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# EFFECT OF AXIAL LENGTH ON PERIPAPILLARY RETINAL NERVE FIBRE LAYER THICKNESS MEASURED BY SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY

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## ABSTRACT

***Objective:*** To determine the relationship between mean axial length and mean peripapillary retinal nerve fibre layer (RNFL) thickness using spectral domain optical coherence tomography (SD OCT) in healthy subjects.

***Study Design:*** Cross sectional study.

***Place and Duration of Study:*** Armed Forces Institute of Ophthalmology (AFIO) Rawalpindi, from Dec 2014 to Aug 2015.

***Material and Methods:*** Data of 300 eyes of 300 healthy volunteers were collected at AFIO from December 2014 to August 2015 and analysed. Axial length and RNFL thickness of each volunteer was calculated using laser interferometer (IOL master) and SD OCT respectively. Eyes were divided in three groups based on axial length. Statistical analysis of the data were done using SPSS version 17.0.

***Results:*** Mean age of study population was 23.16 ± 3.73 years. Mean axial length was 24.40 ± 1.50 millimetres (mm). Mean of average peripapillary RNFL thickness was 128.87 ± 9.94 micrometres (µm). Mean peripapillary RNFL thickness of superior, inferior, nasal and temporal quadrant was 158.27 ± 11.04 µm, 152.92 ± 14.54 µm, 103.85 ± 5.01 µm and 100.45 ± 11.59 µm respectively. Mean RNFL thickness, as well as RNFL thicknesses of each quadrant was also significantly different between hypermetropic, emmetropic and myopic eyes ($p$-value<0.001). There was also a strong negative correlation between axial length and peripapillary retinal nerve fibre layer thickness (r= -0.964, $p$-value<0.001).

***Conclusion:*** Variation in axial length significantly affects the measurement of RNFL thickness and must be counted for, while diagnosing glaucoma on basis of thinning of RNFL.

**Keywords:** Axial length, Myopia, Optical coherence tomography, Retinal nerve fibre layer thickness.



## INTRODUCTION

Measurement of retinal nerve fibre layer (RNFL) thickness is potentially useful and sensitive indicator for early detection of glaucoma as thinning of the peripapillary RNFL may be an early sign of structural damage in patients with glaucoma[1,2]. Moreover, RNFL thinning often occurs prior to clinically detectable vision loss, optic disc changes and appearance of visual field loss[2,3]. Optical coherence tomography (OCT) is a non-invasive diagnostic modality that allows cross-sectional imaging of the retina and optic nerve head, enabling measurement of thickness of RNFL. The new generation of spectral domain (SD) OCT with high speed image acquisition, superior axial resolution (1-5 µm) and generation of 3-dimensional images provides detailed measurements of RNFL and the macula[4]. Moreover, SD OCT permits segmentation and measurement of individual retinal layers using computer-assisted programs[4].

RNFL, as measured by SD OCT, varies with age, gender, ethnicity, axial length, refractive status and optic disc area[2,5-7]. Association of myopia with primary open angle glaucoma is well recognized with 2-3 times higher risk of developing glaucoma in myopes[1,8]. Various studies have measured the effect of axial length or refractive status on peripapillary RNFL thickness using high resolution SD OCT and

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recommended that axial length must be taken into account while evaluating patients for diagnosis and follow-up of glaucoma on the basis of OCT findings. Oner et al in their study found average peripapillary RNFL thickness being thinner in myopic and thicker in hypermetropic eyes as compared to emmetropes[6]. Sowmya et al reported that in increasing myopia, RNFL thickness was seen to decreased, and in increasing hypermetropia the RNFL was increased[2]. The aim of this study was to determine the relationship between RNFL thickness and axial length in Pakistani population.

## MATERIAL AND METHODS

This was a cross sectional study carried out at Armed Forces Institute of Ophthalmology (AFIO) Rawalpindi from December 2014 to August 2015. After approval by the hospital ethical review committee, informed consent was taken from the patients prior to inclusion in the study. Non probability consecutive sampling technique was used and calculated sample size was 300 using level of significance as 0.05, Type II error 10% confidence level of 95% and r-value of 0.741[6]. One eye of each subject was randomly selected for data acquisition through lottery method. Healthy subjects between 16-30 years of age, with best corrected visual acuity (BCVA) of 6/6 in both eyes and refractive error within ± 6.0 D were included. Subjects with media opacities precluding optimal image acquisition, anterior segment pathology, history of glaucoma, optic nerve or macular disease, family history of glaucoma and retinal dystrophies, previous history of ocular surgery or trauma, astigmatism >2.00 D, intraocular pressure (IOP) >21 mm Hg and cup/disc ratio >0.5 or asymmetry >0.2 were excluded from the study. Eligible subjects underwent ophthalmic clinical examination including uncorrected and corrected distance visual acuity assessment, slit lamp examination with fundus examination and IOP measurement. Axial length measurement was performed using partial laser interferometry (IOL Master, Carl Zeiss Meditec, Dublin, CA, USA). Average of three readings was recorded for data analysis. On the basis of axial length, eyes were divided into three groups. Hypermetrope group (axial length: 21-22.5 mm), emmetrope group (axial length: 22.6-24.5 mm) and myope group (axial length: 24.6-27 mm). Peripapillary RNFL measurements were taken using 3D OCT-1000 Mark II, Topcon Co, Tokyo, Japan, after dilating one eye with 0.1% topical Tropicamide eye drops. The pre devised proforma was completed by researcher endorsing subject's demography, ocular examination findings and RNFL thickness of peripapillary area.

