Original article:

An anatomical study: The variation of retinal nerve fiber layer thickness with age and ocular axial length in subjects of West Bengal.

[1]Dr.Alipta Bhattacharya* , [2]Prof.(Dr) Alpana De(Bose) ,[3] Prof.(Dr) Gautam Bhaduri ,

[4]Dr. Swapan Bhattacharya , [5]Dr. Apala Bhattacharya

[1]Demonstrator, Anatomy, Malda Medical College,Malda -732101

[2]Prof & HOD. (Anatomy),R.G.Kar Medical College,Kolkata-700004

[3]Prof & HOD. Regional Institute Of Ophthalmology, Medical College, Kolkata-700073

[4]Additional Prof. Medical College &Hospital , Kolkata.-700073

[5]Assistant Professor, .Regional Institute Of Ophthalmology, Medical College & Hospital , Kolkata -700073

*C**orresponding author:** Email-id. alipta.bhattacharya@gmail.com.

Abstract:

Ganglion cells form the second order neurons of the visual pathway. The Retinal nerve fibre layer (RNFL) consists of unmyelinated axons of Ganglion cells which converge at the Optic nerve head. Increasing age and increased axial length of the eyeball have been noted to cause a reduction in the RNFL thickness. The present work aims to correlate the effects of increasing age and axial length of the eyeball on the Retinal nerve fibre layer thickness in middle aged and elderly subjects of West Bengal. 380 Adults of both sexes and of various age groups , minimum age being above 40 years were chosen for the study. RNFL thickness was measured by Optical Coherence Tomography (OCT) . We have been able to show that RNFL thickness gradually decreases with increasing age and axial length of the eyeball. The results also show that this effect is aggravated for higher values of the independent variables , i.e, at higher decades of age and at moderate or severely increased axial length. We believe that this study will be able to enhance our knowledge regarding the anatomical and pathophysiological relation between an unique organ of our body , the organ of vision , the eye.

Key words : RNFL, age ,axial length , OCT

Introduction :

Retina is the innermost layer of the eyeball. It is a thin, delicate and transparent membrane. It is the most highly developed tissue of the eye[1] .A healthy status of the RNFL is essential for proper maintenance of functional vision. The Retinal nerve fibre layer (RNFL) consists of unmyelinated axons of Ganglion cells which converge at the Optic nerve head. Ganglion cells form the second order neurons of the visual pathway. Loss of this RNFL is essentially loss of ganglion cells of the retina resulting in Glaucoma, characterized by optic nerve damage as evidenced by retinal nerve fibre layer defects. Prevalence of glaucoma [2]in above 50 year age group is about to be 3.4% in India. Some risk factors have shown to affect the RNFL thickness in apparently normal individuals i.e. subjects not having glaucoma. Increasing age and increased axial length of the eyeball have been noted to cause a reduction in the RNFL thickness.[3] Whether these factors increase the risk of glaucoma in apparently normal individuals is yet to be established. The present work aims to correlate the effects of increasing age and axial length of the eyeball on the Retinal nerve fibre layer thickness in middle aged and elderly subjects of West Bengal . With this background the present study was

planned to assess change of retinal nerve fibre layer thickness with changes in age and axial length of the eyeball in middle aged and elderly subjects of both sexes.

Materials and Methods:

The present study was completed at department of Anatomy, R.G.Kar Medical College and Hospital, Kolkata and Regional Institute Of Ophthalmology (RIO) , Medical College , Kolkata . Patients attending RIO out patients department with no posterior segment disorder and having a clear ocular media were selected for the study. Both eyes of 380 subjects of both sexes and aged above 40 years were examined and the results were recorded.

Sample design: 380 Adults of both sexes and of various age groups , minimum age being above 40 years were chosen . It was made sure after careful evaluation that all of them were having a clear ocular media and none were having any posterior segment pathology. Their ocular axial lengths were also measured.

Based on the said sample design, findings were recorded and a randomized Observational and cross-sectional study was undertaken to achieve the above objectives.

Study tools :

- Slit lamp biomicroscope
- Direct and Indirect Ophthalmoscope to exclude posterior segment anomalies.
- USG A scan to measure axial length of the eyeball.
- Goldmann Applanation Tonometer to measure intraoculat pressure in order to rule out frank ocular hypertensives.
- Goldmann gonioscopic mirror to rule out eyes with closed anterior chamber angles.
- Humphrey visual field analyzer to assess visual field of the subjects in order to exclude glaucomatous subjects.
- Stratus Optical Coherence Tomograph (OCT)[4] for RNFL thickness assessment.

