlier be detected by non-

invasive OCT that also quantify if thickness changes alter with favourable or unfavourable response to treatment.

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