Statistical analysis of the data were done using SPSS version 17.0. Descriptive statistics i.e. mean ± standard deviation for quantitative values (age, axial length, RNFL thickness) and frequencies along with percentages for qualitative variables (gender, number of eyes) were used to describe the data. Chi square test was used for comparison of gender between groups. Pearson correlation coefficient was used to determine correlation between axial lengths and mean of average peripapillary RNFL thickness, mean peripapillary RNFL thickness of superior, inferior, nasal and temporal quadrants. One way analysis of variance (ANOVA) with post hoc analysis was used for comparison of demographic data and peripapillary RNFL thickness between different groups and *p*-value <0.05 was considered significant.

## RESULTS

Three hundred eyes of 300 subjects fulfilling the inclusion criteria were analysed. Mean age of study population was 23.16 ± 3.73 years (Range: 16-30 years). About 168 (56%) subjects were males, while 132 (44%) were females. Mean axial length was 24.40 ± 1.50 mm (Range: 21-27 mm). Mean of average peripapillary RNFL thickness was 128.87 ± 9.94 µm (Range: 105.75-152.83 µm), whereas, mean peripapillary RNFL thickness of superior, inferior, nasal and temporal quadrant was 158.27 ± 11.04 µm (Range: 134.70-188.80 µm), 152.92 ± 14.54 µm (Range: 121-184.60 µm), 103.85 ± 5.01µm (Range: 90-118.20 µm) and 100.45 ±

11.59 µm (Range: 77-120.20 µm) respectively. Axial length showed significant negative correlation with mean of average peripapillary RNFL thickness, as well as with mean peripapillary RNFL thickness of superior, inferior, nasal and temporal quadrants (table-I). parameters (*p*-value <0.001) between groups. Post Hoc Tukey's test of multiple comparisons also showed statistically significant differences amongst all groups for all parameters (*p*-value <0.001).

**Table-I: Peripapillary retinal nerve fibre layer thickness (n=300).**

| Quadrant | RNFL thickness (µm) Mean ± SD | Correlation co-efficient (r) | *p*-value |
|---|---|---|---|
| Average | 128.87 ± 9.94 | - 0.964 | <0.001 |
| Superior | 158.27 ± 11.04 | - 0.908 | <0.001 |
| Inferior | 152.92 ± 14.54 | - 0.969 | <0.001 |
| Nasal | 103.85 ± 5.01 | - 0.726 | <0.001 |
| Temporal | 100.45 ± 11.59 | - 0.916 | <0.001 |

**Table-II: Group wise demographic data (n=300).**

| Characteristic | Hypermetrope (n=34) | Emmetrope (n=123) | Myope (n=143) | *p* value |
|---|---|---|---|---|
| Age (Years) Mean ± SD | 23.79 ± 3.96. | 22.88 ± 3.85 | 23.24 ± 3.57 | 0.425 |
| Gender | | | | 0.883 |
| Male | 20 (58.8%) | 67 (54.5%) | 81 (56.6%) | |
| Female | 14 (41.2%) | 56 (45.5%) | 62 (43.4) | |
| Axial Length (mm) Mean ± SD | 21.95 ± 0.47 | 23.47 ± 0.59 | 25.79 ± 0.53 | < 0.001 |

**Table-III: Group wise distribution of peripapillary RNFL thickness (n=300).**

| Quadrant | Hypermetrope (n=34) | Emmetrope (n=123) | Myope (n=143) | *p* value* |
|---|---|---|---|---|
| Average (µm) Mean ± SD | 144.17 ± 4.43 | 134.56 ± 4.44 | 120.35 ± 5.44 | <0.001 |
| Superior (µm) Mean ± SD | 177.09 ± 6.61 | 163 ± 6.55 | 149.72 ± 5.66 | <0.001 |
| Inferior (µm) Mean ± SD | 174.50 ± 5.61 | 161.99 ± 6.09 | 139.99 ± 7.43 | <0.001 |
| Nasal (µm) Mean ± SD | 110.50 ± 3.85 | 105.37 ± 3.51 | 100.96 ± 4.23 | <0.001 |
| Temporal (µm) Mean ± SD | 114.59 ± 3.55 | 107.87 ± 4.91 | 90.70 ± 8.22 | <0.001 |

*Post Hoc Tukey's test of multiple comparisons also showed statistically significant differences amongst all groups.