Study techniques: Complete ocular examination with dilated pupils to rule out posterior segment pathology and media opaciy.Assessment of refractive error was done .Intraocular pressure (IOP) was measured with Goldmann Applanation Tonometer on three successive occasions.Anterior chamber angle of both eyeballs was measured with Goldmann's Gonioscopic mirror. Visual field analysis with Humphrey's visual field analyzer 30-2 program was undertaken . Venous blood was sent for Postprandial blood sugar estimation. Axial length of both eyeballs was determined with USG A Scan Biometry. Peripapillary Fast RNFL thickness scan (3.4) was done on both eyes with Stratus OCT machine.

Inclusion criteria

- Best corrected visual acuity (BCVA) better than 6/9 for distance and N8 for near
- Vertical cup disc ratio (VCDR) ≤ 0.4
- IOP on three successive occasions less than 21 mm of Hg
- Anterior chamber angle open.(more than SHAFFER'S GRADE III)

- Visual field within normal limits.(By Humphrey's Visual Field analyser) .

Exclusion criteria :

- Best corrected visual acuity worse than 6/9 for distance and N8 for near
- Ocular media opacity.
- History of ocular surgery.
- Posterior segment pathology.
- Vertical cup disc ratio (VCDR) greater than 0.4
- IOP on three successive occasions greater than 21 mm of Hg .
- Anterior chamber angle closed.(Less than SHAFFER'S GRADE III)
- Diabetic (Post prandial blood sugar greater than 200 mg/ dl.)

The data thus collected was analysed statistically by using unpaired t test, and correlation analysis

Results:

Fig 4.1: Age and gender distribution of the Study Population

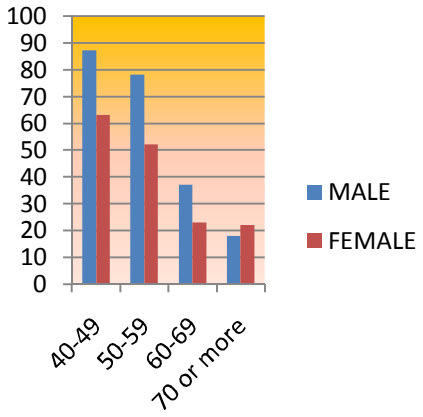


Fig 4.2: Sex Distribution Of The Study Population

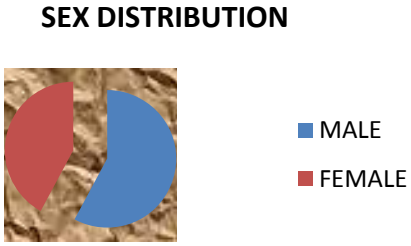
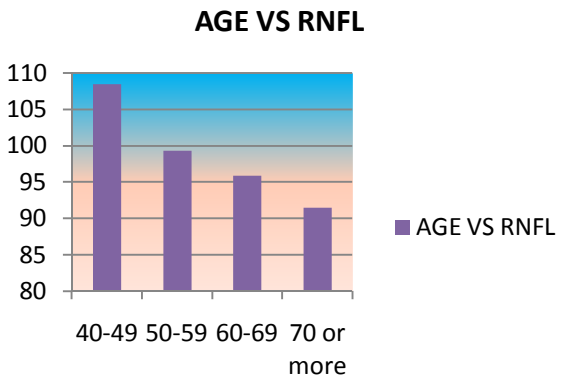


Fig 4.3: Variation Of Age Versus RNFL Thickness In The Study Population



*Age along x –axis in years

Rnfl thickness along y-axis in microns.

AGE (YRS)	MEAN RNFL THICKNESS(μ)
40-49	108.53
50-59	99.39
60-69	95.94
70-79	91.49

Mean RNFL thickness of the study population :101.62 ±10.42 μ

Pearson correlation coefficient for age versus RNFL thickness = -0.649

Confidence Intervals for r= -0.649

C.I.	lower	r		upper
80%	-0.675159	<	-0.649	< -0.621211
90%	-0.682275	<	-0.649	< -0.613042
95%	-0.688346	<	-0.649	< -0.605846
99%	-0.699928	<	-0.649	< -0.591506

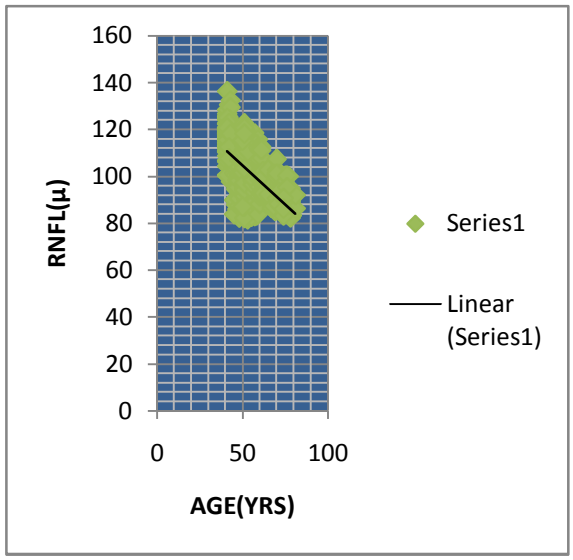
Statistical significance of r= -0.649 against 0

t= -23.48634; df= 758;

the two-tailed P value is less than 0.0001

By conventional criteria, this difference is considered to be extremely statistically significant.

FIG 4.4: Linear regression analysis of correlation between Age Versus RNFL Thickness In The Study Population



Pearson correlation coefficient = -0.649

Unpaired *t* test results

P value and statistical significance:

The two-tailed P value equals 0.8812

By conventional criteria, this difference is considered to be not statistically significant.

Confidence interval:

The mean of MALE minus FEMALE equals 0.1145

95% confidence interval of this difference: From -1.3906 to 1.6197

Intermediate values used in calculations:

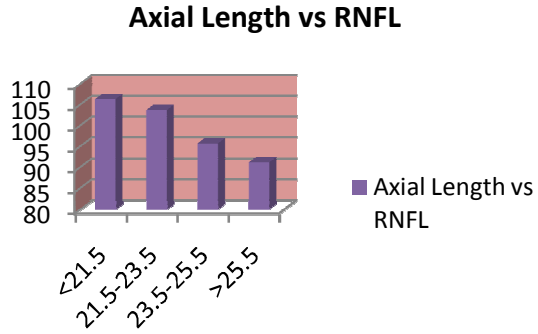
t = 0.1495

df = 758

standard error of difference = 0.766

Hence our study showed that there is **no statistically significant** difference in the RNFL thickness values between **males and females**

Fig 4.5: Variation Of Axial Length Versus RNFL Thickness In The Study Population

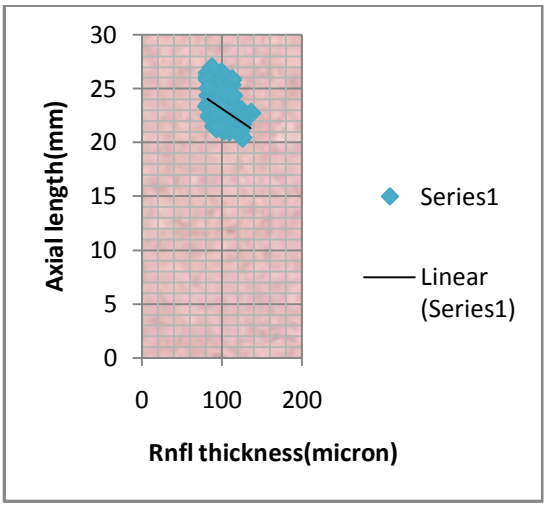


*Axial length in mm along x-axis

Mean rnfl thickness in micron along y-axis.

Axial Length(mm)	Mean RNFL Thickness(µ)
<21.5	106.38
21.5-23.5	103.78
23.5-25.5	95.81
>25.5	91.27

Fig 4.6: Linear regression analysis of correlation between Axial Length Versus RNFL Thickness In The Study Population



Pearson correlation coefficient = -0.45

Confidence Intervals for r= -0.45

Statistical significance of r= -0.45 against 0
t= -13.87336; df= 758;
The two-tailed P value is less than 0.0001
By conventional criteria, this difference is considered to be **extremely statistically significant**.

Discussion:

In the study population number of male patients is more than female patients. These pictures signify the socio-economic condition of our country because of which male patients seek medical attention more than females.