There were 34 (11.33%) eyes in hypermetrope group, 123 (41%) eyes in emmetrope group and 143 (47.66%) eyes in myope group. All three groups were age and sex matched; however, in-between group difference of axial length was statistically significant (table-II). Group wise data on mean of average peripapillary RNFL thickness and mean peripapillary RNFL thickness of different quadrants is given in table-III that shows statistically significant difference in all

## DISCUSSION

As glaucoma is known as "silent thief of eye sight", early diagnosis is of paramount importance in reducing the morbidity related to the disease. Objective analysis of the optic nerve head with measurement of RNFL thickness has overtaken the conservative visual field analysis as an early diagnostic tool in glaucoma management. RNFL thickness is a sensitive indicator for predicting early glaucomatous

changes and the extent of RNFL damage correlates with severity of functional defects in perimetry. Assessment of peripapillary RNFL thickness has been revolutionized with advent of OCT that allows non-invasive measurement of RNFL thickness using sophisticated optics. The previously used time-domain (TD) OCT had multiple drawbacks like slower scan rate, poor resolution and varied factors affecting accurate assessment. With advent of SD OCT, these factors have largely been catered for, allowing quiet reproducible and reliable measurements of RNFL thickness[2]. RNFL, though a sensitive indicator, is influenced by multiple factors like age, sex, axial length, type of OCT, phakic status, pupil dilation and media opacities[2]. Various studies have confirmed the reduction in measured RNFL thickness in subjects with increased axial lengths[2,6-9]. Mean RNFL thickness was also found to be thinner in myopes using cirrus high definition (HD) OCT, but correction for axial length related ocular magnification using correction formula has resolved the relationship between axial length and both RNFL thickness and optic nerve head area[5]. Analysis of the effect of axial length on RNFL thickness by various studies using SD OCT also revealed thinning of RNFL in myopic eyes, where every 1 mm increase in axial length was calculated to cause 2.2-2.4 µm thinning of RNFL[7,10,11]. In our study mean of average peripapillary RNFL as well as mean peripapillary RNFL thickness in each quadrant showed significant negative correlation with axial length. Nafees et al in their study on Pakistani population reported mean RNFL thickness of 94.76 ± 10.22 µm and they also found out a significant negative correlation between axial length and mean RNFL thickness ($r=0.815$, $p$-value $<0.05$)[12]. Rauscher et al found a significant strong association between axial length and RNFL thickness, but they also reported a less strong relationship between spherical equivalent and RNFL thickness[13]. They also found thin RNFL in myopic subjects preferentially at superior and inferior poles, with overall decrease in RNFL thickness of 7 µm for every 1 mm increase in axial length and 3 µm for every 1 dioptre of sphere[13]. Sowmya et al showed increased thickness in temporal and superior quadrants only in hyperopic eyes, and thinning of RNFL in superior and inferior quadrants only in myopic eyes[2]. Several prior studies did not found a significant association between axial length and peripapillary RNFL thickness, though with limitations of older generation OCT, small sample sizes and lack of age and gender matching and variation in ethnicity[14-16].

There are many factors that affect quantitative measurement of macula and optic nerve head like scan centration, sampling density and ocular magnification effect due to variation in axial length[17]. The transverse mirror in OCT is calibrated for an axial length of 24.46 mm and RNFL thickness is measured at a constant distance (1.7 mm) from the optic disc centre[17,18]. Hence, variation in axial length could result in magnification error in the measurement made on OCT. Correction of this ocular magnification effect due to axial length has been possible by incorporating Littman's formula and modification of Littman formula described by Bennett et al[19,20]. In our study, all the subjects were healthy volunteers and demographically matched. SD OCT was used for analysis and only one eye of each subject was used for analysis. Few limitations in our study were unequal sample size, lack of multivariate analysis and non-application of correction formulas to establish whether difference in RNFL measurement was due to axial length related magnification factor only. In view of available literature, one has to be cautious while interpreting RNFL thickness measurements in patients with extremes of axial lengths. Due to availability of limited data in our set up, further studies are warranted to establish the relationship between axial length and RNFL thickness in our setup for accurate diagnosis of glaucoma.

## CONCLUSION

Variation in axial length significantly affects the measurement of RNFL thickness and must be

counted for, while diagnosing glaucoma on basis of thinning of RNFL.

### Disclosure

No author has a financial or proprietary interest in any material or method mentioned, neither the article presented in any conference, seminar, and symposium before submission to PAFMJ.

## CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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