NAME OF STUDY	MEAN RNFL THICKNESS(μ)	ETHNICITY OF THE STUDY POPULATION
Sony, *et al* [5]	104.27±8.51	INDIAN
Ramkrishna, et al [6]	104.8±38.81	INDIAN
Yamada, et al [7]	108±13.5	JAPANESE
Peng, et al [8]	108.7±9.4	TAIWANESE
Budenz, et al [9]	98.1±10.9	CAUCASIAN
Manassakorn, et al [10]	109.3±10.5	THAI
Present study	101.62±10.42	INDIAN (WEST BENGAL)

From the above data and the review of literature we can see that average RNFL thickness in our study was comparable with the studies of ***Sony*** *et al* and ***Ramkrishna et al*** . However, it is to be noted that the average RNFL thickness of the Japanese , Thai and Taiwanese population are significantly higher than the Indians whereas that of the Caucasians is significantly lower. In this regard it should be mentioned that the average age of the study population was higher in our study compared to all the others, as we had selected only people above 40 years of age. The lower value of the mean RNFLT in our case also suggests that with ageing mean RNFLT goes on decreasing.It is to be noted **Parikh RS, *et al***, [11] performed a similar study to determine the normal age-related loss of retinal nerve fiber layer thickness (RNFLT) as measured on Stratus optical coherence tomography (OCT 3; Carl Zeiss Meditec, Dublin, CA) in an Asian Indian population. Simple linear regression was performed to study the effect of age on RNFLT, with age as the independent variable and RNFLT as the dependent variable. Spearman's correlation was studied between the age and RNFLT. An analysis of variance was applied to compare RNFLT between the different age groups. RNFL thickness is significantly correlated with age, but not with gender. Our study corroborates well with the findings as Pearson correlation coefficient for the variation of age versus RNFL thickness = -0.649 (p <,0.0001).The present study likewise failed to find any significant correlation between RNFLT and gender. However in this regard our study differs from that conducted by ***Ramkrishna, et al*** as according to them there is no significant correlation of RNFLT with respect to age. . There was a decrease in mean RNFL thickness with respect to age, but it was not statistically significant. But most of the other studies conducted elsewhere corroborated with the negative correlation between age and RNFLT.

Similarly while comparing the results done on the relation of axial length of the eye and RNFLT our results were comparable to most of

the studies barring one.Our findings are similar to those of **Yasser** ,et al, where they found a larger correlation between axial length and RNFLT for east Asians compared to Caucasians. However their study was conducted upon children and ours on middle aged and elderly adults.comparing data with the other relevant studies we note that our results corroborate more closely to the south east asian studies(***Leung, et al Sang hoon park, et al),*** compared to the Caucasian population studies(***Schweitzer K.D, et al, Rauscher F.M. , et al*** **.**Again, our study ,contradicts the findings of ***Hoh S.T, et al,*** who failed to show any statistically significant correlation between these two parameters.

STUDY	RESULT	ETHNICITY OF STUDY POPULATION
Yasser, et al[12]	r=-0.25, p<0.001 r=-0.14, p<0.001	East asian caucasian
Leung, et al [13]	r=-0.23, p<0.001	Hong kong
Schweitzer K.D, et al [14]	r=-0.712, p<0.001	caucasian
Sang hoon park, et al [15]	r=-0.306, p<0.001	korean
Rauscher F.M. , et al [16]	r=-0.7, p<0.001	caucasian
Hoh S.T, et al [17]	No significant correlation	singapore
Present study	r=-0.45, p<0.0001	Indian (West Bengal)

Conclusion:

From present study it can be said that if more regular evaluation of eyes are done specially for those at higher risks , more number of patients could be benefitted.So it is our recommendation that elderly and myopics , specially moderate to severe ones should have mandatory glaucoma evaluation and workout irrespective of their gender.

Limitations: There have been certain limitations of this study, More number of samples and a longitudinal design for the study would have yielded more accurate results , and such efforts can be made in future. Nevertheless we believe that this study will be able to enhance our knowledge regarding the anatomical and pathophysiological relation between an unique organ of our body , the organ of vision , THE EYE.

Abbreviations:

- POAG – Primary Open Angle Glaucoma
- IOP – Intraocular Pressure
- CI – Confidence Interval
- BP – Blood Pressure
- RNFL-Retinal Nerve Fibre Layer
- OCT-Optical Coherence Tomography
- AC-Anterior Chamber
- PPBS-Post Prandial Blood Sugar
- BCVA-Best Corrected Visual Acuity

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